

Triennial Report 2022 – 2024







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PREFACE

THE DANISH RESEARCH CENTRE FOR MAGNETIC RESONANCE (DRCMR)

is constantly evolving, with new research areas emerging and existing projects maturing. We are proud to have made significant strides in bridging the gap between preclinical research in rodents and applied research in patients. This approach ensures that our discoveries are not only innovative but also have a clear path to clinical application.

A MAGNET FOR TALENT

As a global research hub, DRCMR attracts talented researchers from around the world, creating an inspiring and dynamic environment. This international collaboration plays a vital role in advancing our work in biomedical MR-based imaging, with a strong focus on the brain and its diseases.



Professor Hartwig Siebner, Head of Research at DRCMR.

PUSHING THE CAPABILITY OF BRAIN MRI

Our work in imaging and spectroscopy, especially using ultra-high field strengths, has opened the door to promising clinical research in major brain diseases such as Parkinson's disease, multiple sclerosis, and schizophrenia. These advancements highlight the power of modern imaging techniques in understanding and diagnosing complex brain disorders.

LOOKING AHEAD

Covering the period from 2022 to 2024, this report reflects on the progress we have made over the past three years and offers a glimpse into the exciting directions our research will take in the future. We would like to take this opportunity to express our gratitude to the many foundations and institutions that support our work. Their trust enables us to continue our groundbreaking research. We also extend our heartfelt thanks to the researchers and students who contribute to the DRCMR community. Their passion, expertise, and creativity continue to shape our environment and inspire the next generation of scientists.

As we navigate an increasingly complex global landscape, we remain steadfast in our commitment to scientific excellence, nurturing emerging talent, and making discoveries that will shape the future of neuroimaging and clinical neuroscience. We will continue to push the frontiers of MRI-based brain research and to educate the next generation of scientists. We would also like to thank the management of Copenhagen University Hospital Amager and Hvidovre and the Capital Region of Denmark for their continued support. And – last, but not least – we would like to thank our collaborators and our research staff for their engagement, team spirit, and hard work which make the DRCMR a fantastic place for brain imaging and neuroscience.

Hartwig Roman Siebner Head of Research (DRCMR)

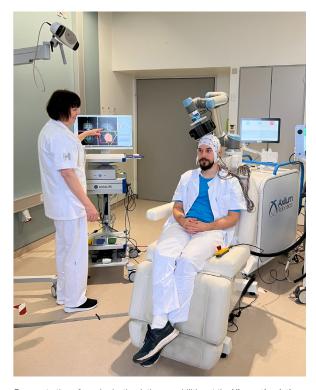
Hartwig Siebus

Clinical Professor with special focus on Precision Medicine (Faculty of Health and Medical Sciences, University of Copenhagen) The professorship is sponsored by the Lundbeck Foundation

HIGHLIGHTS AND MILESTONES 2022-2024

ESTABLISHING A UNIT FOR TRANSCRANIAL STIMULATION THERAPY

From 2022 to 2024, one of the most notable advancements has been the launch of investigational studies utilizing transcranial magnetic stimulation (TMS) as a therapeutic tool. Building on a decade of brain stimulation research, this initiative represents a natural progression towards clinical translation. While TMS is an approved therapy for conditions such as major depressive disorder, the standard one-size-fits-all approach is only effective for some patients and effect size is usually modest. Adopting a precision medicine approach, our goal is to enhance the efficacy of TMS by tailoring therapeutic TMS protocols to each patient's unique brain anatomy and function. Currently, the focus is on Transcranial Magnetic Stimulation (TMS) therapies whereas other brain stimulation modalities such as transcranial focused ultrasound and electrical stimulation will be added later. Thanks to generous support by Hvidovre Hospital, we were able to establish a unit for precision brain stimulation in Center E of Hvidovre Hospital. This unit became functional in 2023 and includes three labs dedicated to therapeutic brain stimulation studies and two offices. To ensure that patients feel welcomed and comfortable between treatments, the center also includes a receiving area along with rest areas where patients can relax between treatments. The treatment labs are equipped with top-shelf brain stimulation equipment, including custom-made high-performance magnetic stimulators, suspension systems for weightless neuronavigated coil control, and a new generation Cobot, enabling robotic precision stimulation. Even with robotic support, precision brain stimulation calls for a group effort. The human infrastructure includes PhD students, research assistants, postdocs, and a clinical neurophysiology assistant that work together to manage ongoing therapeutic trials. The new treatment facility enabled us to initiate three clinical TMS trials in collaboration with clinical partners in RegionH. The therapeu-



Demonstration of new brainstimulation capabilities at the Hjernestimulation, klinik, afs. 128, by PhD Student Sofus Drejer Nygaard and neurophysiology assistant Aino Lindroos Jensen.

tic TMS studies are led by Prof. Hartwig Siebner and test the use of personalized TMS for patients with Parkinson's Disease, multiple sclerosis, and treatment-resistant major depressive disorder. The three studies are described in more detail below.

ADAPT-PD

The ADAPT-PD project (ADAptive and Precise brain-circuit Targeting in Parkinson's disease), initiated in 2021, addresses a crucial question in neuroscience with significant therapeutic implications: How can we normalize the dysfunction of brain circuits in Parkinson's Disease using device-based neuro-



Image right: ADAPT-PD Retreat 2023

modulation? Adopting a multimodal and multiscale approach, the project team investigates alterations in the cortico-basal ganglia circuit in Parkinson's Disease and levodopa-induced dyskinesia. This knowledge is used to develop treatments with tailored non-invasive and invasive brain stimulation. The project is funded by a Collaborative Projects

grant (35 million DKK) from the Lundbeck Foundation, awarded to Hartwig Siebner, Professor Andrea Kühn from Charité Universitätsmedizin in Berlin, Germany, and Professor Angela Cenci Nilsson from Lund University, Sweden.

FANTIMS

The FANTIMS project is a randomized, controlled trial that uses repetitive TMS to alleviate fatigue in patients with multiple sclerosis. Fatigue is one of the most common and debilitating symptoms of multiple sclerosis, and there are currently no effective treatments. This study is funded by the Danish Multiple Sclerosis Society and the Independent Research Fund Denmark.

Precision-BCT

From technological innovation to application: Precision brain circuit therapy of mood disorders: In 2019, Innovation Fund Denmark invested 14 million DKK (Grand Solutions grant) in a five-year project to develop precision brain stimulation as a therapy for major depressive disorder. The Precision-BCT project, led by DRCMR, involves several partners, including Mag-Venture A/S (Farum, Denmark), the Centre for Neuropsychiatric Depression Research of the Mental Health Centre Glostrup, DTU Health Tech, Localite GmbH (Bonn, Germany), and Ludwig Maximilian's University (Munich, Germany).

In the Precision-BCT project, we have developed novel TMS and navigation equipment that enables simultaneous stimulation of multiple brain regions, precise spatial targeting, dose



control, and highly flexible stimulation patterns. These technical advancements have been integrated with structural and functional brain imaging to create a workflow that can efficiently and selectively target individual brain-circuit dysfunctions in patients with major depressive disorder. The project is now in its final phase, and the established workflow is now leveraged in the COMPACT study—a randomized clinical trial funded by the Independent Research Fund Denmark and led by Professor Poul Videbech and Hartwig Siebner.

USING BRAIN MRI TO TEST IMMUNMODULATORY TREATMENTS IN MULTIPLE SCLEROSIS

Another major clinical undertaking over the past three years has been the establishment and operation of the DanNORMS trial. This nation-wide, investigator-initiated clinical trial investigates whether treatment of active multiple sclerosis (MS) with the drug rituximab (Ruxience®, approved for the treatment of several different conditions but not MS) has comparable efficacy and safety to treatment with ocrelizumab (Ocrevus®, approved for the treatment of MS). The DRCMR Reader Centre coordinates the MRI component of the study, which involves MRIs performed at eight different hospitals across Denmark. The Reader Centre receives scans from all participating sites and is responsible for the quality assessment and data analysis of all MRI data. The study has successfully recruited 600 patients, with nearly half of them being scanned at DRCMR in collaboration with the Radiology Section. Each patient is scanned up to 7 times over a course of 5 years.

NEW MRI SCANNERS

In the autumn of 2022, three out of four clinical MRI scanners at the hospital were replaced. The Siemens Verio and Avanto scanners from 2009 and the Siemens Espree scanner from 2006 were replaced by two Siemens Vida scanners (3T) and a Siemens Sola scanner (1.5T). These new scanners, financed by the Capital Region of Denmark as part of a large tender spanning multiple hospitals, were installed in two phases to ensure minimal disruption to clinical and research activities. The new scanners provide state-of-the-art tools for clinical and research imaging, resulting in more efficient scans, reduced patient discomfort, and improved image quality. The scanners were inaugurated in March 2023 by the chairman of the Regional Council, Lars Gaardhøj, and the hospital director, Birgitte Rav Degenkolv.

In November 2024, the hospital's new building, Center A, was inaugurated, which marked a new era for the Radiology Section of the department. The new building hosts a new emergency ward with a radiological satellite function. This includes conventional X-ray imaging, ultrasound, 2 CT-scanners and an MRI scanner. A Philips Ingenia Ambition X 1.5T scanner was installed in the new emergency ward and will be operated by staff from the Radiology section. This scanner, the first of its



Installation of new MRI Scanner in the hospital's new emergency ward in Center A $\,$



Installation of new MRI Scanner in the hospital's new emergency ward in Center A.

kind at the hospital, uses the latest magnet cooling technology, operating with only seven litres of liquid helium and being fully sealed. This eliminates the need for large quantities of liquid helium for cooling the magnet as well as the risk of magnet quenches.

NEW NAME AND NEW LEADERSHIP

2024 also brought significant changes in department leadership and a new department name. In line with a regional move towards more patient-friendly department names, the clinical department that includes DRCMR changed from the Center for Functional and Diagnostic Imaging and Research to the Department of Radiology and Nuclear Medicine (in Danish from Funktions- og Billeddiagnostisk Enhed to Afdeling for Røntgen, Skanning og Nuklearmedicin). Additionally, there was a leadership change in early 2024. Chief physician Claus Leth Petersen stepped down, and Hartwig Siebner served as acting chief physician until Mads Barløse was recruited as the new chief physician in mid-2024. The department leadership was also expanded to include a chief radiographer position, filled by Omar Muharemovic. The leadership team now consists of a chief physician, a chief radiographer, and a head of research.

FOCUS ON DIVERSITY

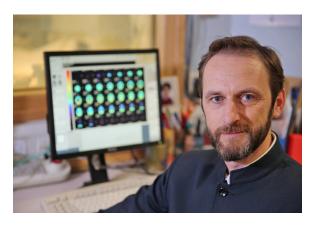
At DRCMR, we remain committed to fostering an environment where researchers of all backgrounds, identities, and experiences are valued, respected, and supported. Taking an active stance, our team includes researchers from more than 20 countries, merging expertise from diverse fields such as physics, engineering, computer science, biology, psychology, sports science, and medicine. This diverse mix of talents enables us to tackle complex challenges from multiple angles and push the boundaries of neuroimaging research.

The REFRESH Initiative

In 2022, senior researcher Kathrine Skak Madsen received a Diversity grant from the Lundbeck Foundation for the initiative entitled "REtaining Female RESearcH talent at DRCMR: Supporting successful transition to senior research roles (REFRESH)". Like many research environments, DRCMR has seen an underrepresentation of females in senior research positions, despite having comparable numbers of male and female PhD students and Postdocs. The REFRESH initiative aims to uncover the reasons behind this gender imbalance and implement both short- and long-term strategic changes within our department. The initiative focuses on several key areas: raising awareness about gender bias within the research community, gathering data through surveys to understand the extent and nature of the gender imbalance, conducting workshops to develop strategies for addressing gender disparities, organizing a seminar series and networking events to highlight female role models in neuroscience, and establishing a mentoring programme specifically for women in neuroscience. The REFRESH initiative is strongly supported by the leadership at DRCMR, and successful components of the project will be integrated into the department's practices when the initiative concludes in 2025. Since the start of REFRESH, there has been a gradual improvement in the gender balance among research fellows and senior researchers at DRCMR.

VISITING PROFESSORSHIP

James B. Rowe, Professor of Cognitive Neurology at the University of Cambridge and adjunct Professor of Clinical Neuroscience at the University of Copenhagen, revisited the DRCMR in the autumn of 2024 where he stayed at the DRCMR for four months – thanks to generous funding by the Lundbeck Foundation. James is a world-leading expert in frontotemporal dementia, Parkinson's disease and other neurodegenerative diseases. Especially the "Movement Disorders" research group benefited from his engagement in ongoing projects, helpful comments, and advice. James will continue visiting the DRCMR on a series of shorter visits in the spring 2025.



James Rowe, Professor of Cognitive Neurology at the University of Cambridge & adjunct Professor of Clinical Neuroscience at the University of Copenhagen

NEW PROFESSORSHIPS

Tim Dyrby - Professor at DTU

In 2023, Tim B. Dyrby was appointed Full Professor at the Technical University of Denmark (DTU) in the Department of Applied Mathematics and Computer Science (DTU Compute). In 2024, he was also appointed as the Coordinating Professor at the newly established Technical University Hospital of Greater Copenhagen (TUH). In this role, he is establishing a bridge of communication between the hospital and DTU, fostering collaboration between clinical and academic research. Tim shares his time equally between DTU and DRCMR and leads the Microstructure and Plasticity research group and co-leads the Preclinical methods group at DRCMR.

Tim's research focuses on mapping how the structure of brain pathways modulates neuronal signaling between functional regions — specifically, the signal timing of the brain. His research investigates how this timing changes when diseases affect pathways and the process of restoration. This mapping is analogous to creating a train timetable for the Copenhagen area



Professor Tim B. Dyrby

while also accounting for renovations. Tim and his research group take a holistic approach to studying brain structure by integrating 3D imaging technologies, ranging from millimeter-scale MRI down to nanometer-resolution imaging, where individual fibers forming neural connections are visualized and analyzed. Their research includes both animal models and human subjects, employing a combination of techniques such as optogenetic brain stimulation, electrophysiological recordings, preclinical and clinical MRI, X-ray synchrotron imaging, light-sheet fluorescence microscopy, biophysical modeling, and artificial intelligence.

Carl-Johan Boraxbekk - Professor at KU

In 2022 Carl-Johan Boraxbekk was inaugurated as professor of Neurology at Copenhagen University. The main research focus for his position is to better understand how physical exercise can be used to mitigate cognitive decline in aging, with a particular focus on the underlying neural mechanisms. Therefore, it is natural that DRCMR is a strong player in Carl-Johan's work and although Carl-Johan is physically located at Bispebjerg Hospital and the Institute of Sports Medicine, he is no stranger for DRCMR after joining the center back in 2016. Carl-Johan maintained dual affiliation with DRCMR until mid-2023, and continues to collaborate with DRCMR. One example of an existing joint project between the DRCMR and the ISMC is the LISA study, a longitudinal study about the potential of resistance training for healthy brain aging. With a recent grant from the DFF on the mental aspects of strength training, the coming years will surely result in further fruitful collaborations.



Professor Carl-Johan Borakbexx

Mattias Rickhag - Associate Professor at KU

In 2022, Mattias Rickhag was appointed associate professor of neuroscience at Department of Neuroscience, Faculty

of Health and Medical Science at University of Copenhagen (KU). His research focuses on the cortico-basal ganglia circuits in Parkinson's disease and implements advanced genetic and viral-based manipulation tools together with experimental mouse models of Parkinson's disease to disentangle circuit mechanisms. His



Assc. Professor Mattias Rickhag

research will yield fundamental insights into how distinct cortical neuronal subpopulations govern motor actions and which cortico-striatal circuits that are enrolled to control these biological processes. Novel biological insights into these brain circuits will have clinical relevance for people affected by movement disorders such as Parkinson's disease. Mattias shares his time between KU and DRCMR.

Oliver Hulme - Associate Professor at KU

In 2023, Ollie Hulme was appointed Associate Professor of Cognitive Computational Neuroscience at the Department of Psychology, at the University of Copenhagen (KU). At Psychology, he joins the Cognition and Neuropsychology Cluster, a major research theme that closely aligns with the



Assc. Professor Oliver Hulme

Cognitive and Computational Research Theme at DRCMR. His research focuses on mapping the reward system using computational modeling techniques applied to fMRI, physiological, and behavioral data. Specifically, his work aims to answer some basic questions. How does the reward system work and why does it work the way it does. Specifically, he is interested in how reward processes are mapped over the brain, and how cortical and subcortical reward maps encode reward, and calculate reward values. His work leverages advanced Bayesian methods to jointly analyze and interpret neural and cognitive

data. In addition to his research, he is actively involved in teaching, covering topics such as modeling cognition using Bayesian methods, neuroimaging, and statistical analysis. Through his work, Ollie contributes to advancing our understanding of how the brain represents and processes rewards, with potential applications in both clinical and theoretical neuroscience. Ollie divides his time between KU and DRCMR.

Lasse Christiansen - Associate Professor at KU

In 2023 Lasse Christiansen was appointed associate professor at the Department of Neuroscience, University of Copenhagen. Lasse's appointment further solidifies the long-standing collaboration between DRCMR and the department of Neuroscience, while reviving the collaborative efforts to detail human central nervous control of movement in health and disease. Lasse's research combines electrophysiology with neuroimaging and brain stimulation to delineate the underlying principles of sensorimotor control and neuroplasticity.



Assc. Professor Lasse Christiansen

Henrik Lundell - Associate Professor at DTU

Henrik Lundell was appointed associate professor at the Technical University of Denmark (DTU), Department of Health Technology in 2023. Henrik has a large interest in diffusion MRI techniques with a focus on acquisition methods providing specificity directly in the data in contrast to fitting conventional data through model assumptions. This is realized through both gradient encodings and readouts of both water and metabolite mobility. His work spans all scanners at the department from the preclinical animal scanner to the ultra-high field 7T scanner. His methodology is applied in multiple projects but with a focus on multiple sclerosis. His affiliation creates a strong connection to his methodological work and contact to talented students through his lectures



Assc. Professor Henrik Lundell

and projects. Henrik is awarded with an ERC starting grant and has also recently received grants from the Danish Multiple Sclerosis Society to support his work.

JOINING MAGNIMS

The NeuroImaging in Multiple Sclerosis (NiMS) group at DRCMR has taken a big step forward in contributing to MS research at the European scale. In 2023, the NiMS group became a MAGNIMS centre, affiliated to the well-known MS Centre at VUMC Amsterdam under the leadership of Frederik Barkhof and Menno Schoonheim. MAGNIMS is the European consortium of centers working in the field of Magnetic Resonance Imaging in Multiple Sclerosis (MS). As leaders in the field of MRI research in MS, the MAGNIMS network has since 1990 worked on establishing radiological guidelines for the diagnosis and monitoring of MS. Over the past decade, as data analysis and multi-center studies moved into the foreground



MAGNIMS steering committee at one of the biannual workshops. The MAGNIMS steering committee represents central MAGNIMS site and leading MS-MRI centres in Europe.

of MS research, the MAGNIMS network has become increasingly valuable to not only share knowledge but also data. Gathering data to enable large scale studies is an important part in establishing relevant biomarkers, allowing to account for site and scanner variations, as well as cohort specific geographical and ethnical differences. Large data sets also play to the strength of artificial intelligence tools which are gaining relevance in most areas of modern MS-MRI research.

DRCMR is now actively collaborating with other MAGNIMS centers, sharing valuable data set such as from our national, multi-site DanNORMS to answer questions on the role of late-onset MS characteristics and the comparison of MS from mimicking diseases such as NMOSD and MOGAD. Our own research leverages the MAGNIMS network to further explore the impact of fatigue in MS. Postdoc Mads Madsen is currently holding a MAGNIMS fellowship award and pursuing a study on structural and functional network alterations linked to fatigue during a one year stay in Amsterdam. Another DRCMR study aims to establish the timeline of macro- and microstructural brain changes in deep brain regions in relationship to fatigue via event-based modelling and other data-driven approaches. We are excited to establish a 7T-subconsortium within MAGNIMS in the future, fostering cutting-edge research at ultra-high magnetic field strength by overcoming the otherwise still limited number of patients scanned in individual centers.

PARKINSONFORENINGEN

Professor Hartwig Siebner, Chairperson of the Research Council, presented the newly funded research projects at the Danish Parkinson Association's (Parkinsonforeningen) annual research event in 2024. More than 20 projects were chosen for their scientific value and relevance to patients. These projects reflect the Association's dedication to advancing basic and clinical research and care of patients affected by Parkinson's disease (https://parkinson.dk/).



Professor Hartwig Siebner at Parkinsonforeningen

LF INVESTIGATOR NETWORK

The DRCMR is proud to have seven members in the Lundbeck Foundation Investigator Network (LFIN): Oula Puonti, Vanessa Wiggermann, Lasse Christiansen, David Meder, Naiara Demnitz, Mathias L. Mathiasen, & Melissa Larsen.

The LFIN is a network for early- to mid-career researchers in Denmark working in neuroscience or related fields. LFIN aims to establish a network where neuroscientists from different labs and fields get to know each other, discuss science and establish collaborations at their meetings. The network also provides a space for sharing experiences amongst researchers at similar stages of their career, seeking help and sharing advice. This is aided by meetings revolving around career and development training for its members. Finally, LFIN members are engaged in promoting Danish neuroscience by participation in public outreach events, but also by training and inspiring young researchers at the LFIN winter school. With our seven members, amongst them two previous and one current LFIN board members guiding the network, we are proud to have a strong representation of DRCMR within the network.

MAJOR NEW GRANTS IN 2022-2024

Our talented pool of researchers at DRCMR continues to grow and attract major funding for groundbreaking projects.

Michael J. Fox Foundation Grant for Parkinson's Research

The overarching aim of this project is to elucidate the role of sensorimotor cortical areas and different corticostriatal projection neurons in the genesis of motor symptoms in Parkinson's disease using experimental mouse models. This collaborative grant focuses on Circuits and Cellular Targets for PD's symptoms and comprise three principal investigator teams in Sweden and Denmark (Prof. Gilad Silberberg, Karolinska Institute, Sweden; Prof. Angela Cenci, Lund University, Sweden and Associate Prof. Mattias Rickhag, Copenhagen University & DRCMR at Hvidovre Hospital). The project was granted 498,958.81 USD (3.300.000 DKK) for a two-year study. This project will fill major knowledge gaps regarding the role of corticostriatal systems in the genesis of parkinsonian and dyskinetic motor symptoms.

Modelling the induced electric field and neuronal response evoked by transcranial brain stimulation

Professor Axel Thielscher was awarded a grant from the NIH in 2022 as part of an applicant team together with Professors Angel Peterchev and Warren Grill from Duke University, USA. The project aims to extend an open-source software solution for simulating the electric field generated in the brain during non-invasive brain stimulation (SimNIBS) to incorporate estimations how these fields stimulate neurons (NeuroSimNIBS).



The DRCMR Lundbeckfonden Investigator Network: Oula Puonti, Vanessa Wiggermann, Lasse Christiansen, David Meder, Naiara Demnitz, & Melissa Larsen

The same year, Axel also received a significant grant from the German Research Council along with a large network of collaborators in Germany as part of the MeMoSLAP project. Axel's subproject in that collaboration focuses on validating and optimizing personalized current flow simulations across the human lifespan using in-vivo magnetic resonance current density imaging.

NeuroImaging of Babies during natural Sleep to assess typical development and Cerebral Palsy (NIBS-CP)

In 2022, Senior Researcher Kathrine Skak Madsen received a grant from the Elsass Foundation for the NIBS-CP project. The aim is to advance MRI techniques for babies without the need for sedation. These protocols will be used to image babies at high risk of developing cerebral palsy. The NIBS-CP project is a collaborative effort with paediatricians, physiotherapists, and IT scientists at Hvidovre Hospital and Rigshospitalet.

European Research Council Consolidator Grant

In 2022, Professor Tim B. Dyrby was awarded a prestigious European Research Council (ERC) Consolidator Grant of €2 million (15,000,000 DKK) for Non-Invasive Conduction Velocity Mapping in the Brain Network (CoM-BraiN). The overarching goal of the

CoM-BraiN project is to utilize a clinical MRI scanner to map signal transmission speed—specifically, conduction velocity—along the pathways of the brain. The fundamental research component will involve preclinical studies, while its applications will be implemented in patients with neurodegenerative diseases. The host institution for the project is Copenhagen University Hospital Amager and Hvidovre, in collaboration with the Technical University of Denmark.

XTREME-CT: Advancing multiscale label-free 3D x-ray imaging

In 2023, our XtremeCT project was awarded a €2 million (15,000,000 DKK) Synergy Grant from the Novo Nordisk Foundation. This four-year synergy project involves four principal investigators: Professor Tim B. Dyrby (DRCMR), Anders Dahl (DTU Compute, Technical University of Denmark), Henrik Birkedal (iNano, Aarhus University), and Professor Henning Friis-Poulsen (DTU Physics, Technical University of Denmark), who also serves as the project coordinator. The overarching goal of XtremeCT is to establish a new sub-micrometer X-ray imaging setup for biomedical imaging having a large field-of-view at the DanMAX beamline at the MAX IV synchrotron in Lund. The project focuses on two key applications: 3D imaging of brain structures and bones.

OTHER GRANTS

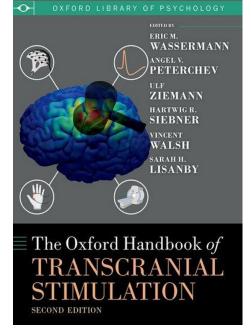
In addition to the major grants mentioned above, many other smaller grants have also been secured:

- Senior researcher Melissa Larsen received a grant from Independent Research Fund Denmark in 2024 under their special programme for psychiatric research. The project examines multidimensional trajectories of cortical neurodevelopment in adolescents at high risk of psychiatric disorders – an extension to the ongoing VIA study.
- Naiara Demnitz, Simon Steinkamp and Mikkel Malling Beck, received postdoc grants from the Lundbeck Foundation in 2022, 2023 and 2024 respectively
- Research fellow Petr Bednarik and senior researcher Lasse Christiansen were awarded Lundbeck Foundation Experiment grants in 2022 and 2023, respectively, allowing them to pioneer novel lines of MRI-based neuroscientific research
- Mads Just Madsen, Mikkel Malling Beck, Mikkel Vinding, Armita Faghani Jadidi, David Meder, Janine Bühler and Amin Ghaderi Kangavari received postdoc grants from the Capital Region of Denmark Research Fund in 2022-2024

We are immensely proud of our researchers for securing funding to pursue their scientific goals, and we extend our gratitude to the supporting funding agencies for their strong support.

BOOK PUBLICATION

In August 2024, we celebrated the publication of the Oxford Handbook of Transcranial Stimulation, which is an updated and expanded overview of the rapidly evolving field of transcranial neuromodulation with contributions from established and rising authorities, including Prof. Hartwig Slebner. This edition covers the scientific bases of non-invasive modulation of brain circuits with time-varying and static magnetic and electric fields, as well as focused ultrasound and infrared energy. The book will be useful to neuroscientists, clinicians, bioengineers and others with an interest in neuromodulation.



EDUCATION AND RECOGNITION

At DRCMR, we offer comprehensive in-house education to prepare young scientists for conducting innovative brain research. Our intra-mural educational programs actively involve all staff, creating an inspiring multidisciplinary environment built on openness and mutual respect among disciplines.

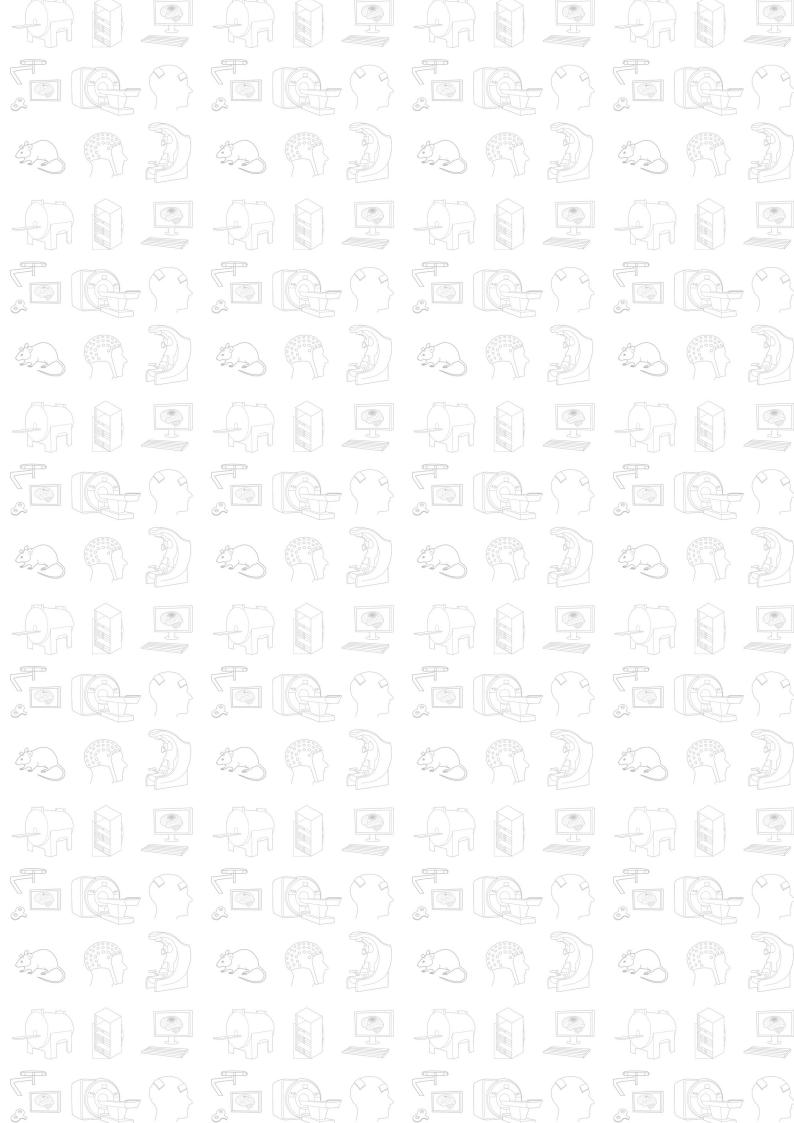
We place great emphasis on mentoring researchers and supporting their career development, helping them realize their scientific potential while prioritizing their well-being. We take immense pride in their achievements, whether it's securing grants, receiving awards, or gaining recognition in Danish media. To celebrate these milestones, our researchers share their success—and their joy—by bringing cake for the entire staff – and there has been quite some cake in 2022-2024....

THE GREATEST HIGHLIGHT IS OUR TEAM

Over the past three years, DRCMR has successfully attracted new talent from both Denmark and abroad. 18 new researchers at the postdoctoral level or higher have joined our team. We are delighted to welcome them in this report. They have quickly become vital members of the DRCMR team, making valuable contributions to our work. In addition, we have welcomed many students who have been part of DRCMR for varying durations. The greatest highlight of the past years has undoubtedly been our outstanding team. Researchers, students, support staff, and administrative personnel have all contributed to making

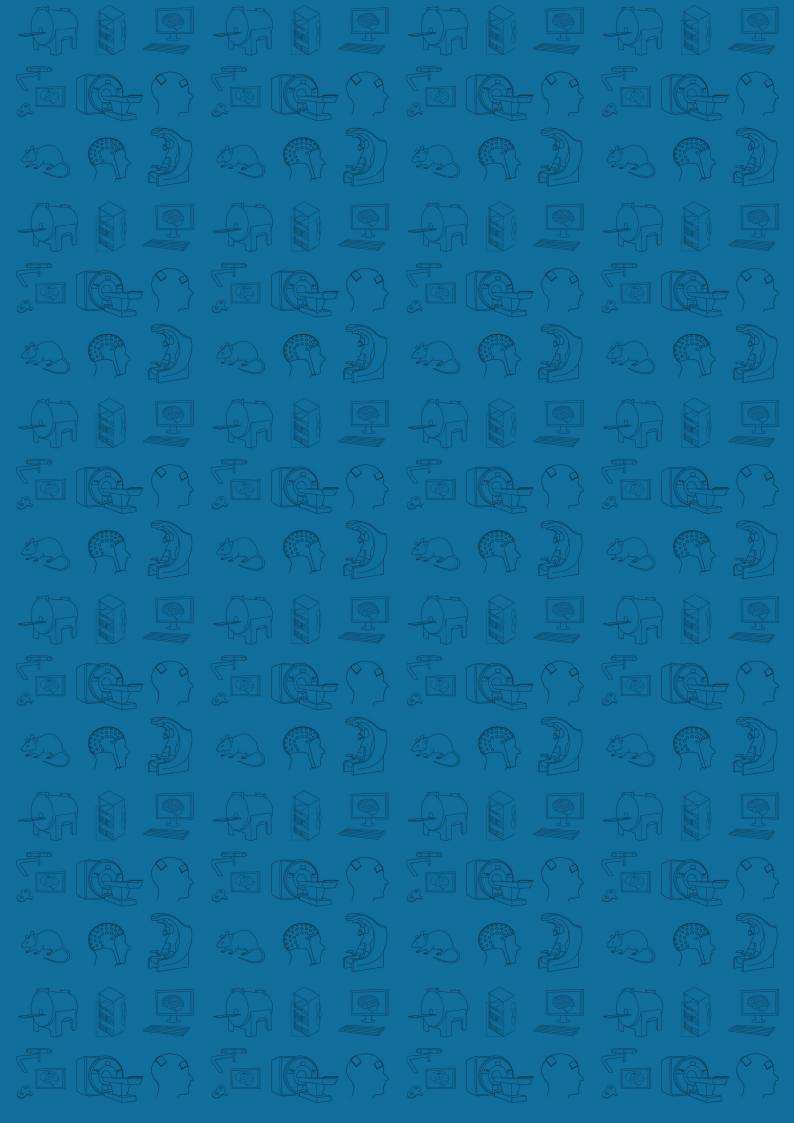
DRCMR a truly inspiring workplace. Their dedication to achieving excellence and innovation, paired with a deep commitment to collaboration, has been fundamental to our success. Looking back on three successful and productive years, we feel proud and optimistic, confident that our exceptional team will continue to make groundbreaking strides in understanding the human brain and its disorders.

2025 marks the start of DRCMR's fifth decade. As we look back on three memorable and productive years, we do so with pride and optimism, certain that our dedicated team will keep advancing research and deepening our understanding of the human brain and its disorders.



KEY PROJECTS

At DRCMR, we have a large number of interesting ongoing projects. Some projects are quite big, involving numerous researchers and are carried out in close collaboration with national or international partners while others are smaller projects involving a single PhD student and his/her supervisor. In this section, you can get a taste of some of the projects we have been working on in 2022—2024, listed roughly alphabetically according to funding body.



MEMO-SLAP

MODULATION OF BRAIN NETWORKS FOR MEMORY AND LEARNING BY TRANSCRANIAL ELECTRICAL BRAIN STIMULATION: A SYSTEMATIC, LIFESPAN APPROACH

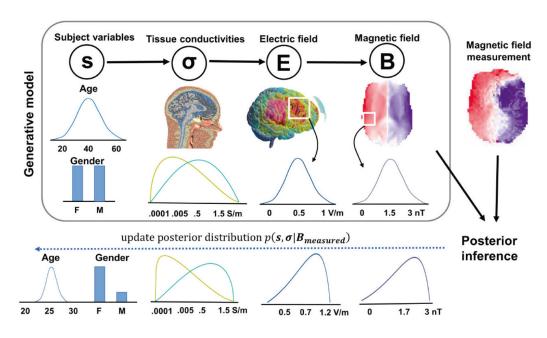
BACKGROUND

Non-invasive transcranial direct current stimulation (tDCS) has recently received substantial attention in experimental and clinical science, because it allows modulation of human brain function without significant adverse effects. However, despite widespread and often successful use of this technique, little systematic research into the mechanisms underlying frequently observed highly variable effects of tDCS has been accomplished. Currently, this results in suboptimal use of this promising technique in experimental and clinical contexts. The Research Unit 5429 (RU) MemoSLAP (modulation of brain networks for memory and learning by transcranial electrical brain stimulation) received funding by the German Research Foundation (DFG) in 2022 to address this knowledge gap, led by the University of Greifswald. MemoSLAP aims at investigating tDCS effects for the first time in a systematic, comprehensive

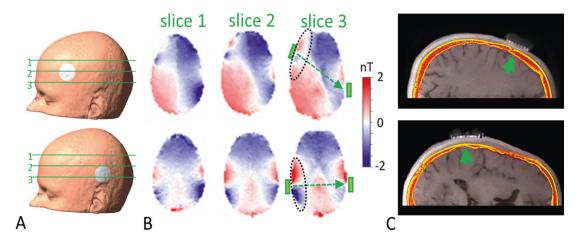
FUNDED BY



and coordinated way, leveraging a multidisciplinary team of leading groups at six German universities and research institutes, and DRCMR as international partner. Due to its high relevance for experimental and translational research, human learning and memory function serves as a model in Memo-SLAP to study tDCS effects across four functional domains (i.e., visual-spatial, language, motor, and executive) and across the



Overview of the Bayesian Modeling Framework that we aim to use identify factors that cause differences between measured and simulated current flow, in turn giving us the opportunity systematically improve the simulated current flow.



MRCDI measures the small magnetic fields that are caused by the tDCS current flow through the head. Comparison of the measured to simulated fields enable systematic validations of the tDCS field simulations. This pilot data shows the dependence of MRCDI measurements on the electrode position for a tDCS montage with two electrodes on the left and right side of the head, respectively. (A) Only the position of the left electrode was changed as indicated. (B) The magnetic field pattern changes due to the position change. In addition, the strength of the field closest to the left electrode clearly changes (black dashed ellipses), likely caused by differences in the local skull thickness. (C) Skull from low-dose CT overlays on UTE images of the electrode positions. The green arrows indicate the skull region underneath the electrode centers.

human lifespan. MemoSLAP comprises eight empirical projects with aligned methods, individualized and targeted stimulation, highly controlled experimental settings, and tDCS application during concurrent functional imaging. MemoSLAP will generate fundamental insights into the neural mechanisms and predictors of tDCS response across the human lifespan, thereby informing theoretical concepts of the mechanisms-of-action by which current flow alters neural activity. From a methodological point of view, we will be able to optimize and validate biophysical models of current flow using an unprecedented dataset.

Together, this will substantially advance future experimental and translational applications of tDCS in health and disease.



STATUS

DRCMR contributes to two overarching projects that integrate the data of the empirical projects, with the aim to (1) relate the outcomes of biophysical models of individualized current flow to behavioral and neural modulations using the large, coordinated dataset acquired in the empirical projects and (2) cross-validate and improve current flow simulations by using in-vivo magnetic current density imaging measurements (MRCDI, Fig. 2). We will help analysing selected aspects of the rich MRI dataset and current flow patterns to identify anatomical and biophysical factors that contribute to the variability of the TDCS effects on functional brain activity and behavior. In addition, we will acquire a large MRCDI dataset of healthy participants across a wide age range which we will use to systematically test and optimize the accuracy of the current flow simulations (Fig. 1) that are employed in MemoSLAP for planning and analysing the tDCS interventions.

















FANTIMS

FATIGUE ALLEVIATION WITH NEUROMODULATION THERAPY IN MULTIPLE SCLEROSIS

BACKGROUND

Excessive fatigue during everyday life (trait fatigue) and increased fatigability during motor or cognitive activity (state fatigue) affect up to 75% of all patients with multiple sclerosis (MS). Fatigue-induced functional impairment causes substantial societal burden in Denmark, due to reduced work capacity and increased unemployment levels. Functional (f)MRI studies suggest that the individual expression of fatigue arises from brain-network dysfunction, resulting from an imbalance between excitation and inhibition in affected networks. Specifically, that perceived trait fatigue associates with task-related hyperactivation of the premotor cortex during a non-fatiguing grip force task, and those patients who were able to increase premotor activity after performing a fatiguing motor task were less affected by fatigue during everyday life.

PROJECT GOALS

We will conduct a double-blind, randomised, controlled trial. We are investigating the use of repetitive Transcranial Magnetic Stimulation (rTMS), as a potential intervention targeting fatigue

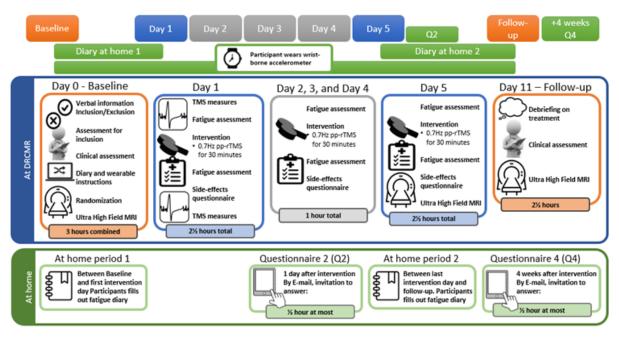
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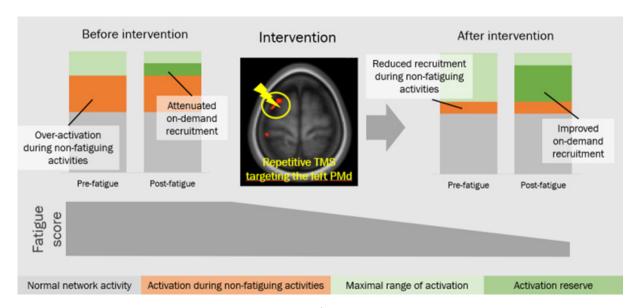




in MS, targeting the dorsal premotor cortex. The dorsal part of the premotor cortex is a prime candidate area, for rTMS aiming at alleviating fatigue. It is accessible and it is implicated in the excitation-inhibition imbalance of fatigue. We will use a novel rTMS pulse paradigm, validated using fMRI to have broad network-wide suppression of the premotor-motor network.



Overview of project methodology and outcome measures. The study consists of a total of 7 visits: Baseline; 5 intervention days; follow-up. Participants will be MR-scanned on baseline, day 5 of the intervention and on follow-up. The study is supplemented by at-home activity tracking and patient-reported outcomes.



Overview of the project hypothesis. Before the intervention, there is an excitation/inhibition imbalance. The intervention alleviates this, allowing for improved on-demand recruitment. This results in a decrease in perceived fatigue.

The hypothesis is, that this network-wide suppression will allow for improved on-demand recruitment, resulting in lower perceived fatigue, as shown in the first figure.

In close collaboration with the Danish Multiple Sclerosis Center at Rigshospitalet Glostrup, we will recruit 60 moderately to severely fatigued participants with stable MS and no other major disease. The protocol is shown in figure 2, and participants will undergo:

- A baseline period with 1 visit to our site (D0) and an at-home period
- 5 treatment days
- Follow-up period with one visit to our site (D11), an at-home period and two follow-up questionnaire invitations

IMPACT

Treating multiple sclerosis related fatigue is one of the most urgent, unmet needs of MS management. This proposed RCT will be pivotal in determining the role of rTMS in the future treatment of MS-related fatigue symptoms. Additionally, the neurophysiological and MRI assessments will also allow us to gain important novel insights into the underlying mechanisms of fatigue amelioration which will aid in future protocol optimization.

The primary outcome is the difference in change from baseline to follow-up, between the 2 arms, in Fatigue Scale for Motor and Cognitive symptoms (FSMC). In addition, we will perform a total of 3 7T MRI sessions with spectroscopy to capture excitation-/inhibition balance. Enabling further illumination of the (pato-)physiology of fatigue.

STATUS

Starting in the second half of 2023, we piloted the protocol, and began recruiting participants in the second quarter of 2024. The investigation protocol and procedures have been developed, in part, together with MS patients, in order to ensure real-world applicability.

FACTS

Project period: 01.09.2023 - Spring 2026

PI: Hartwig Siebner

Collaboration: Danish Multiple Sclerosis Centre,

Rigshospitalet Glostrup; Danish MS Society

Funding: The Danish Multiple Sclerosis Society;

Amager-Hvidovre Hospital intramural funds; Independent Research Fund

Denmark

COMPACT

COPENHAGEN MAGNETIC PERSONALIZED ACCELERATED BRAIN CIRCUIT THERAPY FOR TREATMENT RESISTANT DEPRESSION

BACKGROUND

Major depressive disorder (MDD), affecting 30% of the population, poses significant personal and societal challenges. Up to 30% of MDD patients develop treatment-resistant depression (TRD), marked by non-response to multiple treatments, leading to prolonged disability and reduced quality of life. Repetitive transcranial magnetic stimulation (rTMS) targeting the left dorsolateral prefrontal cortex (DLPFC) is an established treatment for MDD, particularly for patients who do not respond to conventional therapies, including antidepressants and psychotherapy. Commonly, rTMS treatments are given in a one-size-fits-all fashion and thus, do not account for individual brain circuit variations.

The COMPACT project aims to advance understanding and treatment of TRD in a randomized, sham-controlled trial that integrates clinical, technical, and methodological advances. We will test a novel "accelerated" rTMS protocol, applying multiple daily rTMS sessions to the cortex over five consecutive days to induce a fast antidepressive response. Each session consists of a so-called theta burst stimulation. The CoMPACT protocol uses a novel type of repetitive burst stimulation protocol. Each burst consists of three pulses given at a within-burst frequency

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FACTS

Partners:

Funding: DKK 4.4 million from Independent

Research Fond Denmark

Period: 2024-2028

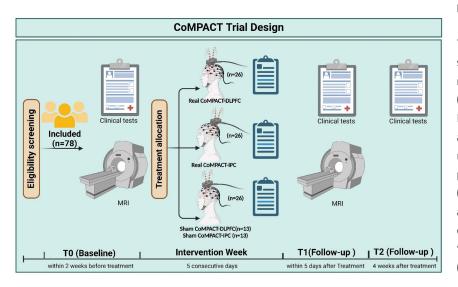
PI: Professor Poul Videbech from CNDR

Professor Hartwig Siebner form DRCMR and Professor Maj Vinberg from Mental

Health Centre North Zealand

of 130 Hz, using a customized stimulator (MagPro-XP Orange Edition, Magventure, Farum). Personalization is achieved using electrical field modeling based on individual brain scans. Using a parallel-group design, the CoMPACT protocol will target either the dorsolateral prefrontal cortex (DLPFC) or a novel target, the left inferior parietal lobule (IPL). Multimodal brain mapping, including functional scans and EEG, will assess protocol impacts on depression-related brain networks and identify biomarkers

predicting response.



The COMPACT team consists of scientists from the Center for Neuropsychiatric Depression Research (CNDR), Mental Health Centre North Zealand, DTU Health Tech, and DRCMR. The CoMPACT project received funding from the Independent Research Fund Denmark (awarded to Prof. Poul Videbech) and builds on technologies developed in the Grand Solutions project "Precision Brain-Circuit-Therapy" (PI: Prof. Hartwig Siebner).

NIBS-CP

ESTABLISHING PROCEDURES FOR CLINICAL INFANT AND TODDLER MRI DURING NATURAL SLEEP

BACKGROUND

Today, diagnostic MRI of infants and toddlers with suspected brain damage is typically conducted using sedation or general anesthesia (GA) and is mainly based on conventional structural MR images focusing on identifying major structural brain pathology. NIBS-CP aims to establish procedures for clini-



cal infant and toddler MRI during natural sleep, eliminating the use of sedation or GA. NIBS-CP will assess early brain and motor function development in 200 infants at risk of cerebral palsy enrolled in the national CP-EDIT study (led by Prof.

Christina Høi-Hansen) and in typically developing infants. Infants will be followed longitudinally (in three waves) between the ages of 3 to 24 months with comprehensive assessments

of motor functioning and advanced MRI. We aim to establish a normative material of early brain development of Danish children, as well as conduct normative modeling of typical and atypical development to identify deviations in brain development at the level of the single child. We will also map how early brain development relates to motor function and motor development. Identifying predictive brain structural features of motor function and motor development is key to the future use of early MRI in the clinical work-up, as this promotes early diagnosis and (clinical) intervention strategies tailored to the individual child.

FUNDED BY





STATUS

In NIBS-CP, we utilize the knowledge from international research initiatives on early brain development to set up and implement infant and toddler MRI during natural sleep in Denmark, as well as translate these methods from healthy research populations into clinical practice. In 2023, we visited multiple research labs in the USA and Europe to learn how to scan infants and toddlers without GA. Further, we acquired the necessary equipment and implemented the procedures through pilot scans. Recruitment of participants started in 2024.



NIBS-CP pilot baby together with NIBS-CP project member Line Korsgaard Johnsen

C-MORPH

THE MICROCOSMOS BEYOND WHAT IS VISIBLE WITH CONVENTIONAL IMAGING

BACKGROUND

The project is funded by an ERC (European Research Council) starting grant given to Associate Professor at DTU and Senior Researcher at DRCMR Henrik Lundell who is using MR imaging and spectroscopy as a tool to identify specific fingerprints of underlying disease processes. C-MORPH stands for cell type specific morphometry and has the primary goal of stratifying the shape and size of different cell types in the brain and changes related to neuroinflammatory and -degenerative processes with end goal applications in multiple sclerosis (MS). These processes are in a tight interplay in MS but to a different degree active in different disease stages and phenotypes. While this heterogeneity across time and individuals is known from histology, the diagnostic tools are still lacking to understand the right treatment strategy for the individual patients at a given time. The methods developed in C-MORPH could be

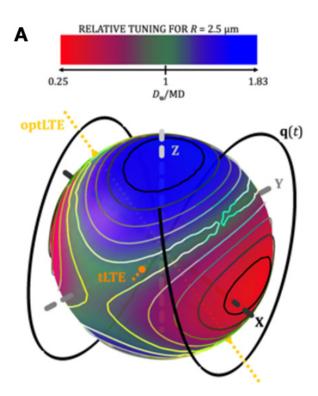
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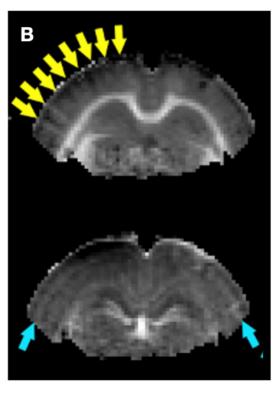




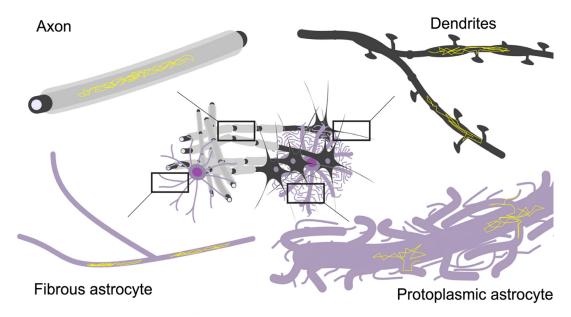
thought of as a prism separating disease processes by identifying morphological changes to individual cell types, such as neurons and glial cells in the human brain.

To achieve these goals, Henrik Lundell has developed two independent spectroscopic MR methods. The first MR method is called Powder averaged diffusion weighted spectroscopy





Advanced gradient trajectories (black curve) can be tuned to probe molecular mobility in 3D at different length and time scales (color scale). B) In practice, these new methodologies can provide direct contrasts to relations between the shape and size of cellular restrictions. The maps shows different organizations of radial anisotropic fibrous structures (top) and tangential layers of restrictions in the rat cortex (Lasic et al, in submission 2024).



A central goal for C-MORPH has been reached: the detection of cell type specific morphology in the human brain in vivo. The figure is a graphical interpretation of how the DDES method detects very different conditions in different cell types and tissue types (Lundell et al, Neuroimage 2021).

(PADWS) and can provide an unbiased marker for cell specific structural degeneration. The second method uses Spectrally tuned gradient trajectories (STGT) which can isolate cell shape and size. In the C-MORPH project, Lundell and co-workers push these techniques further and combine them for MR-based precision medicine on state-of-the-art MR hardware.

STATUS

In 2019, Dr. Samo Lasic joined the C-MORPH project and this kickstarted development of theory, simulations, and analysis methods. An early outcome of this work has been a massive book chapter, covering novel diffusion encoding techniques. The chapter gave the opportunity to collect the theoretical foundation for the project, but the chapter is also looking into the future and brings in several new concepts.

In 2021, Dr. Nathalié Just came onboard the project. She has brought her expertise in preclinical MRI in general with a special focus on the experimental preclinical aspects of the project. This has included implementation of new theories into the real world and evaluations of applications in models of neuroinflammation and neurodegeneration in rodents. The new methodologies provide unprecedented independent contrast mechanisms that can be directly extracted from raw data.

In 2023, MSc. Kristin Engel joined the group as a research assistant and enrolled as a PhD-student in 2024 on method developments and applications in human ultra-high field settings with a highlight on optimizing hardware performance.

On the human in vivo side a key methodology has been double diffusion encoded spectroscopy (DDES) demonstrating the feasibility of stratifying glial and neuronal morphologies in gray and white matter, a central goal of the project. The direct measurements of metabolite mobility in this work provide remarkably detailed views into differences in neuronal and glial morphologies in human gray and white matter.

Knowledge attained prior to and during the C-MORPH project was also incorporated in a recent consensus paper on diffusion weighted spectroscopy and a review paper on disentangling cerebellar microstructure. Further, the still ongoing work in the C-MORPH project has already spun off into applications in characterization of cardiomyocytes in collaboration with Irvin Teh, University of Leeds, UK, which demonstrates the wide interest and power of these new methods. The project also benefits from strong local collaborations with Centre for Neuroscience and Stereology at Bispebjerg Hospital and the Danish Center for Multiple Sclerosis, Rigshospitalet. Methods related to the project are also part of the protocol in the ongoing DanNORMS project.

COM-BRAIN

UNDERSTANDING THE BRAIN'S INTRICATE COMMUNICATION NETWORKS

BACKGROUND

Professor Tim Dyrby was awarded a prestigious European Research Council (ERC) Consolidator Grant, receiving €2 million to support his groundbreaking research. The five-year project, titled "Non-invasive Conduction Mapping in Brain Networks: A Novel Imaging Framework for Axonal Fingerprinting of Brain Connections in Health and Disease" (CoM-BraiN), is hosted at the DRCMR, with co-hosting by the Technical University of Denmark.

The CoM-BraiN project focuses on understanding the brain's intricate communication networks, where countless axons—tiny "cables"—carry signals between different regions to power our thoughts, actions, and decisions. These axons, wrapped in a fatty substance called myelin, transmit signals at different speeds based on their size and the thickness of their myelin sheath. However, diseases like ALS and MS can damage these structures, disrupting communication in the brain and leading to severe functional and cognitive impairments.

Our goal in CoM-BraiN is to transform structural MRI into a kind of "in vivo microscope." As discussed at the kick-off meeting in Copenhagen (Figure below). This means making it possible to use MRI scans to examine these microscopic features



Kick off meeting for the CoM-BraiN project.

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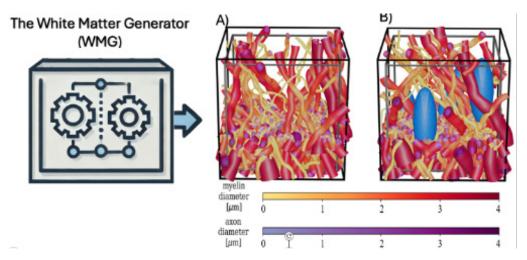
European Research Council

inside living brains. By doing this, we can predict how structural changes in axons and myelin might affect the brain's ability to function. This kind of insight, which is typically only available by studying donated postmortem brains under a microscope, could revolutionize how doctors detect and treat brain diseases. Although traditional structural MRI can only capture details at the millimeter scale, it is sensitive enough to reveal microstructural patterns beyond this resolution. Over the years, MRI methods have been developed to estimate axon diameters, but these methods often have biases that limit their reliability in real-world clinical settings. In CoM-BraiN, we are creating a new generation of MRI-based models that address these limitations, enabling higher precision in estimating axon diameters. Early in our work, we discovered that traditional ways of building models, based on assumptions about axon anatomy, are unstable when applied to more detailed data. These limita-

> tions stemmed from the fact that the MRI signals for some microstructural details were too similar to differentiate.

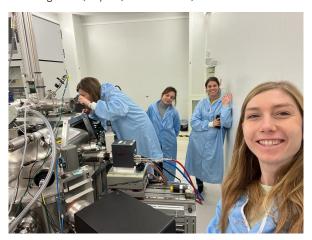
STATUS

To solve this, we turned our focus to machine learning (ML) techniques, which are not limited by the same assumptions as traditional models. The ML methods showed exceptional results in controlled settings, but their performance declined significantly when tested on real MRI data. We are now testing novel data preprocessing approaches to address this challenge, and the preliminary results are prom-



The White Matter Generator (WMG) is a software tool for creating realistic 3D meshes of White Matter microstructural features, including axons, myelin, and cells. Based on X-ray Nano Holotomography (XNH) imaging. Adapted from Winther et al., 2024, Front. Neuroinform.

ising. A key challenge in developing these models is the need for ground-truth data: how can we know what these axons and myelin look like in detail without directly seeing them? To overcome this, we used X-ray Nano Holotomography (XNH), a cutting-edge 3D imaging technique that allows us to visualize brain microstructures with astonishing detail—down to 75 nanometers. This technology requires access to synchrotron facilities like ESRF in Grenoble or MAXIV in Lund and produces massive datasets. To analyze these datasets, we developed an advanced image processing pipeline using deep learning. This pipeline takes sparse, manually labeled training data and uses it to accurately segment entire 3D images into tissue classes, including axons, myelin, blood vessels, and cells.



ERSRF synchrotron facility in Grenoble, France at the ID16 beamline. Team and beamline people placing one of our tiny samples in the machine.

With this detailed understanding of brain microstructures, we developed a software tool called the White Matter Generator (WMG). This tool allows us to create synthetic 3D models of

realistic brain environments, representing both healthy and diseased states, such as axonal degeneration or myelin loss - Figure above. These models are used to train and test MRI methods, bridging the gap between the anatomical features seen in XNH images and the signals captured by MRI scans.

Myelin is a particularly important part of this story because it plays a crucial role in speeding up signal transmission in the brain. Changes in myelin are often linked to diseases, but current MRI methods cannot easily distinguish whether the myelin is being damaged or if it is in the process of repair—a vital clue for understanding disease progression and recovery. In CoM-BraiN, we have explored a new MRI-based approach that may reveal these dynamics. We tested this technique in animal models of demyelination (myelin loss) and remyelination (myelin repair), comparing the results with traditional microscopic analysis. The results were highly promising, showing that this new method could provide valuable insights into the state of brain diseases. The CoM-BraiN project is paving the way for a deeper understanding of the brain while creating new possibilities for diagnosing and treating neurological disorders. So far, the project has achieved several promising results. We have developed a new generation of MRI-based axon diameter models and an innovative myelin metric, both of which offer doctors and neuroscientists more precise tools to detect early signs of brain disease and track disease progression. Additionally, our deep learning-based framework for analyzing massive XNH datasets, together with the WMG software, will be made publicly available. These resources will provide an invaluable foundation for future research, enabling scientists worldwide to advance their understanding of brain microstructures.

FAMILY

UNDERSTANDING & PREDICTING THE INTER-GENERATIONAL TRANSMISSION OF MENTAL ILL NESS

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BACKGROUND

A family history of severe mental illness significantly heightens the likelihood of mental health issues in offspring, with over 50% developing disorders by early adulthood. However, intergenerational transmission of risk for mental illness in one's children is insufficiently considered in clinical practice, nor is it sufficiently utilised in diagnostics and care for children of ill parents. FAMILY is a multidisciplinary initiative that aims to improve the lives of mentally ill persons and their families.

FACTS

Project period: 01.10.2022 - 01.09.2027

Pls: Melissa Larsen, Kathrine Skak Madsen, and William Baaré.

Collaboration: Prof. Neeltje van Haren, Erasmus Univer-

sitair Medisch Centrum Rotterdam

Funding: EU Funding: 10 million Euro

The initial focus is on better understanding the mechanisms of intergenerational transmission of mental illness from parent to child. FAMILY will try to build models to predict whether mental illness will be transmitted across generations or not. Furthermore, FAMILY addresses key ethical and social issues raised by risk prediction for clinical use, such as the right not to know

and the risk of stigma. FAMILY collaborates with the family advocacy and support organisation EUFAMI and the not-for-profit association ESCAP to increase awareness and foster active engagement of families, and translate new discoveries to patients and mental health care professionals. The DRCMR is involved FAMILY as part of the Capital Region of Denmark (see link) through its partnership with the Danish High Risk and Resilience Study-VIA and is represented by researchers Melissa Larsen, Kathrine Skak Madsen, and William Baaré.

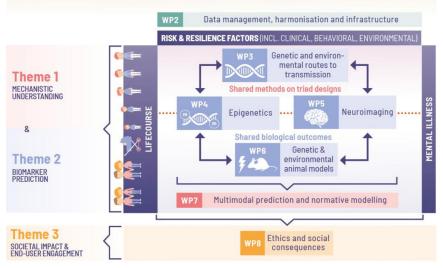
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IMPACT

FAMILY leverages longitudinal population and familial high-risk cohorts and integrates diverse data types, including clinical, genetic, and neuroimaging information. Additionally, it expands datasets with novel epigenetic and parental brain imaging data. The initiative's impact spans scientific advancement, ethical guideline development, and public awareness efforts. Through open-access publications and tool development FAMILY aims to inform both scientific and clinical communities. Moreover, by engaging stakeholders and policymakers, FAMILY seeks to facilitate the integration of risk prediction models into mental healthcare services. Educational campaigns aim to reduce stigma and empower families to manage their mental health proactively. FAMILY's holistic approach promises to inform future strategies for disorder prevention and health promotion, ultimately improving outcomes for generations to come.

INTERGENERATIONAL TRANSMISSION OF RISK OF MENTAL ILLNESS



LIFEBRAIN

OPTIMISING THE USE OF EUROPEAN BRAIN IMAGING COHORTS - HEALTHY MINDS FOR 0-100 YEARS

BACKGROUND

Lifebrain was initiated in 2017 after successfully securing EU Horizon 2020 funding. Lifebrain brought together top European brain research centres and a small-medium-sized enterprise, VITAS, that specializes in measuring and monitoring biomarkers in dried blood spots). The Lifebrain project officially ended on June 30, 2022. However, the partners initiated an "after Lifebrain" consortium with their own funding and continue to work on the unique Lifebrain data.

The Lifebrain consortium aims to identify determinants of brain, cognitive, and mental health at different stages of life and establish foundational knowledge for understanding how brain, cognitive, and mental health can be optimized throughout the lifespan. The project produced important new knowledge about risk and protective factors influencing brain health. It also brought new insights into public perceptions of brain health, by means of a large-scale international survey regarding the views and perceptions of healthy adults regarding brain health. The survey was made available in 14 languages and closed in August 2020. More than 27,590 people from 81 countries responded to the survey, including more than 1,000 people from Denmark. Key findings challenged previous assumptions in cognitive neuroscience and emphasised the importance of longitudinal data and avoiding global conclusions from selective datasets.



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STATUS

Socioeconomic status (SES) 's relationship with brain and cognition varies across samples, with stronger associations in the US than in European cohorts. In Lifebrain, we found that SES was more related to intracranial volume (ICV) than grey matter volume (GM). Since ICV is mainly driven by early brain growth, our finding suggests that SES-cognition relations are already established in early development.

Using longitudinal analyses, we showed that the popular methodological concept of "brain age" captures brain differences that have been present throughout an individual's life. Our finding indicates that cross-sectional studies, with one single brain scan per participant, are unable to predict the pace of ageing in someone's brain. As part of its commitment to advancing brain research, Lifebrain has developed novel statistical tools. These tools, designed to address challenges in assessing brain changes, are now freely available for researchers. By

providing these tools, Lifebrain aims to empower researchers in their longitudinal study planning, data analysis, and meta-analysis across studies, thereby fostering a more collaborative and impactful research community.

Lifebrain consortium, June 29th, 2022, Oxford, held at the Blavatnik School of Government: William Baaré, Naiara Demnitz, Anna Plachti, Carl-Johan Boraxbekk, Kathrine Skak Madsen



http://www.lifebrain.uio.no

PRECISION-BCT

PERSONALIZED MULTI-TARGET BRAIN STIMULATION TO RESTORE BRAIN FUNCTION IN TREATMENT-RESISTANT DEPRESSION

BACKGROUND

In Precision–BCT, we combine leading clinical, technical, and methodological expertise of Danish and international partners to implement a new treatment of major depressive disorder (MDD), based on personalized non-invasive transcranial magnetic stimulation (TMS). Supported by a Grand Solutions grant from Innovation Fund Denmark, it is led by DRCMR and involves MagVenture A/S (Farum, Denmark), the Centre for Neuropsychiatric Depression Research of the Mental Health Centre Glostrup, DTU Health Tech, Localite GmbH (Bonn, Germany) and the Ludwig-Maximilians-University (Munich, Germany) as partners. Our aim is to improve and innovate on all aspects of TMS-based MDD treatments to boost their clinical efficacy.

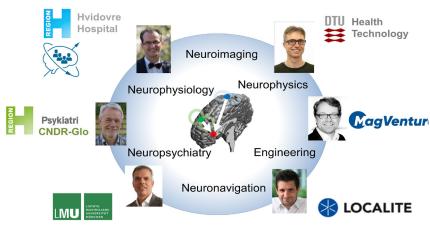
MDD is among the most frequent brain disorders and severely affects the social life and relationships of the patients. It increases their risk for lowered financial income and unemployment and can result in somatic comorbidities and a lower life expectancy. MDD also poses a huge economic burden for society as a whole. However, not all patients respond to the available treatment options, including various antidepressants and different types of psychotherapy, even when these are given in combination. Repetitive TMS (rTMS) of prefrontal brain areas is currently developed as a promising and much-needed alternative treatment. It is approved as MDD treatment in the USA and EU, especially because it has been shown to be efficacious in many of the patients that are deemed resistant to standard therapies. RTMS applies a series of strong electromagnetic field pulses to cause highly synchronized neural activity in the

targeted brain area. It is safe, pain-free and non-invasive and can successfully restore normal activity in the dysfunctional brain networks and by that reduce the clinical symptoms of the disease. So far, rTMS is given as "one-size-fits-all" therapy that does not account for the substantial between-patient variability of the disease-related brain circuit alterations, which currently limits clinical efficacy. Precision-BCT aims to tackle this challenge by personalizing the treat-

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ment, with the aim to further increase its clinical value. During the initial project period, we developed novel TMS stimulation and navigation equipment that enable precise spatial targeting and dose control, highly flexible stimulation patterns, and simultaneous stimulation of several brain regions. In addition, a personalization workflow that uses structural and functional brain imaging to identify the relevant individual brain circuit has been successfully tested in healthy participants. While the methodological research will continue, the project is now focused on translating the new findings and tools into clinical testing in a MDD patient cohort. We have received additional funding from The Independent Research Fond Denmark that will enable us to substantially increase the scope from methodological proof-of-concept testing towards a full clinical trial. Within the new COMPACT (Copenhagen Magnetic Personalized Accelerated Brain Circuit Therapy) trial, 70 MDD patients will undergo an intense one-week rTMS therapy based on the Precision-BCT approach. This will enable us to ensure the efficiency and maturity of our clinical workflow for personalized rTMS treatment of MDD that will be grounded in the underlying circuit-dysfunction and will pave the way for large-scale clinical studies aiming at a broad clinical adoption.



DEUTERIUM IMAGING

NOVEL DEUTERIUM SPECTROSCOPIC IMAGING

BACKGROUND

Mapping the brain's metabolic rate of glucose (Glc) with positron emission tomography (PET) is a diagnostic core of neurodegenerative brain diseases. Senior researcher Petr Bednarik acquired funding for a 2-year project from the Lundbeck Foundation (Experiment grant, 2 Mio DKK), where we propose a proof-of-concept experiment to demonstrate the potential of a novel quantitative mapping method: deuterium magnetic resonance spectroscopic imaging (DMRSI).

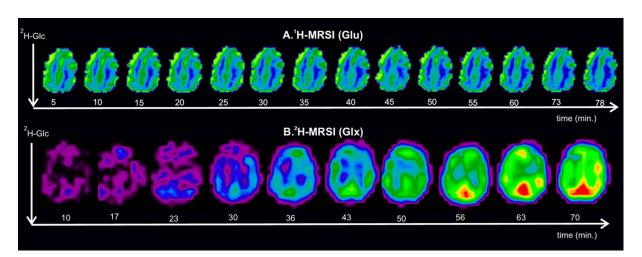
Deuterated glucose and its downstream metabolites will be detected either directly with a radiofrequency coil tuned to deuterium frequency (2H-MRS) or indirectly utilizing standard radiofrequency hardware tuned to protons (1H-MRS). Thus, DMRSI has the potential to overcome all major drawbacks of PET, as DMRSI maps both regional Glc uptake and downstream metabolism using orally or intravenously administered non-harmful stable tracers. While 2H-MRS reveals the shift from aerobic towards anaerobic glucose metabolism in pathologies (Warburg effect), the indirect approach (1H-MRS) quantitates the synthesis rate of major excitatory (glutamate) and inhibitory (GABA) neurotransmitters, thus allowing to reveal alterations in various brain disorders such as major depressive disorder and Alzheimer's disease.

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The current project will benefit from a new deuterium head coil for our 7T scanner, which allows comprehensive metabolic modeling in the human brain with high spatial specificity on 7T. In addition, the feasibility of both the direct and indirect deuterium detection on 3T MR scanners facilitates clinical translation of DMRSI. Therefore, we obtained funding from Hvidovre Hospital (170 K DKK) to advance currently available techniques at 3T for clinical studies.

Our advancement in DMRSI will set the stage for future metabolic brain studies, measuring how aging, neurodegeneration and other brain disorders impair the brain's aerobic and anaerobic metabolism, using nonharmful tracers. DMRSI offers a reliable and affordable method desperately needed to unravel the contribution of metabolic mechanisms to debilitating brain diseases with a massive impact on mental health.



Time-course of signals from brain metabolites (glutamate:Glu and glutamate+glutamine:Glx) after oral administration of deuterated glucose (2H-Glc) collected with two different MR spectroscopy methods. . Bednarik, Nat Biomed Eng. 2023;7:1001-1013.

ADAPT-PD

ADAPTIVE AND PRECISE BRAIN-CIRCUIT-TARGETING IN PARKINSON'S DISEASE

BACKGROUND

ADAPT-PD is a collaborative project that addresses a central question in neuroscience with enormous therapeutic implications: How can the dysfunction of brain circuits in Parkinson's disease be normalized with device-based neuromodulation? Parkinson's disease (PD) is a common and disabling, multi-system neurodegenerative disease which affects motor and non-motor brain networks. The symptoms of PD are motor symptoms like bradykinesia and tremor as well as non-motor symptoms such as autonomic dysfunction and cognitive decline. As of today, the main therapeutic approach is dopaminergic replacement therapy like levodopa. Unfortunately, most patients develop adverse effects with time. One common and disabling adverse effect is levodopa-induced dyskinesia (LID) which are involuntary movements coursed by the non-physiological fluctuations in dopamine concentrations and maladaptive plasticity at the cortico-striatal synapses. The project is led by Professor Hartwig Siebner at DRCMR, who is collaborating with Professor Andrea Kühn, Charité Universitätsmedizin in Berlin, Germany, and Professor Angela Cenci Nilsson, Lund University, Sweden. Each site focuses on different aspects of PD and by combining the different levels of analysis, this project can achieve a unique understanding of the disease and how to treat it.

We use an array of well-aligned methods to characterize how the cortex and its projections to the basal ganglia contribute to motor and non-motor disabilities in PD and LID. Invasive recordings and opto-/chemogenetic stimulation in rodent models of PD and LID yield novel insights into critical cortico-basal ganglia circuit features that constitute candidate targets for ADAPT. In humans, we use an array of neuroimaging techniques (functional MRI, EEG, TMS) to map the functional circuit changes dynamically over time as the brain goes from an unmedicated state to a medicated one.

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In our dedicated clinic for brain stimulation, we then apply this knowledge to test how non-invasive cortical stimulation can normalize the dysfunctional brain circuits. We develop novel brain stimulation therapies that primarily target the dysfunctional cortex. ADAPT-PD will greatly advance the mechanistic understanding of cortico-basal ganglia circuit dynamics in health and PD and create a powerful hub for causal brain circuit discovery, paving the way for personalized device-based neurostimulation, with therapeutic implications beyond PD.

IMPACT

Using a multimodal and multiscale approach, we will investigate how the cortico-basal ganglia circuit is altered in Parkinson's disease as well as levodopa-induced dyskinesia. Based on this knowledge we will develop treatments with tailored non-invasive and invasive brain stimulation.

FACTS

Funding: 35 mill. DKK Lundbeck Foundation

Collaborative Projects grant

Period: 2021 - 2026

Led by: Professor Hartwig Siebner

Partners: Professor Andrea Kühn, Charité
Universitätsmedizin in Berlin, Germany

Professor Angela Cenci Nilsson,

Lund University, Sweden



HARTWIG SIEBNER



DRCMR, AHH & Neurology, BHH

Transcranial brain stimulation and brain imaging

- · Human Imaging & Stimulation
- Ex-Vivo Animal Recordings
- · Chemogenetic Animal Stimulation





ANGELA CENCI NILSSON



Lund University

Basal ganglia circuits ain rodent PD models

- In-Vivo and Ex-Vivo Animal Recordings
- · Optogenetic Animal Stimulation





ANDREA A. KUHN

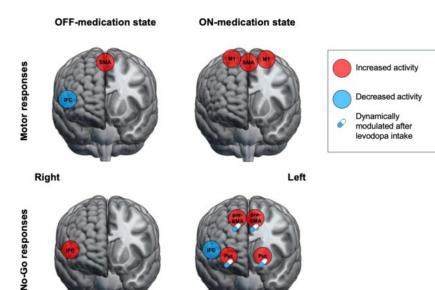


Charite, Berlin

Interventional neurophysiology and deep brain stimulation (DBS)

- Human Deep-Brain Stimulation
- · Human Direct Cortical Recordings
- Ex-Vivo Animal Recordings





Example figure from the systematic review on brain mapping studies on levodopa-induced dyskinesia. This figure summarizes the changes in brain activity during motor- and response-control tasks in PD patients with LID relative to PD patients without LID.

7T-MS

CORTICAL LESIONS AND GREY MATTER DYSFUNCTION IN MULTIPLE SCLEROSIS

BACKGROUND

In multiple sclerosis (MS), cortical pathology contributes significantly to disability and has therefore attracted considerable interest in the last decade. However, we are yet to understand the impact of cortical damage on both the connectivity and functional integrity of the affected area and other parts of the central nervous system. Clinical magnetic resonance imaging (MRI) at 1.5 or 3 Tesla is indispensable to the diagnosis and monitoring of MS-related brain damage. However, common MRI features, such as atrophy and lesions, are insufficient predictors of disability in MS as they only partially reflect functional properties of affected brain networks.

The greater sensitivity of 7 Tesla MRI is needed to assess cortical damage more comprehensively. 7T MRI doubles the number of detectable cortical lesions (Madsen et al. 2021), and

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Amager og Hvidovre Hospital

IMPACT

This project will reveal key insights into how cortical demyelination and damage, both regionally and globally, contribute to cognition and motor impairment in MS, two major disabling problems for patients. We will advance the possibilities of MRI to capture cortical involvement in Danish MS patients with the goal to improve individual stratification, monitoring of disease progression and capturing of the individual response to therapy.

FACTS

Project period: 01.01.2017 - 01.01.2026

Pls: Hartwig Siebner & Vanessa Wiggermann

Collaboration: Danish Multiple Sclerosis Center,

Rigshospitalet Glostrup

Funding: Scleroseforeningen, Independent Research

Fund Denmark, Hvidovre Hospital, Gangsted fonden, The Lundbeck Foundation.

Day 1: Behaviour and

Day 2: Multimodal MRI

Day 3: Electrophysiological examination



Clinical assessments

- Neurologic disability
- Depression
 Fatigue



Functional 7T MRI

Sensorimotor mapping of digit representation



TMS

- Corticospinal conduction
 inhibition/excitation
- Intracortical conduction



7T MRI

- High-resolution structural imagin
- structural imaging
 Quantitative MRI



Myelin MRI

- Diffusion tractography Myelin water imaging
- Myelin water imaging Magnetization transfer imaging



EEG

- Som atosensory potentials
 Sensory conduction time
- Sensory conduction tim
 High-frequency oscillations



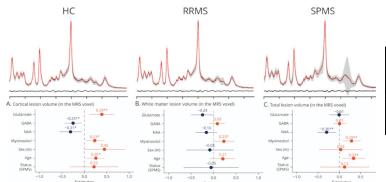
Cognitive and

- behavioural testing
 Sensorimotor testing of
- the hands
 Memory and cognitive processing speed



MR spectroscopy Glutamate

- Glutan
 GABA
- GABA
- Myo-inosito



Average spectra (black) and LCModel fit results (red) obtained with 1H-MRS at 7T. The gray areas represent ± SD for participant

groups. The corresponding example MRS voxel placement for the primary sensorimotor hand area is shown on the right side. (Bottom) Standardized beta-coefficients from the mixed linear models with (A) cortical lesion volume, (B) white matter lesion volume, and (C) total lesion volume within the IH-MRS voxel as the dependent variable. This data shows a clear relationship of only cortical lesion volume with Glutamate

and GABA concentrations in the SM1-HAND voxel, which were not present for white matter lesion or total lesion volume in the

allows for high-resolution myelin mapping of the cortex. This project exploits the increased resolution of 7T MRI to map cortical lesions and diffuse changes in cortical myelination using quantitative MRI in patients with MS. We also use transcranial magnetic stimulation (TMS) as a complementary tool, which allows investigations into functional cortical integrity and conduction properties of the corticospinal system.

By using state-of-the art anatomical and quantitative MRI at 7T, supplemented by TMS, we aim to identify radiologically visible and invisible features of cortical grey matter damage that contribute to physical and cognitive impairment in MS. The ongoing project aims are:

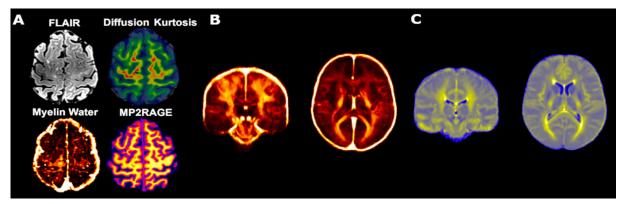
- To utilize submillimeter anatomical MRI to map the distribution of the different types of cortical lesions in relapsing remitting, secondary progressive and primary progressive MS patients.
- To characterize and compare cortical lesions, perilesional grey and white matter as well as normal appearing grey matter using quantitative myelin-sensitive MRI sequences.
- To explore the relationship between MRI measures of focal and diffuse myelin injury with neurophysiological integrity of the corticospinal system and clinical disability in order to establish novel stratification tools and predictive biomarkers.

In close collaboration with the Danish Multiple Sclerosis Center at Rigshospitalet Glostrup, we are in the unique position to investigate these questions in MS patients at all stages of the disease.

STATUS

Starting from 2017, we developed and optimized high-resolution MR sequences for our 7T MRI system and set up a neurophysiological experimental protocol for measurements of sensorimotor conduction time and cortical integration, using TMS and electroencephalography (EEG). To date, we have collected data from 38 relapsing remitting patients, 12 patients with secondary progressive MS, 29 patients with primary progressive MS and 38 matched, non-neurological controls.

Our results so far show that having a cortical lesion in the primary sensorimotor hand area is associated with a significant reduction in both manual dexterity and sensory acuity of the fingers. Additionally, our results demonstrate that TMS is sensitive to the disruption of cortical function due to cortical lesions, and that this disruption might be related to increased disability (Madsen et al. 2022). Digging even deeper into the pathology of cortical lesions, we showed that cortical lesions are associated with local changes in the concentration of excitatory and inhibitory neurotransmitters, using 7T MR-spectroscopy (Madsen et al. 2024).



Exemplary advanced MRI metrics capture cortical myelin changes in a leukocortical lesion in a primary-progressive MS patient. Here shown: FLAIR for general MS pathology – Diffusion Kurtosis shows changes in tissue microstructure – Myelin Water detects specifically reductions in myelin – MP2RAGE for very high-resolution mapping of the cortex and cortical changes in T1 relaxation. (B) High-quality average templates of myelin water fraction and intra-extracellular T2 (C) can be created.

VIA19 - BRAINMAP

THE DANISH HIGH RISK AND RESILIENCE STUDY

BACKGROUND

Children of parents with schizophrenia and bipolar disorder are at high risk for developing mental illnesses. Studies of groups at high risk for schizophrenia and bipolar disorder provide opportunities to gain insight into the processes that contribute to or protect against the emergence of symptoms. The Danish High Risk and Resilience Study - VIA 19 includes 19-year-old adults whose parents have been treated for bipolar disorder, schizophrenia disorders or none of these disorders. VIA 19 is the fourth follow-up study of a Danish cohort of 522 children who have already been studied at the age of seven (VIA7), eleven (VIA11), and fifteen (VIA15). When children took part in VIA 11 and VIA15, they underwent magnetic resonance imaging of the brain at the DRCMR or the Centre for Integrative Neuroscience (CFIN), Aarhus University. We are now re-scanning the children at the age of 19. Approximately half of the participants are additionally be examined with EEG at the DRCMR or with MEG at CFIN.

PROJECT GOALS

The design and scope of brain mapping in the VIA 19 study is unique on a global scale. Since brain imaging is performed repeatedly, before puberty (i.e., at the age of 11), during puberty (i.e., at the age of 15), and after puberty (i.e., at the age of 19) we have the opportunity to identify patterns of abnormal struc-

tural and functional brain development. We will particularly focus on developmental changes of brain networks involved in social cognition, reward processing, and executive functions. Furthermore, the brain imaging-based measures of brain network function and structure will be linked to the environmental, genetic, clinical, and neurocognitive data. This will enable us to elucidate underlying pathophysiological mechanisms and develop models predictive of risk, disease initiation and development, and resilience. We have now required funding to add 7T spectroscopy imaging in VIA19, which will allow us to relate neurochemical features to the functional read-out, allowing a mechanistic understanding of impairments.

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IMPACT

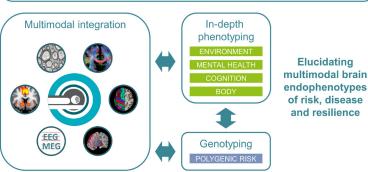
The combination of a multidimensional assessment of cognition, environment, and genetics with multimodal imaging in the VIA 19 Brainmap study allows to identify brain risk and resilience markers which may help to develop targeted treatments that prevent the transition to these disorders.

FACTS

VIA 19 started in 2024 and is led by Prof. Merete Nordentoft from the Research Unit, Mental Health Center Copenhagen, University of Copenhagen. VIA 19 received funding from the Lundbeck Foundation, the Mental Health Services of the Capital Region of Denmark and the Novo Nordisk Foundation.

THE DANISH HIGH RISK AND RESILIENCE STUDY: VIA19 - BRAINMAP





SOCO

THE DEVELOPMENT OF NEW BIOMARKERS & TREATMENTS FOR PSYCHOSIS

BACKGROUND

The diagnostic process in psychiatry is time intensive and shows low inter-rater reliability for many diagnoses. The diagnosis is currently not supported by objective biomarkers but consists of clinical assessment that can be subjective. In addition to this, treatment of various diagnoses is not effective given the "one fits all" approach. For example, in Major depressive disorder up to 30% are non-responders to pharmacological treatment. Therefore, there is a need for new biomarkers, not only to guide the diagnosis but further to help in the prediction of treatment response.

The SoCo project is led by Prof. James Blair from the Child and Adolescent Mental Health Centre and is funded by a grant from the Lundbeck Foundation to James. The SoCo study tackles this challenge as part of a larger study with the overall focus on the development of new biomarkers for psychosis as well as treatment response for psychosis. Particularly, SoCo is taking its departure within the social cognition domain, which is known to be disrupted in patients with adolescent schizophrenia. This project therefore has the aim to develop new fMRI social cognition classifiers and determine the extent that disruption of

nonnormative social cognition neural response is found in adolescent schizophrenia.

PROJECT GOALS

180 typically developing adolescents in the age range 14-18 years will be included to generate the normative dataset. Later, 100 adolescents with early onset psychosis will be included to test to what extent they social cognition responses deviates from the norm. Besides the social cognition paradigm, the study further includes structural scans. We therefore have high synergy between SoCo and the VIA study. The VIA research group involves multiple clinical and research centres across Denmark.

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IMPACT

The new class of fMRI biomarkers examined and developed in the SoCo study offer a far more individualized approach to treating adolescent psychiatric patients. They could serve as objective indices aiding reliable diagnosis, allowing the prediction and assessment of treatment

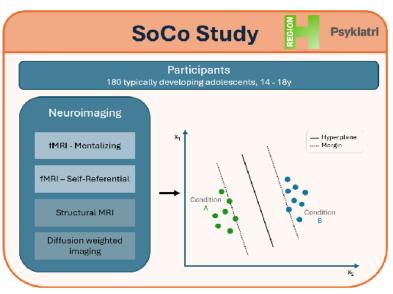
FACTS

Project period: 2024 - 2027

Pls: Prof. James Blair, Child and Adolescent

Mental Health Centre, Capital Region DK

Funding: Lundbeck Foundation



Normative dataset based on 180 typically developing adolescents. Social cognition assessed in task-based fMRI using a mentalizing and a self-referential paradigm. A support vector machine classifier is applied to generate a hyperplane differentiating the BOLD response of two conditions within the social cognition tasks.

REFRESH

ACHIEVING GENDER PARITY

BACKGROUND

Achieving gender parity continues to be a challenge in Science, Technology, Engineering, and Mathematics (STEM) fields, particularly in senior and leadership positions. This also applies to the Danish Research Centre for Magnetic Resonance (DRCMR), where females are underrepresented in senior research positions despite comparable numbers of male and female PhD students and Postdocs.



Prof. Sarah Louise Muhr from Copenhagen Business School at REFRESH 2023

The REFRESH (REtaining Female RESearcH talent at DRCMR: Supporting successful transition to senior research roles) initiative aims to tackle the gender imbalance at senior research levels at the DRCMR. The REFRESH initiative wishes to identify challenges and develop strategic initiatives for change to retain female research talent in neuroscience and promote and support female researchers' transition into senior academic roles.

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The REFRESH group is working on the following topics:

- increase awareness of gender bias at the DRCMR through strategic workshops
- increase the visibility of female role models in neuroscience via a seminar series and related networking
- mentorship program for female researchers with academic career aspirations
- survey-based data collection to assess the current perception of gender bias in the department and track changes over time as a measure of the impact of the REFRESH initiative

STATUS

REFRESH started in September 2022. We have currently had one workshop on bias awareness and a second workshop for early career researchers on career development, that took place April 2024. All female postdocs, research fellows, and senior researchers, have been offered to participate in the mentoring program that we have initiated. We have developed a survey to identify obstacles and barriers in career development where the first round of answers have been collected. Finally, we have started our REFRESH seminar series, increasing the exposure to female role models.



The audience of the 2023 REFRESH Retreat

BLOOM

THE DEVELOPMENT OF NEW BIOMARKERS & TREATMENTS FOR PSYCHOSIS

BACKGROUND

Eating Disorders (ED) such as Anorexia Nervosa (AN), Bulimia Nervosa (BN) and Binge Eating Disorder (BED) are severe psychiatric disorders with the highest mortality rate of all psychiatric disorders. Patients with ED show abnormal reward processing, motor inhibition control, social information processing, and general cognitive control functions. Moreover, evidence of neurobiological differences (both in brain structure and function) in ED is strong. Although these findings are extremely useful in paving the way for an understanding of the neurobiology of EDs, they cannot help us disentangle whether characteristics identified are correlates or biomarkers/endophenotypes (i.e., neurobehavioral traits that index genetic susceptibility for a psychiatric disorder of ED). Studies of populations with an increased risk of disease are highly relevant for investigating the development of the disease and resilience. Children at familial high risk (FHR) of ED, i.e. children born to parents suffering from ED, are ten times at higher risk of developing ED compare to controls. However, many of them do not develop an ED. Therefore, this makes healthy offspring of individuals with EDs to be a suitable population to study longitudinally to investigate important risk and protective factors for ED.

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IMPACT

The project holds significant implications for public health in terms of preventing ED. By examining high-risk offspring, it will facilitate a deeper comprehension and clarification of the risk/protective factors associated with ED, ultimately leading to more precise early interventions, prevention strategies, and the identification of individuals at risk over the medium to long term.

FACTS

BLOOM started fall 2024 and is led by Professor Nadia Micali from the Center for Eating and Feeding Disorders Research at the Mental Health Services in the Capital Region of Denmark.

PROJECT GOALS

The BLOOM study includes a clinical part and a brain mapping part. The aim of the brain mapping part of BLOOM is to investigate if FHR offspring show brain structural and functional abnormalities before any ED onset, and to establish whether structural and functional Magnetic Resonance Imaging (MRI)

data can provide patterns of vulnerability and identify specific neurobiological precursors that may predict ED in the future. The overall BLOOM study consists of a cohort of 510 8-9-year-old children from different familial risk profiles of eating disorder in a follow-up design based on register data from the Danish National registers. A

thorough examination of 360 children aged 8-9-years with a mother with a lifetime diagnosis of ED, as well as an examination of 150 peer children with a mother with no active/lifetime psychiatric diagnosis is performed. The brain mapping part of BLOOM will be conducted in a subset of participants N = 100).



XTREME-CT

UTILISING HIGH ENERGY X-RAY IMAGING TO IMPROVE DISEASE UNDERSTANDING & DIAGNOSTICS

BACKGROUND

The Xtreme-CT project is a five-year synergy project supported with 15 mill DKK by the Novo Nordisk Foundation (NNF) that began with a kick-off meeting in January 2023. The project synergistically cross-links diverse research fields, including big data analysis and machine learning, synchrotron X-ray physics and optics, and MRI physics, with applications to nanoscopic 3D imaging of brain and bone structural anatomy. The project includes five Principal Investigators (PIs): Professor Anders Dahl from DTU Compute, Henning Friis Poulsen from DTU Physics, Henrik Birkedal from iNANO, Aarhus University, and Professor Tim B. Dyrby from the DRCMR, Copenhagen University Hospital Amager and Hvidovre. The project coordinator is Professor Henning Friis Poulsen. In addition to the Pls, the research team includes Senior Researcher Rajmund Mokso (DTU Physics), Postdoc Ulrik Olsen (DTU Physics), Postdoc Nis Gellert (DTU Physics), Adrian Palomo (iNANO), Beamline Scientist Innokenty Kantor (MAX IV), Postdoc Thorbjørn Christensen (MAX IV/DTU), Postdoc Emma Thomson (DRCMR), and Professor Martin Bech (Lund University).

Biological tissues, such as bones and brains, are composed of hierarchical structures ranging from cellular organization to entire organs. Both normal function and disease progression depend on complex interactions across these different levels. Creating detailed 3D images that span these scales—from cellular to macroscopic—is a central goal of the Xtreme-CT project.

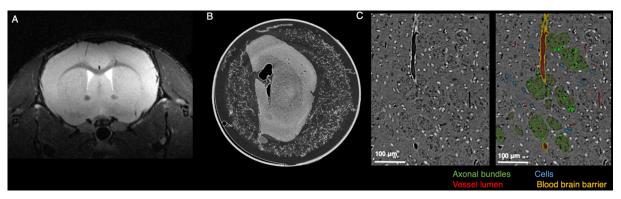
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Benefitting people and society

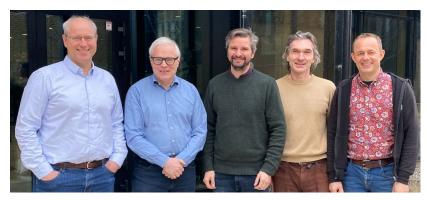
By combining high-energy X-ray tomography across different length scales, high-field MRI, animal models of health and disease, and machine learning, this synergy project aims to unravel the intricate microstructural organization of the bone structures and the cerebral cortex. Understanding tissue microstructure is essential for studying how different brain regions function and connect via neural pathways. Gaining deeper insights helps map these pathways, identify subtle structural differences, and understand how diseases disrupt normal processes. High-resolution 3D imaging techniques, such as synchrotron-based X-ray imaging, allow visualization of brain microstructure at the sub-micrometer level. When this detailed data is combined with low-resolution, in vivo MRI scans at the millimeter scale, it bridges the gap between cellular-level insights and whole-brain imaging, enhancing the interpretation of MRI signals.

Clinical techniques like diffusion MRI often struggle to differentiate specific structural changes without detailed knowledge



MRI image of a mouse brain in-vivo, B) A large-field synchrotron image of a mouse hemisphere, C) A small section of B both without and with manual annotations...

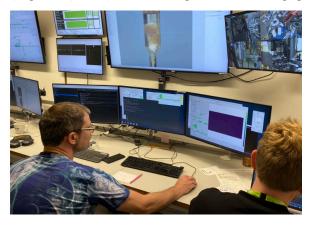
of the microstructural environment. We aim to address this limitation by pairing different imaging modalities, such as the sub-micrometer resolution of synchrotron X-ray imaging with the millimeter resolution of MRI and animal models using cell-type-specific labeled neurons. We hope that this deeper understanding will enhance diffusion MRI's diagnostic potential and aid in identifying new biomarkers for early disease detection.



The five Principal Investigators of the XTREME-CT Project. From left to right: Henrik Birkedal, Henning Friis Poulsen, Anders Dahl, Rajmund Mokso, and Tim Dyrby

STATUS

Utilizing the DanMAX beamline at MAXIV in Lund, we are developing X-ray optics to perform both large-field-of-view imaging



Beamline experiment preparing tomography imaging of mouse brain.

and high-resolution zoom-in imaging, with the trade-off of a reduced field-of-view. This imaging setup generates massive datasets that must be managed and analyzed efficiently. By employing advanced machine learning techniques, such as super-resolution algorithms, we can integrate these two length scales to extract sub-cellular-level information across large sample sizes without the challenges of data size.

This research hopes to provide:

- Improved knowledge of the 3D microstructure of various tissues
- A deeper understanding of disease mechanisms
- The discovery of new imaging biomarkers for disease
- Enhancements to clinical imaging techniques, such as MRI, making them more precise and effective

The Xtreme-CT project aims to utilise high energy X-ray imaging to improve disease understanding and diagnostics. These efforts will combine cutting-edge imaging with the development

of advanced algorithms to process and analyse the massive datasets produced—often hundreds of gigabytes per image.

We are dedicating significant time at the DanMAX beamline at MAXIV to setting up and testing new optics and sample preparation procedures. The top figure shows some of the team members during a beamline experiment, which typically lasts a few days and involves 24/7 teamwork and involves a lot of fun. The bottom figure shows one example of sample preparation is a mouse brain, prepared by Emma Thomson, positioned on the rotation stage and ready for X-ray illumination. Innokenty Kantor is shown in the control room preparing for tomography imaging of the brain sample bottom figure.



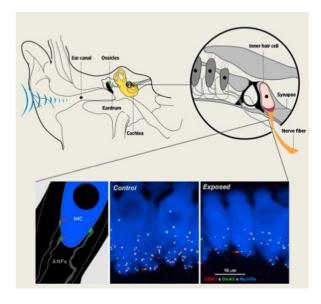
Beamline experiment preparing tomography imaging of mouse brain.

UHEAL

UNCOVERING HIDDEN HEARING LOSS

BACKGROUND

Age-related hearing loss is among the most prevalent chronic health conditions in the world. In the EU alone, untreated hearing loss is estimated to cost more than 185 billion Euros each year. Untreated hearing loss in mid-life is the highest known risk factor for developing dementia later in life. The conventional view has been that the primary cause of age-related hearing loss is loss of the outer hair cells that amplify vibrations in the inner ear. Loss of these cells make soft sounds inaudible and require external amplification by a hearing aid. In 2009, seminal work from the auditory physiologist Charles Liberman and co-workers at the Massachusetts Eye and Ear Infirmary (MEEI) at Harvard Medical School challenged this conventional view. Mice exposed to noise for 2 hours showed no damage to hair cells, but instead an acute loss of synapses between the sensory cells and the auditory nerve. Despite extensive neural damage, the noise exposure did not make soft sounds inaudible. In consequence, the neural damage to the ear remained 'hidden' in standard clinical tests of hearing. The existence of such hidden hearing loss may help explain why many people experience difficulties following speech in noisy situations already in mid-life, although they may have normal hearing



Loud sounds damage synapses and nerve fibres in the inner ear. Clinical hearing tests today do not capture this synaptopathy. Hence the term 'hidden hearing loss' (histology data from MEEI)

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in standard clinical tests. Adding insult to injury, these neural damages set off a cascade of neurodegenerative processes that eventually lead to clinical hearing loss later in life. Diagnosis of this type of hidden hearing loss is critical to enable early interventions but is currently missing.

In the UHEAL synergy project supported by the Novo Nordisk Foundation, auditory researchers from DTU Hearing Systems (Torsten Dau, Jens Hjortkjær), and MEEI (Charles Liberman) have teamed up with the DRCMR (Hartwig Siebner, Tim Dyrby) to tackle this challenge. The project combines animal and human physiology with structural and functional MRI, computational modelling and psychophysics to investigate auditory neural degeneration and its consequences for hearing. In WP1 of the project, ears exposed to noise at MEEI are sent to DRCMR for preclinical imaging with the goal to detect microstructural changes. WP2 develops measures of neural degeneration by using functional and structural MRI at DRCMR and electrophysiology at DTU in a large cohort of human listeners. WP3 combines this evidence with behavioral listening tests and measures of central brain processing to understand what the consequences of hidden hearing loss are, for instance, in terms of listeners' ability to decode speech in noisy environments.

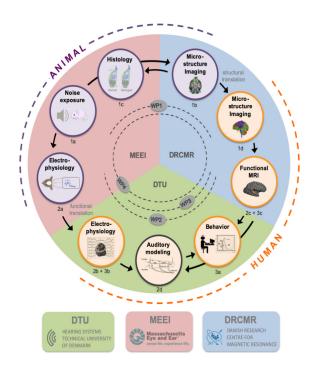
Collection of data in the UHEAL project was completed in 2024, but sub-studies and preliminary results already disclose promising results. With Charles Liberman at MEEI, the DRCMR group investigates the microstructure of the inner ear of healthy and noise-exposed animals. Diffusion imaging at ultra-high field (7T) is performed at DRCMR to image the soft tissue of the ear otherwise only seen through a microscope. The group has been able to push image resolution to visualize the 3D morphology of the inner ear. Maps of fractional anisotropy, for instance,

reveal the stria vascularis curling inside the spiral ligament of the cochlea, a structure that is responsible for maintaining a positive potential inside the healthy ear. This level of detail has not previously been seen with MRI of the ear. Other imaging techniques, including micro-CT and synchrotron imaging, are currently being pursued in the project to push resolution even further.

tion critical. Frequency-following responses as those pursued in the UHEAL project can readily be adapted in the hearing clinic. Along with MRI biomarkers of hearing health, such measures present a considerable advance in our current tools for characterizing hearing loss and identifying signs of auditory decline at an early stage.

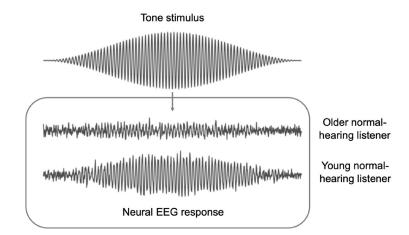
In another sub-study in the UHEAL project, PhD-student Jonatan Märcher-Rørsted combines electrophysiology and computational modelling to understand how loss of auditory nerve fibers affects the nerve's ability to transmit temporal information to the brain. By presenting tones while recording EEG signals inside the ear canal, Jonatan observes how well the brain potentials follow the frequency of the tone. In older listeners with clinically normal hearing, this ability to code fast fluctuations in sounds is reduced, despite the fact that the tones can still be heard. AT DTU, a computational model of the auditory nerve was combined with human histopathology from MEEI to show that this reduction in frequency-following neural responses is consistent with an age-related loss of auditory nerve fibers. Paradoxically, the studies also revealed that the coding of slow variations in sound signals are restored and even enhanced in the aging auditory system. This points to a compensatory brain mechanism that can help restore the detection of sounds after neural damages to the ear, but the fine temporal information needed for accurate sound perception is lost.

Therapies to reverse auditory nerve damages are currently under development, making diagnostic markers of auditory degenera-



DRCMR collaborates with DTU and MEEI in the multidisciplinary UHEAL synergy project. The project combines imaging of the auditory system with animal and human physiology, computational modelling and clinical audiology.





Left: diffusion MRI image of the inner ear showing its spiral structure and the auditory nerve within the cochlear modiolus. Right: frequency-following EEG responses to a tone in older and young normal-hearing listeners.

TECTO BRAIN IMAGING

TREATMENT EFFECTS OF FAMILY-BASED COGNITIVE THERAPY IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER

BACKGROUND

A growing number of studies have related obsessive-compulsive disorder (OCD) symptomatology to structural and functional brain changes in specific regions of parallel dorsal and ventral cortico-striato-thalamo-cortical (CSTC) circuits. Normal functioning of these regions is known to be imperative to successful response inhibition in healthy subjects. During treatment with cognitive behavioral therapy, including exposure and response prevention (CBT-ERP), patients with OCD are purposefully exposing themselves to anxiety-provoking stimuli (e.g. by touching something dirty) whilst refraining from acting on the desire to respond (e.g. by not excessively washing hands immediately after). Although CBT-ERP is effective for some patients, about half of all children and adolescents with OCD do not or only partially benefit from the treatment, and it is largely unknown how the brain of patients that benefit from treatment differs from the brain of patients that do not.

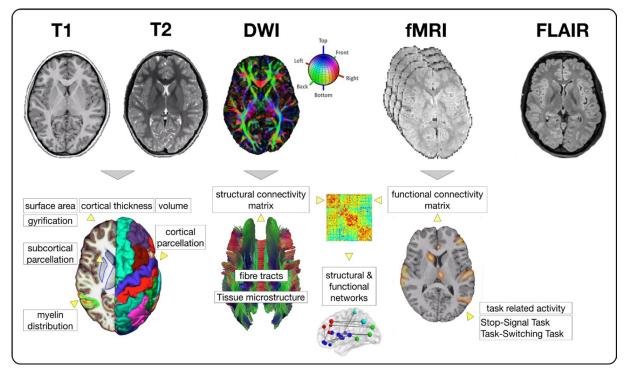
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GANGSTEDFONDEN

Exploring why some benefit from treatment and others do not is an important step to improving individualized treatment. The wide use of CBT-ERP for pediatric OCD stands in contrast to the lack of knowledge about the mechanisms underlying the treatment effect. Previous studies using imaging have demonstrated abnormal response-inhibition-related activation of CSTC-circuits in patients with OCD, and changes in the activation of these regions is potentially critical to treatment outcome. However, most studies of the underlying mechanisms



Multimodal brain imaging. High resolution structural T1-weighted and T2-weighted scans, diffusion-weighted imaging scans and blood-oxygenation level dependent weighted functional MR scans (fMRI) are obtained on a Philips 3 Tesla scanner. Structural and diffusion-weighted imaging scans will be used to quantify regional cortical thickness, surface area and gyrification, microstructural properties and volume of cortex, subcortical nuclei, and white-matter tracts, T1/T2 ratio-based myelin distribution as well as structural network connectivity. Response-inhibition-related brain activity will be measured with fMRI using a Stop-Sig-nal Task (SST) and a Task-Switching (TS) paradigm. SST and TS tap different aspects of response inhibition processes. In the SST, a selected and initiated motor response must occasionally be inhibited (action cancellation), whereas in TS, the correct response to a target must be selected from a bimodal task-response set with interference from an irrelevant and incongruent response (interference control).

of CBT-ERP for OCD have focused on behavioral changes, whereas studies documenting neurobiological changes are rare. One recent functional imaging study on pediatric OCD shows a potential CBT-ERP-related normalization of regions in CSTC-circuits after treatment, but this study did not use an RCT design. A direct comparison of CBT-ERP and an active control treatment is necessary to distinguish between brain changes that occur due to the putative effective component of the treatment (i.e., exposure and response prevention) and changes that occur due to general features of psychotherapy (e.g., psychoeducation, the therapeutic alliance or family problems being dealt with). Furthermore, a direct comparison of patients with OCD and healthy control subjects is required to distinguish between effects of time (e.g., normative maturation of the brain) and effects of treatment..

TECTO-BRAIN

TECTO-brain is a collaborative sub-project to TECTO that is carried out in close collaboration between the Child and Adolescent Mental Health Centre (BUC), Gentofte Hospital and the Danish Research Centre for Magnetic Resonance (DRCMR), Hvidovre Hospital. The overarching goal of TECTO-brain is to delineate structural and functional brain profiles of pediatric OCD and elucidate connections between neural and neurocognitive measures and treatment response.

The most important aims are as follows:

- To determine the structural and functional brain profile of pediatric OCD by comparing patients with healthy control subjects matched on age and gender.
- To investigate changes in the neural profile of the brain in patients after treatment with CBT-ERP or psychoeducation and relaxation therapy (PRT).
- To identify neural and neurocognitive factors that are predictive of treatment response.

The entire TECTO study includes 128 patients, age 8 through 17 years, with a primary diagnosis of OCD and 128 age- and sexmatched healthy control subjects. Patients are randomized at the allocation ratio 1:1 to receive either CBT-ERP or PRT. Both treatments comprise 14 sessions of 75 minutes each, delivered over 16 weeks by trained and supervised doctors or psychologists. All participants of TECTO are offered participation in TECTO-brain. The brain of both patients and healthy control subjects partaking in TECTO-brain are magnetic resonance (MR)-scanned at baseline and immediately after treatment (week 16). In TECTO-brain, we take a multimodal approach to brain imaging. TECTO-brain utilizes modern methods and technology to reduce the amount and significance of move-

ment during scanning. All our structural scans include online motion correction as children generally have more difficulties lying still during scanning. Our pilot data show a systematic underestimation of gray matter volume from structural images when motion is present and uncorrected, and online motion correction improved image quality substantially even in the presence of significant movement. Sequences have been tailored to scan children and have been validated in a pilot study on both patients and healthy control subjects. Because comorbid anxiety disorders are common among OCD patients, we use a narrated virtual reality environment that has been developed for this project, in which the participants can experience being virtually scanned in 3D. Finally, we use a mock-scanner to train the tasks and train lying still on the first day of scanning.

Results from TECTO-brain are expected, as a minimum, to improve our understanding of pediatric OCD and of CBT-ERP as an intervention for OCD. However, we aim to also make significant contributions to the development of individually tailored interventions for pediatric OCD. TECTO-brain can realistically do so by illuminating the neural mechanisms underlying the treatment effects.

The data acquisition in the study has been concluded. A total of 161 participants: 90 patients with 71 healthy controls for session one, and 62 patients with 58 helathy controls in session two have been included in TECTO-brain.

IMPACT

TECTO will improve understanding of the interplay of factors that predict, moderate, and mediate treatment response by combining neural, cognitive, emotional, and neuroendocrine measures. Results are crucial to improve psychotherapy and targeted interventions for pediatric OCD that can minimize medication use, prevent chronicity, and reduce the substantial socioeconomic burden of the disorder.

FACTS

TECTO is led by Prof. Anne Katrine Pagsberg from the Research Unit - Child and Adolescent Mental Health Centre (CAMHC), Mental Health Services, Capital Region, Denmark.

The study was initiated by Prof. Kerstin Plessen, who is now at the University of Lausanne, Switzerland.

The Copenhagen Trail Unit, led by Director Dr. Christian Gluud, oversees RCT procedures and statistical analyses.

TECTO received funding from the Mental Health Centre for Child and Adolescent Psychiatry, the Lundbeck Foundation, Capital Region Psychiatry, the Capital Region Research Fund, Gangstedfonden and Psykiatrisk Forskningsfond af 1967.

CANID

A BRAIN-BODY INTERACTION STUDY OF NEUROVASCULAR COUPLING AND SPLANCHNIC BLOOD FLOW

BACKGROUND

Diabetes is a growing global health care challenge affecting almost half a billion patients worldwide with a prevalence estimated to reach 629 million in 2045. These patients are at greatly elevated risk of developing severe short- and long-term complications, of which the neuropathies are amongst the most prevalent. Neuropathies are caused by hyperglycemia and comprise a heterogeneous group of conditions, which affect both the central and peripheral nervous system. Detection and prevention are key as the neuronal damage often is irreversible and treatments are lacking. Cardiovascular autonomic neuropathy (CAN) has a prevalence between 20 and 65%. CAN has major implications for the patients' health and can directly result in severe cardiovascular issues. CAN may also be associated with cerebral dysfunction and

FACTS

The CANiD study, led by prof. Hartwig Siebner, is a collaboration between Steno Diabetes Center, the dept. of Endocrinology at Hvidovre Hospital and DRCMR where the imaging is nested in the Brain-Body Interaction group, headed by Mads Barløse. Involved partners include Christian Bauer (DRCMR), Esben Thade Petersen (DRCMR), Sten Madsbad (Endocrinology, Hvidovre Hospital), and Christian Stevns Hansen and Birgitte Brock (Steno).

IMPACT

This study will add significant new insight into the association between diabetic autonomic neuropathy and impaired cerebral function and gastrointestinal reflexes. It will contribute to a better understanding of how diabetes affects the brain and cognitive function as well as why glycemic control becomes especially challenging in patients with autonomic neuropathy.

FUNDED BY

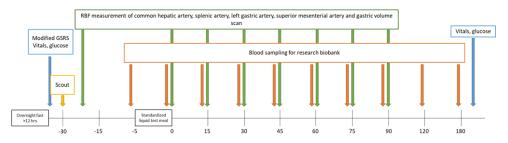


patients with diabetes are at an elevated risk of cognitive impairment. These deficits are theorized to be a consequence of lower resting cerebral perfusion and impairment of neurovascular coupling and may be involved in neurovascular uncoupling. The result of which is persistent imbalance between local neuronal metabolic demand and blood flow. In addition to affecting the cardiovascular system and cerebral homeostasis, autonomic neuropathies also induce gastrointestinal changes including gastroparesis, constipation and diarrhea. It is well known that in diabetics with autonomic dysfunction, achieving optimal glycemic control becomes very challenging. This is potentially caused by impaired gastrointestinal reflexes, but little is known about the mechanisms driving these changes. We aim to:

- Characterize cerebrovascular reactivity as a measure of neurovascular coupling in diabetics with and without CAN and compare this to healthy controls.
- Characterize gastro-intestinal vascular responses to a standardized meal in patients and controls as a measure of the function of the enteric nervous system.

STATUS

We aimed to include thirty participants in each group who would undergo two visits (see flow-chart below). This has been accomplished and data analysis is ongoing. Visit number 3 was delayed due to the installation of new clinical scanners. Ten participants from each group have undergone this visit and we are currently performing an interim analysis.



Overview of the standard liquid meal test. Fasting participants ingest a meal in the scanner before and after which blood flow in the superior mesenteric artery is measured by means of phase contrast MR.

THE LISA STUDY

WHY DO SOME INDIVIDUALS AGE BETTER THAN OTHERS?

BACKGROUND

In the LISA study, a rich longitudinal dataset which has followed participants for up-to 7 years, we are uniquely equipped to address this question and – ultimately – contribute to our understanding of how we can prevent or delay age-related brain and cognitive impairments.

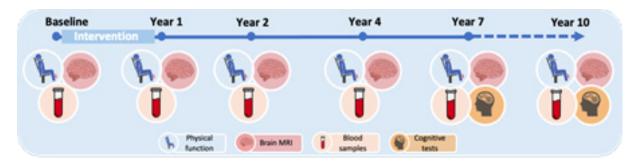
The LISA study examined the effects of two different 1-year resistance training programs (high intensity vs. moderate intensity), in comparison to a non-exercising control condition, on the muscle strength of 451 older adults. One of the things that makes this study particularly special is that data on brain health, physical function, lifestyle and cognition continued to be collected long after the end of the intervention (Fig. 1). This cross-disciplinary study was made possible by a collaboration between us at DRCMR, the Institute of Sports Medicine at Bispebjerg Hospital, and the department of Public Health at the University of Copenhagen. At DRCMR, we collect a MRI battery that includes structural scans, diffusion weighted imaging, perfusion and resting state connectivity.

STATUS

Initial findings showed that 1-year of muscle strengthening successfully improved leg strength, and that significant benefits extended to various markers of strength and physical function, such as muscle mass and leg power. More recently, we have shown that even 3-years after the end of the intervention, participants from the high-resistance training group still showed greater muscle strength than the control group. These findings indicate that resistance training with heavy loads at retirement age can give long-term effects over several years. We believe

these results have important implications for practitioners and policy makers, as well as encourage older individuals to engage in heavy resistance training.

Changes in the brain have been less clear cut. At the end of the intervention, the hippocampus – a brain region important for memory and often affected in ageing – did not differ in volume between the intervention groups. By examining trajectories of physical function over 4 years, we found that participants showing improvements in physical function showed baseline differences in a brain region called the cerebellum. As the study has now completed data collection for year 7, and begun its 10-year wave of assessments, we are ideally placed to map individual brain trajectories even further and identify predictors and risk factors for healthy brain ageing.



Schematic overview of the LISA dataset. Repeated assessments of physical function, brain MRI and blood samples have been conducted from baseline to Year 7.

UPCOMING KEY PROJECTS

COPENHAGEN CEREBROSPINAL FLUID LEAK EVALUATION OF MAGNETIC RESONANCE IMAGING

BACKGROUND

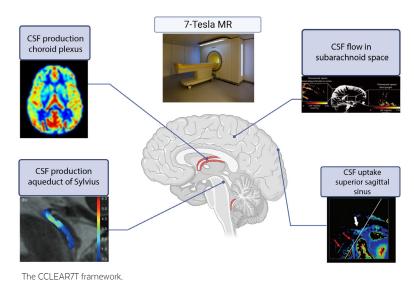
Spontaneous intracranial hypotension (SIH) is a severe neuro-logical disease where cerebrospinal fluid (CSF) leakage in the spine causes orthostatic headache, cognitive dysfunction, tinnitus, mental dullness, diplopia and, in worst cases, coma. Yet, if correctly diagnosed, it is a fully treatable disease. If the clinical suspicion of SIH is lacking, a multitude of scans, misdiagnoses and fatal diagnostic delays are the result. The estimated

annual incidence rate is at least 5 per 100,000 in the general population, close to other serious neurological disorders such as subarachnoid hemorrhage. Several epidemiological and pathophysiological aspects of SIH are currently unexplored. The CCLEAR7T-project uses ultra-high field MRI in combination with newly developed MRI sequences to measure CSF production and circulation as well as structural alterations in fine CSF pathways around the brain. We aim to gain new and unique knowledge on how the brain and

CSF regulation are altered when SIH causes a decrease in intracranial pressure and how and whether these alterations are reversed upon following successful treatment. Due to its mechanical nature and simple reversibility, SIH is a unique con-

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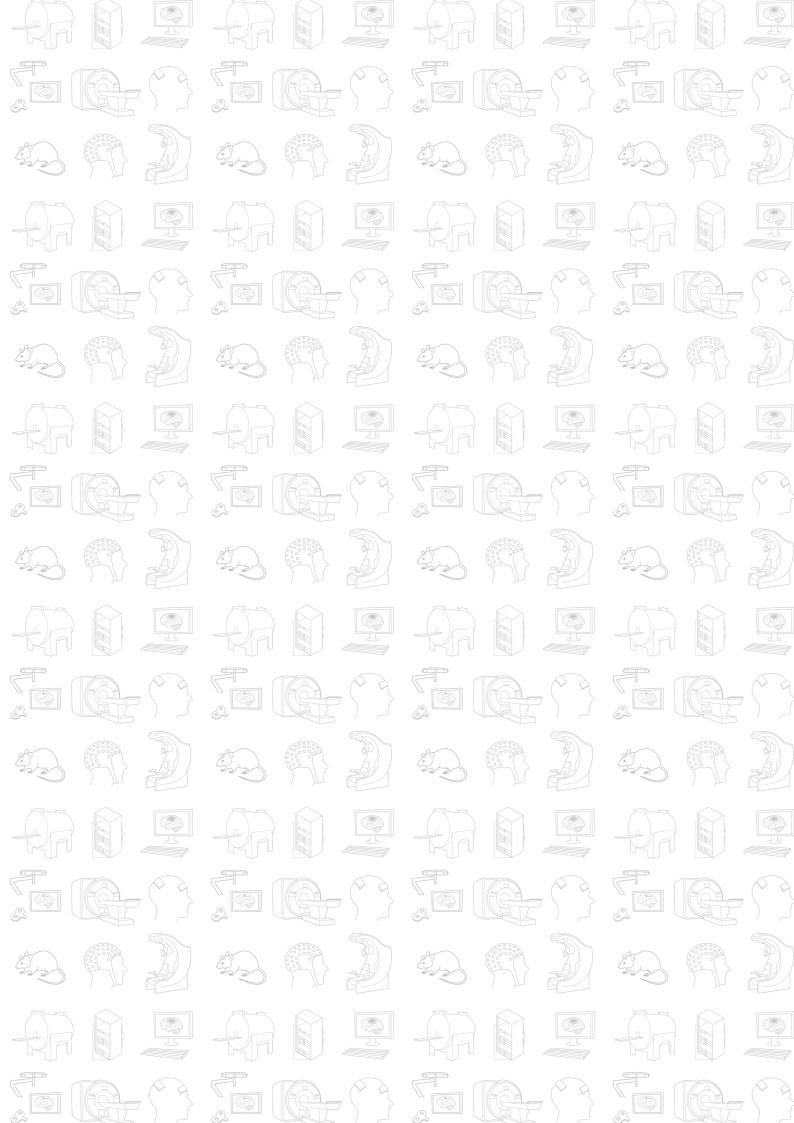




s a decrease in dition to study CSF dynamics and their influence on brain waste clearance pathways safely in humans. The results will

also serve as input for developing a state-of-the-art diagnos-

tic evaluation of SIH.



RESEARCH AT DRCMR

OUR VISION

Mapping brain dynamics to promote health and to tailor therapy. We use advanced magnetic resonance imaging to create knowledge about the brain –knowledge that can be used to optimize treatments in individual patients and to boost public and individual health, potential, and well-being.

OUR MISSION

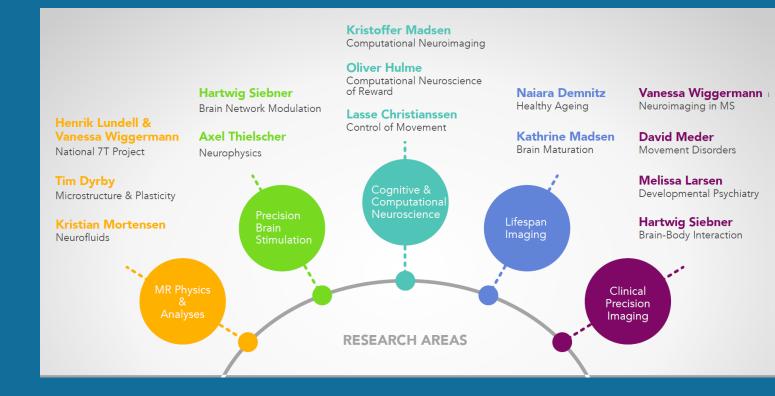
We use brain mapping to unravel causal dynamics in the human brain.

We study beneficial brain dynamics that secure physical and mental health as well as detrimental brain dynamics that cause brain disorders across the lifespan.

IMPACT

This knowledge will help us tailor therapeutic interventions in the brain dynamics expressed in individual patients (precision medicine).

And in general contribute to future efforts to boost public and individual health, potential, and well-being.



MR PHYSICS AND ANALYSES



While the research at DRCMR is multidisiplinary and involves a number of different techniques, MR-based methods are at the core of most projects. The continuous development of new methods enables new research questions to be raised. We take active part in the forefront of methods research and follow the achievements of the MR community closely to reach new goals in neuroscientific and clinical research.

MR methods range from high resolution anatomical imaging to studying brain anatomy in better detail, quantitative imaging and spectroscopic techniques reflecting different microstructural molecular features of tissue to dynamic imaging methods tracing neuronal activation and physiology. Increasing interest is also put into body imaging, e.g. the heart and the liver.

In our work, ultra-high field MRI is crucial for innovation in experimental and clinical research as well as the integration of multimodal approaches during the scanning session. Translation of experimental methods in preclinical and ultra-high field settings to clinically feasible routines is also in the heart of

our work. This requires efforts in the construction of new hardware, scanner sequences and not at least computational methods to analyse new types of data. We have a particular interest in spectroscopy, diffusion, perfusion and functional MRI but are also extending to combined approaches, e.g. using MRI and transcranial magnetic stimulation.

To unleash the powers of new methods, we coordinate our work with other research areas at the department as well as external collaborators in Denmark and internationally. This ensures the synergy needed to span from basic research to clinical work. The MR Physics and Analysis research area is coordinated by Senior Researcher Henrik Lundell.

Microstructure & Plasticity





Ultra-High Field MR

Acquisition Technology

Neurofluids









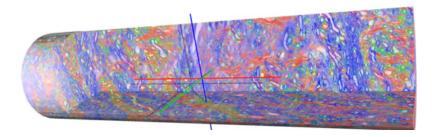


MICROSTRUCTURE AND PLASTICITY

We aim to develop a fundamental understanding of brain structure, its plasticity, and how it encodes function. Our vision is to create a brain map, spanning scales from submicrometers to millimeters, by integrating diverse 3D imaging modalities. These advancements are applied preclinically in animal models and translated to clinical MRI. The MaP group operates across two sites: DRCMR and DTU Compute. From 2022 to 2024, we expanded our technological capabilities within core 3D imaging modalities, including Light-Sheet Imaging, diffusion MRI, quantitative MRI, and X-ray synchrotron imaging. A LF Experiment grant enabled advancements in Light-Sheet Imaging, focusing on modeling and processing large datasets, further supported by a DFF-1 grant.

In 2022, Tim Dyrby was awarded a prestigious ERC Consolidator Grant for his CoM-BraiN project, which investigates axon diameter mapping with MRI, its relationship to neuronal signal speeds, and the impact of brain diseases. Marco Pizzolato received a DFF-1 grant to develop new diffusion MRI-based models, enhancing our understanding of the axonal environment in disease contexts. Meanwhile, Sidsel Winther completed her PhD, demonstrating that incorporating the real 3D shape of axons and accounting for susceptibility effects from myelin enhances dMRI's ability to detect irregular axonal shapes, as confirmed with synchrotron imaging.

A Novo Nordisk Foundation synergy grant, in collaboration with DTU Compute, DTU Physics, and Aarhus University, supports the development of X-ray optics at the DanMAX beamline at MAX IV in Lund, advancing multi-resolution tomography toward the nanometer scale. Beyond imaging technologies, we are incorporating artificial intelligence (AI) to streamline data processing, enhance dMRI model robustness, and improve semantic segmentation, such as in synchrotron imaging.



Synchrotron X-ray Nano Holotography (XNH) image volume of crossing fibers in the brain in 75 nm resolution. RGB colors overlay show 3D orientation of structure tensors. Note the fiber (colored) layer organisation. Kjer et al. 2024 (eLife).

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- · Postdoc Mahsa Amirrashedibonab
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- · Postdoc Piyush Swami
- · Postdoc Samo Lasic
- · Postdoc Hanna Vila
- · Postdoc João Lima
- · Postdoc David Romascano
- · PhD student Sidsel Winther
- · PhD student August Høeg
- · PhD student Thina Thøgensen
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- Associate Professor Emmanuel Caruyer
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- · Professor Henrik Birkedal
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- · Professor Henrik Birkedal

HOMEPAGE

www.drcmr.dk/map

KEY PUBLICATION

Axon morphology is modulated by the local environment and impacts the non-invasive investigation of its structure-function relationship, Andersson M, Kjer HM, ..., Dahl VA Dyrby TB, Proceedings of the National Academy of Sciences, 2020, 117:33649-33659

ULTRA-HIGH FIELD MR

The vision of the ultra-high field MRI group is to enable cutting-edge spectroscopic and imaging research via state-of-the sequences and hardware, to contribute to earlier and accurate diagnostics in precision medicine research areas such as aging, metabolic and neurodegenerative diseases.

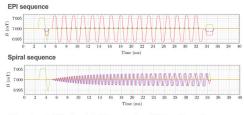
With a focus point on spectroscopy, the studies are currently exploring metabolic changes in healthy older adults in relation to single exercise sessions and cognition, in an add-on treatment study in first episode psychosis patients and in patients with anorexia nervosa. Neurotransmitter changes in the predorsal motor cortex are also a key outcome measure in an ongoing multiple sclerosis clinical trial on fatigue. Novel high-resolution functional spectroscopy has been developed and combined with 3T TMS-MRI.

The full potential of the 7 tesla MRI system is unleashed through innovation. Software solutions include novel sequences that deliver new clinical information as well as new ways to speed up the acquisition of existing modalities. Consistent image quality, also at extreme high resolution, is one of our targets. Current novel developments include high-resolution myelin water imaging, diffusion-weighted spectroscopy and deuterium MRI.

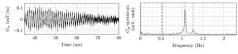
Hardware solutions have focused on improving FOV coverage to enable reliable imaging of the brainstem, cervical spinal cord, cerebellum or carotid arteries as well as eddy current corrections. Novel quantum-based field monitoring equipment will help in the future to correct k-space trajectories, improving image sharpness and reducing distortions. This will be a game changer for all sequences relying on quickly shifting gradient trajectories, including ultra-short echo time sequences, diffusion and fMRI. These achievements are only possible through strong collaborations between DRCMR, DTU Health Tech, the TU of Eindhoven, and the Niels Bohr instute.

Field measurements in 7 T MRI scanner Potential applications in image corrections

Only technology delivering continuous, interferencefree, fast, and accurate measurements



Clearly visible instabilities in the MRI coil system



In collaboration with the Niels Bohr Institute, Hans Stærkind has developed a unique, quantum based high-field optical magnetometer, which uses the Zeeman lines shifts of cesium vapor cell to measure MR field fluctuations continuously.

GROUP MEMBERS

- · Assoc. Prof. Esben Thade Petersen
- · Assoc. Prof. Henrik Lundell
- · Research Fellow Vanessa Wiggermann
- · Research Fellow Michal Povazan
- · MR Clinical Scientist Paul de Bruin
- Research Radiogr.apher Jasmin Merhout
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- · Research Fellow David Meder
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- · Postdoc Mads A.J. Madsen
- · Postdoc Hans Stærkind
- · Postdoc Fanny Kozak
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HOMEPAGE

www.drcmr.dk/7t

KEY PUBLICATION

Linking lesions in sensorimotor cortex to contralateral hand function in multiple sclerosis: a 7 T MRI study. MAJ Madsen, V Wiggermann, ... HR Siebner, Brain 145 (10), 3522-3535

ACQUISITION TECHNOLOGY

The acquistion technology group focuses on both phase-sensitive MRI and MRI safety . The robustness, sensitivity and specificity of MRI is improved using fundamental physics and advanced analysis.

MR Current Density Imaging (MRCDI) is developed with Axel Thielscher's Neurophysics group. Post doc Frooi Gregersen and co-workers developed fast and robust methods for mapping of currents in the human brain as part of a Lundbeck Experiment project headed by Lars G. Hanson. The study (see figure) showed that EPI-based MRCDI is superior to established techniques when limited spatial resolution is acceptable. Consistent results indicated that MRCDI can pick up inaccuracies in computational head models and thus can guide systematic improvements.

In MRCDI magnetic fields in the human brain arise from injected currents of <20 Hz. There are applications where higher frequencies are of interest, e.g., measurement of neuronal currents, transcranial alternating current stimulation, temporal interference stimulation, and tumor-treating fields. Froði and co-workers developed a method extending the frequency range much beyond that of earlier published methods (ISMRM 2024).

Lars G. Hanson promotes MRI safety and MR physics locally and worldwide, e.g. using YouTube (~200k views). On behalf of 4 national organizations with an interest in promoting safe MR practices, he headed a working group formulating a national guideline on the topic. Also, general MR safety courses and a new MR Safety Officer (MRSO) course were given in collaboration with colleagues from Region H hospitals. Participants attended from all over Denmark.

Most studies involve the MR section at DTU Health Tech, including hyperpolarized MRI and MR monitoring of brain tumors during radiotherapy, for example.

GROUP MEMBERS

- · Assoc. Prof. Lars G. Hanson
- · Assoc. Prof. Kristoffer H. Madsen
- · PhD stud. Froði Gregersen

EXTERNAL COLLABORATORS

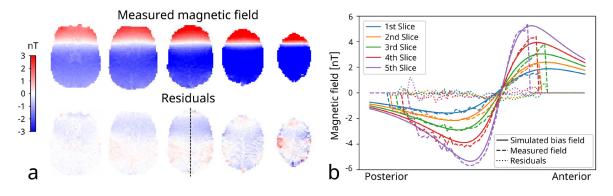
- · Prof. Jan Henrik Ardenkjær-Larsen
- Prof. Klaus Scheffler
- · Dr. Zhentao Zuo

HOMEPAGE

www.drcmr.dk/acquisition

KEY PUBLICATION

Tracking of rigid head motion during MRI using an EEG system. Laustsen, M., Andersen, M., Xue, R., Madsen, K. H. & Hanson, L. G. Magnetic Resonance in Medicine. 88, 2, p. 986-1001, 29251. 2022.



Maps of current-induced fields (Gregersen et al, Imaging Neurosci 2024). For validation, currents flow in a wire around the head enabling simulation. High accuracy results in small differences between measurements and simulations (the residuals)

NEUROFLUIDS

The flows and exchanges of fluids in the brain are crucial to maintain brain function. Blood flow supplies nutrients and removes waste metabolites, interstitial fluid mediates neurotransmitter transport, and cerebrospinal fluid (CSF) provides cushioning and boyancy to the brain. CSF also drives the 'glymphatic system': CSF circulates around the brain, entering the spaces between neurons and glial cells, which helps to clear waste products from the brain's interstitial fluid. Dysfunction of the glymphatic system has been linked to various neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, and other conditions that involve the buildup of toxic proteins in the brain.

Few MR-methods exist to measure glymphatic system-related flows in humans, hindering the translation of the glymphatic system to human research and clinical use. The aim of the neurofluids research group is to develop and implement new methodology and sequences to measure the flows and exchanges of neurofluids. We also facilitate, support and advance all neurofluids-related research at DRCMR and with external collaborators.

GROUP MEMBERS

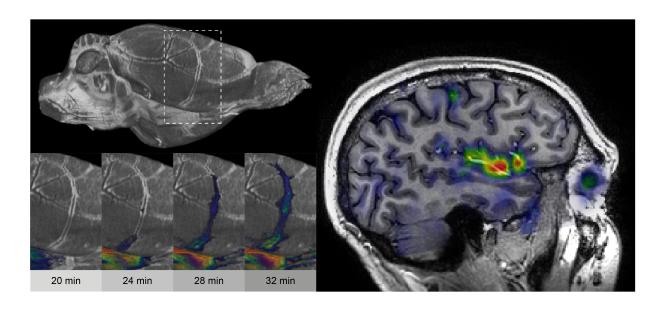
- · Postdoc Kristian Nygaard Mortensen
- · Senior Researcher Henrik Lundell
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- Research Fellow Rasmus Hvass Hansen

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- · Prof. Christina Kruuse
- · Ass. Prof. Henrik W. Schytz

HOMEPAGE

www.drcmr.dk/neurofluids



Glymphatic cerebrospinal fluid flow in pial perivascular spaces of the middle cerebral artery visualized with dynamic MRI of a paramagnetic tracer in the rat brain (left) and low b-value dynamic diffusion imaging in the human brain (right).

PRÉCISION BRAIN STIMULATION



Towards causal neuroscience

Non-invasive Transcranial Brain Stimulation (TBS) techniques directly interact with intrinsic brain activity and can induce long-lasting effects on human brain function. These features make them unique complements to neuroimaging techniques such as MRI that are correlative in nature, with limited possibilities to determine whether the measured brain activity patterns play critical roles in the observed behavior. In contrast, combining TBS with neuroimaging in a perturb-and-measure approach can reveal causal insights into the function and dynamics of the complex brain networks that underlie our thoughts, feelings and actions. TBS can also shape and normalize dysfunctional brain activity patterns that underlie neuropsychiatric diseases, making it a promising therapeutic option. Yet, our understanding of how TBS affects the brain activity is still limited, which reduces its specificity when used as a neuroscience or therapeutic tool, and prevents a systematic optimization of the treatment efficacy.

Mission and Vision

We strive to advance TBS as a unique interventional tool to study causal brain dynamics and enhance cognitive, affective and motor function in health and disease. We aim to overcome current limitations through innovative approaches that shape electrical signaling in the brain with unprecedented spatial, temporal, and functional precision. Our goal is personalized TBS interventions that integrate neu-

roimaging-based phenotyping with computational dose control of the stimulation patterns in the brain to increase the specificity of the stimulation effects and minimize their inter- and intraindividual variability. We further work on establishing novel TBS modalities with complementary application profiles, such as ultrasound stimulation for spatially precise modulation of subcortical activity. We will exploit the potential of precision TBS, tailored to the individual brain, to uncover the causal dynamics of the human brain and translate these insights into powerful neuropsychiatric therapies for the 21st century.

A unique infrastructure for brain stimulation

The DRCMR houses a unique infrastructure to support 'brain imaging informed' and '-controlled' TBS. This includes five state-of-the-art laboratories where all TBS modalities can be applied independently or combined. Brain activity can be continuously monitored with EEG, offering open- and closed-loop applications. Neuro-navigated TMS-fMRI and TESfMRI on a state-of-the-art 3T MR system enable measurements of the immediate and lasting stimulation effects on brain activity. In addition, we are currently establishing dedicated facilities for clinical trials that are equipped with a robotic system for automated and spatially highly precise TMS therapies. Last but not least, personalized computational modeling of stimulation fields and waves is supported by dedicated software infrastructure on the DRMCR computer cluster.



Brain Network Modulation



Neurophysics



BRAIN NETWORK MODULATION

We explore the transformative potential of non-invasive transcranial brain stimulation (NTBS), focusing on transcranial magnetic stimulation (TMS) to induce neuroplasticity and treat conditions like major depressive disorder, multiple sclerosis, and Parkinson's disease. Our work has two main objectives: advancing NTBS as a tool for modulating brain networks and developing next-generation therapies.

We investigate NTBS effects using electrophysiology (EMG/EEG) and advanced magnetic resonance imaging or spectroscopy to link neurophysiology with behavior. In our clinical trials, we employ precision NTBS guided by neuroimaging of target networks, developing stimulation protocols based on the brain's natural activity and tailoring timing in both open- and closed-loop setups.

Our translational efforts are enhanced by a recently established, dedicated outpatient unit for therapeutic brain stimulation, where we currently run three randomized clinical trials to test novel TMS treatments. One trial, the Copenhagen Magnetic Personalized Accelerated Brain Circuit Trial (COMPACT), tests a novel accelerated TMS protocol for treatment-resistant depression in collaboration with the Mental Health Services in the Capital Region of Denmark. The Fatigue Alleviation with Neuromodulation Therapy in Multiple Sclerosis (FANTIMS)-trial investigates the use of a TMS protocol for rebalancing excitation-inhibition in the premotor area, to alleviate fatigue in multiple sclerosis.

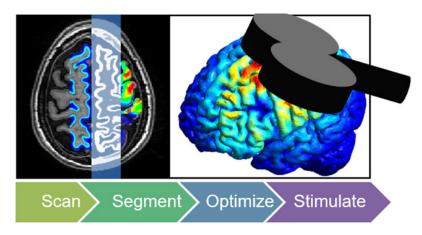


Illustration of the various aspects/ steps of precision targeting based on the individual brain MRI

GROUP MEMBERS

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- · PostDoc Xavier Corominas
- · PostDoc Armita Faghani Jadidi
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- · Research assistant Thomas Thomsen
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- · Student Assistant Mifuyu Hori
- Neurophysiology Assistant Aino Lindross Jensen

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- Associate Professor Annemette Lykkegaard

HOMEPAGE

www.drcmr.dk/brain-network-modulation

KEY PUBLICATION

Transcranial magnetic stimulation of primary motor cortex elicits an immediate transcranial evoked potential.

Beck MM, Christiansen L, Madsen MAJ, Jadidi AF, Vinding MC, Thielscher A, Bergmann TO, Siebner HR, Tomasevic L.Brain Stimul. 2024 Jul-Aug;17(4):802-81

NEUROPHYSICS

Our vision is to boost the efficiency of non-invasive Transcranial Brain Stimulation (TBS) and increase its relevance as therapy for neuropsychiatric diseases. TBS can modulate neural plasticity and normalize function in the targeted disease-related brain networks at a level of spatial specificity that surpasses any other non-invasive method, in particular pharmacological approaches. However, the efficacy of TBS is still hampered by a large inter-individual variability of the treatment outcome. We suggest that understanding the physics and biophysics of TBS is important to optimize TBS and identify factors that contribute to its outcome variability at the physiological and behavioral level.

Our group has pioneered the use of computational dosimetry methods for the personalized control and optimization of the current flow patterns induced by transcranial magnetic and electric stimulation in the brain (www.simnibs.org). In internal and international collaborations, we employ the newly developed methods to assess whether they can help to reveal variablity sources of TBS and be used to optimize the intervention to increase its clinical impact. Complementary to the application of dosimetry methods to empirical research, we are working on extending our methods from current flow simulations to predictions of the impact of the induced currents on neural activity.

An important aspect of our research is the use of MR imaging to inform, complement and validate our dosimetry methods. This comprises the development of new MR image segmentation methods based on deep-learning to enable fast and robust personalized dose simulations. In addition, we have successfully implemented novel and highly sensitive MR methods to measure the current flow patterns induced by TBS in the in-vivo human brain. We are now employing this approach to validate and improve the accuracy of simulated current flow patterns that are the mainstay of computational dosimetry methods.

Bone density Differences C

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- · Postdoc Björn Sigurðsson
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- · Prof. Thomas Knösche
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- Prof. Angel Peterchev
- · Prof. Warren Grill
- · Assoc. Prof. Anders R. Korshøj

HOMEPAGE

www.drcmr.dk/neurophysics

KEY PUBLICATION

A head template for computational dose modelling for transcranial focused ultrasound stimulation. Hosseini S, Puonti O, Treeby B, Hanson LG, Thielscher A (2023) Neuroimage 277:120227.

Examples of current research. A) Transcranial magnetic stimulation therapies often use complex coil geometries that are difficult to simulate and optimize. We are developing new approaches to realistically position the coils on the patient head during simulations, ensuring that the simulated coil fits on the head instead of intruding into it. B) We work on new methods to convert MR images into tissue density maps to inform simulations of focused transcranial ultrasound stimulation, aiming to make the use of CT images unnecessary. C) MRCDI measurements and simulations of a transcranial electric stimulation montage that induces currents flowing from the front to the back of the head. The relatively good correspondance to the measurements validates the simulation approach.

COGNITIVE AND COMPUTATIONAL NEUROSCIENCE



Both cognitive and computational neurosciences constitute major research themes here at DRCMR. What exactly is cognitive and computational neuroimaging? The word cognitive refers to a focus on cognition, a wide spectrum of mental faculties that we all take for granted. Learning, decision-making, attention, reasoning, memory, language, and motor control are all examples of the faculties we rely on as part of our mental toolkit. Cognitive neuroscience, naturally, is the subfield of neurobiology charged with investigating the neurobiological underpinnings of these faculties. Computational Neuroscience, on the other hand, is a subfield in which mathematical tools are used to develop and test theories of brain function. Putting this all together, cognitive and computational neuroimaging thus studies the neural basis of cognition from a computational perspective, using neuroimaging as its primary technique. Our research area's long-term vision is to pioneer new methods for bridging computational modelling of cognition and neuroimaging and to use this to understand the brain's functions and dysfunctions. Principal among these efforts is to develop advanced multi-modal methods for integrating computational models into the modelling of brain, cognition, and behavior.

The Computational Neuroscience of Reward group, seeks to build and test fundamental theories of

reward value that are grounded in our physiology and evolutionary history. The group's primary research interest concerns the brain's reward system. Put simply: how does it work, and why? They explore computational theories that constrain how it should work and then test the predictions of these theories against behavioural, economic, physiological, and neuroimaging data.

The Control of Movement (CoMo) group, studies how the central nervous system orchestrates movements. They combine neuroimaging, neuromodulation and computational modelling of sensorimotor networks. The group adopts a triple-M approach to decipher the causal neuro-dynamics in sensorimotor brain networks by combining multimodal brain mapping with computational modelling and non-invasive modulation of sensorimotor networks.

The Computational Neuroimaging group focuses on modelling and analysis of neuroimaging data based on machine learning methodology. The efforts within the group aim to improve sensitivity and interpretability of the vast amounts of data that are acquired with neuroimaging techniques through sophisticated modelling and analysis methods. Furthermore, the group makes significant contributions to a wide range of projects running within DRCMR.



Computational Neuroimaginging



Computational Neuroscience of Reward



Control of Movement



COMPUTATIONAL NEUROIMAGING

The Computational Neuroimaging group conducts research in modelling and analysis of neuroimaging data from several modalities, including functional and structural magnetic resonance imaging, electrophysiology, brain stimulation and behavior. The methodological focus is on applied statistical machine learning and spans from simple supervised linear models to non-linear and unsupervised learning. Efficient feature extraction methods are important as neuroimaging experiments are generally high-dimensional and often cover several modalities with markedly different noise characteristics. To this end, the Computational Neuroimaging group works on developing unsupervised decomposition methods, which can improve generalization performance of prediction algorithms based on functional connectivity data, especially when faced with datasets recorded across several sites and acquisition manufacturers.

In active machine learning, the idea is to actively plan data acquisition while it is ongoing to optimize a learning objective. This has the potential to vastly improve efficiency of the data acquisition process but is a demanding endeavor in neuroimaging as it requires more sophisticated model and online learning. A key concept in this setting is uncertainty quantification as it enables the model to be aware of its shortcomings and thereby spend time on acquiring data which enable it to learn what it does not already know. Consequently, the Computational Neuroimaging group both develops efficient models with uncertainty quantification and real-time data analysis, in an effort to enable more efficient treatment and data acquisition procedures in the future.

GROUP MEMBERS

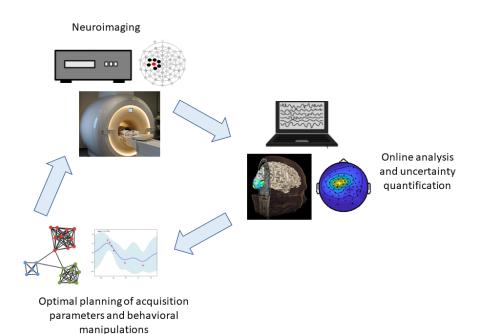
- · Assoc. Prof. Kristoffer H. Madsen
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- · Prof. Lars Kai Hansen
- · Prof. Fang Wang
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HOMEPAGE

www.drcmr.dk/computational-neuro-imaging



Active data acquisition procedures have the potential to improve the data collection procedure. In this setting, online analysis and uncertainty quantification is used to optimally inform future data collection procedure in a closed loop.

COMPUTATIONAL NEURO-SCIENCE OF REWARD

Our main research interest concerns the brain's reward system. Put simply: how does it work, and why? We explore theories that constrain how it should work, and then test the predictions of these theories against behavioral, physiological, and neuro-imaging data. There are two strands to the group's research agenda:

The first strand asks, how do reward computations shape behavior to regulate the physiological systems of the body. Specifically, how are the values of primary rewards such as food and water, configured by homeostatic states, and how should they be configured according to the constraints of survival. We are particularly interested in how models of this sort could provide a unified explanatory account of basic behavioral phenomena such as risk preferences, loss aversion, and temporal discounting. This work involves collaboration with endocrinologists, metabolic scientists, food scientists, and computational neuroscientists.

The second strand draws on a concept in physics known as ergodicity, and is the basis of the group's connection to the London Mathematical Laboratory. Ergodicity here refers to thinking carefully about the types of averages that are relevant to behaviour, with a particular emphasis on how decisions unfold over time. We are interested in the constraints that ergodicity imposes on decision-making, and whether such considerations can also offer a unified account of a number of disparate behavioral phenomena. We received funding from the Novo Nordisk Foundation to work together on experiments that expose subjects to different dynamical settings, testing how these dynamics modulate reward computations, and risk-taking behavior.

The group is committed to open science, and all future experiments will pre-register and release all code, materials, and data wherever possible. We also teach courses on the methods most central to our research, namely Bayesian statistics, as well as Bayesian modelling of cognition and the brain.

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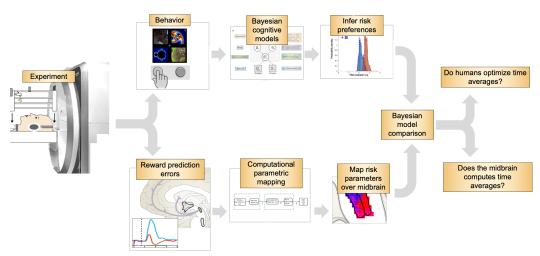
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- · Dr. Ole Peters
- · Prof. Sten Madsbad
- · Assoc. Prof. Tobias Andersen
- · Prof. Duda Kvitsiani

HOMEPAGE

www.drcmr.dk/reward-group

KEY PUBLICATION

Ergodicity-breaking reveals time optimal economic behavior in humanss. Meder D, Rabe F, Morville T, Madsen KH, Koudahl MT, Dolan RJ, Siebner HR, Hulme OJ., 2021, PloS Computational Biology, 17(9): e1009217



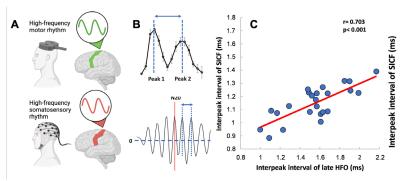
An overview of the methods deployed in our upcoming research project on ergodicity and the brain. It shows how the different methods combine to allow us to ask how the reward system computes time averages when making risky decisions.

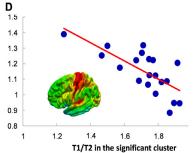
CONTROL OF MOVEMENT

The Control of Movement (CoMo) group combines neuroimaging, neuromodulation, and computational modelling of sensorimotor networks to eliucdate how the brain orchestrates movements. We meet every week to discuss new findings in movement neuroscience and relate these findings to our own research. We are interested in how sensory inputs shape our motor outputs and how brain micro- and macro structures support sensorimotor behavior. Two highlights from the past two years:

Tomasevic et al. (2022) found a close connection between high-frequency (HF) cortical responses in the somatosensory (S1) and motor (M1-HAND) hand representations. They measured the HF oscillatory component (HFO) of the somatosensory evoked potential in S1 and the inter-peak interval of short-interval intracortical facilitation (SICF) with paired-pulse transcraniual magnetic stimulation (TMS) of M1. The intervals between the first two peaks in HFO and SICF displayed a clear positive linear relationship. Structural MRI revealed that the regional cortical myelin content scaled with fast cortical responses: The higher the regional cortical myelin content, the faster were S1 and M1 rhythms. Together these results show a novel link between HF activity and micro-structure in S1 and M1-HAND.

Bonnesen et al. (2022) combined TMS of M1-HAND with electrical stimulation of the digital nerves from the index (D2) and little finger (D5) to show that recent sensory experiences modulate motor ouput excitability. Sensory inputs from D2 resulted in stronger immediate effects on the motor output to the First Dorsal Interosseous (FDI) compared to inputs from D5. Reversely, D5 inputs affect the output to FDI for several seconds but only in the absence of immediate sensory stimuli. Combined, these results show that somatosensory inputs shape the motor output on multiple timescales with distinct spatial organization.





A) We found brain rhythms from sensorimotor cortices to relate to cortical micro-structure. B) High-frequency signals in sensorimotor cortices as reveled by facilitatory peaks following paired TMS pulses with varying interstimulus interval as well as the inter-peak interval of high-frequency EEG oscillations following median nerve stimulation. C) Strong linear relation between these measures of high frequency sensory and motor activity and D) between peri-central TI/T2 ratio and the paired pulse facilitatory peaks. From Tomasevic et al., 2022 (J Neurosci).

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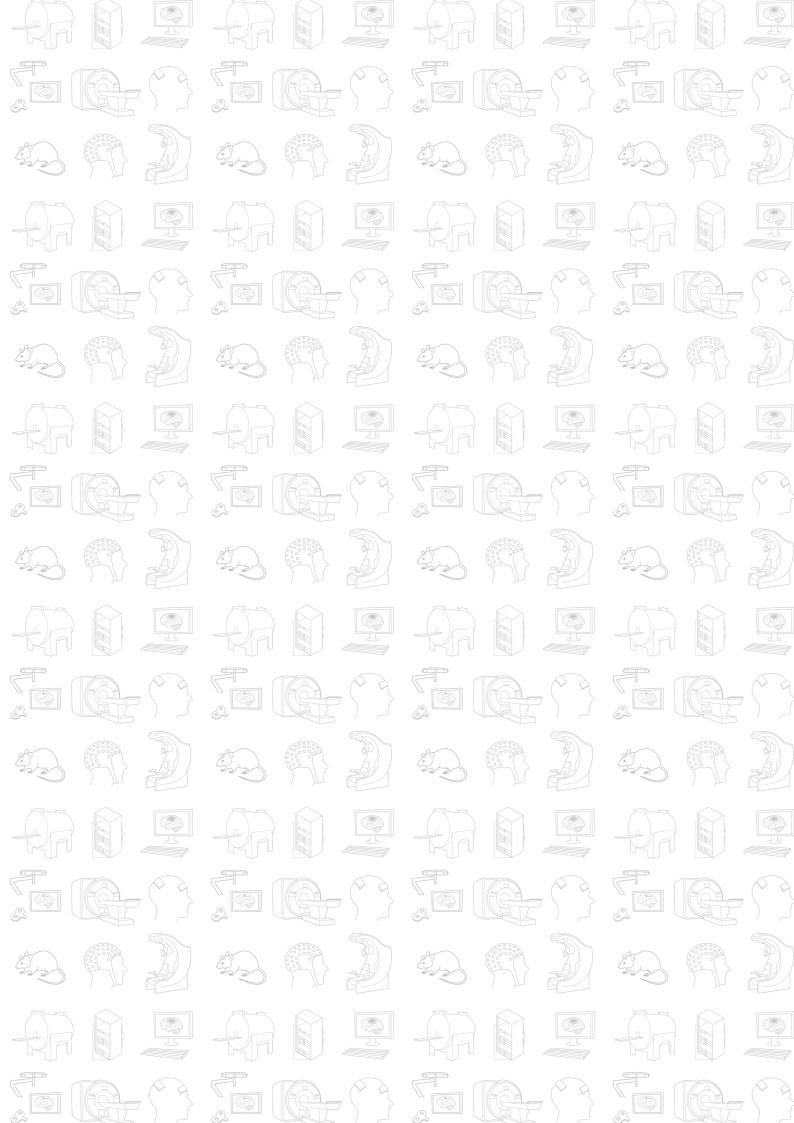
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- · Neurologist Raffaele Dubbioso
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- · Prof. Angelo Quartarone
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HOMEPAGE

www.drcmr.dk/control-of-movement

KEY PUBLICATION

Multipulse transcranial magnetic stimulation of human motor cortex produces short-latency corticomotor facilitation via two distinct mechanisms. Kesselheim, J., Takemi, M., Christiansen, L., Karabanov, A.N. and Siebner, H.R., 2023. Journal of Neurophysiology, 129(2), pp.410-420.



LIFESPAN IMAGING



Lifespan imaging centres around understanding the development of brain structure, function and chemistry throughout the lifespan from birth to the end of life. We are interested in both typical and pathological development and in understanding the drivers, either biological or socio-environmental, of such development. Ultimately, we would like to predict whether individuals are at risk of negative development and provide recommendations for interventions that may alter such a trajectory for a particular person.

A multi-dimensional prospective approach

We tackle these questions using a multi-dimensional prospective approach that combines state-of-the-art multimodal imaging techniques with advanced analysis methods and perform elaborative assessments of biological, physical, environmental and behavioural variables. We believe that the key lies in longitudinal data, with following and examining the same individuals over time to accurately measure life span trajectories in (brain) health and disease. We also perform various intervention studies testing effects on brain health from e.g., physical exercise. In our studies, we have both healthy individuals and specific patient groups.

We have established expertise and research infrastructures for detailed cross-sectional and longitudinal assessments of large cohorts and nurture active and elaborative regional, national and international collaborations. In the last couple of years, we have started up new projects in both the Brain Maturation and the Healthy Ageing research groups, which you can read more about in specific sections of this report.

Our passion

In all our projects, we strive for high academic standards, interdisciplinary collaborations, innovative methods and techniques, and an ambitious, fun and diverse environment.



Healthy Ageing



Brain Maturation



HEALTHY AGEING

The vision for the Healthy Ageing group is to identify and optimize interventional strategies for promoting healthy brain ageing. Over the past two years, work from our group has demonstrated the role of modifiable lifestyle factors, such as sleep and education, in promoting healthy brain aging. Honing in on one particular modifiable lifestyle factor – physical exercise – we have explored how individual differences influence brain changes in response to physical activity. For example, we have observed that white matter lesion load determines the extent of exercise-induced dopaminergic changes and working memory benefits in older adults.

Taking a leap towards better understanding the mechanisms behind the effects of exercise on the brain, we have begun data collection on a new project: the HINT study. The HINT study harnesses the power of 7T MRI to examine exercise-related changes in glia-related metabolites in older individuals. For this, we continue our long-standing collaborations with the Insitutite of Sports Medicine Copenhagen and the Ultra-High Field MR group.

The LISA study, originally a randomised-controlled trial of a muscle strengthening programme in older adults, has reached it's 7th year of data collection. This rich longitudinal dataset has allowed us to examine trajectories in physical function, which we have shown to be associated with gray matter volumes in motor brain regions. By collaborating with other groups in Europe, we have also been able to replicate and cross-validate our findings in a British cohort of older adults.

In the years to come, we will continue to focus on longitudinal multimodal datasets to better characterise brain ageing. Understanding which factors promote healthy brain ageing – and the mechanisms by which they do so – is a crucial step for the development of tailored and effective healthy ageing interventions.



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- · Prof. Klaus Ebmeier

HOMEPAGE

www.drcmr.dk/healthy-ageing

KEY PUBLICATION

Is it all in the baseline? Trajectories of chair stand performance over 4 years and their association with grey matter structure in older adults. Demnitz, N., Gates, A. T., Mortensen, E. L., Garde, E., Wimmelmann, C. L., Siebner, H. R., &

Celebration of Professor Carl-Johan Boraxbekk at his inaugural lecture as Professor of Neurology at the University of Copenhagen.

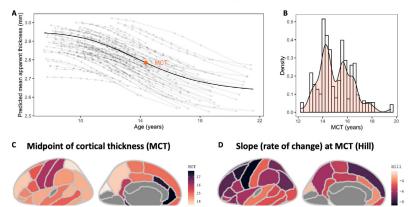
BRAIN MATURATION

The brain maturation group studies brain and behavioral development during infancy, childhood, and adolescence. We characterize brain and behavioral developmental trajectories in health (typical) and disease (atypical) and elucidate how brain networks map onto developing cognitive and motor functioning. We employ multimodal MRI techniques, and environmental, biological, cognitive, and clinical assessments in cross-sectional and longitudinal studies of typically developing and at-risk pediatric populations. In November 2022, we initiated the NIBS-CP project. In NIBS-CP, we examine early brain and motor function development in infants at risk for cerebral palsy and typically developing infants at three time points between the ages of 3 to 24 months with comprehensive assessments of motor functioning and neuroimaging. Read more about NIBS-CP under key projects page XX.

The MORE2SLEEP project was initiated in 2024 in collaboration with Faidon Magkas (PI) and Jesper Lundbye-Jensen (co-PI), University of Copenhagen. MORE2SLEEP aims to investigate the effect of extra sleep in 6-11-year-old children on body weight, metabolism, cognition, and brain structure and function. A total of 300 children will be recruited to the project over the next couple years. All MR scans are performed at the DRCMR.

The longitudinal HUBU project followed 95 typically developing children (aged 7-13 years at baseline) over 9 years, with up to 12 waves of MRI, clinical, and cognitive assessments. It aims are to uncover individual differences in the maturational trajectories of brain networks and their links to cognitive, emotional and neuroendocrine development. Recent findings highlight significant variability in cortical thinning trajectories during childhood and adolescents (Figure X). Since 2017, the HUBU project has been part of the Horizon 2020 project Lifebrain, in which we are partners.

Maturation of cortical thickness during childhood and adolescence



Midpoint of cortical thickness (MCT), the age of most rapid thinning (a), varies among children (b) and cortical regions (c) with anterior cingulate showing the most protracted development. MCT's slope (d) also varies and is independent of the MCT.

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- · Stud. Mathilde Marie Hansen
- · Stud. Franchesca Edwards
- · Stud. Emilie Winther Tolstrup
- · Stud. Ho Man Him
- · Intern Eliza Varju

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- · Prof. Wesley Thompson
- $\boldsymbol{\cdot}$ Assoc. Prof. M. Ganz-Benjaminsen
- · Prof. Christina Hoi-Hansen
- · Assoc. Prof. Helle Pfeiffer
- $\cdot \ \mathsf{Assoc.} \ \mathsf{Prof.} \ \mathsf{Jesper} \ \mathsf{Lundbye}\text{-}\mathsf{Jensen}$
- Prof. Faidon Magkos
- · Lecturer Delia Fuhrmann
- · Prof. Rogier Kievit
- · Prof. Kristine Walhovd
- Assoc. Prof. Øystein Sørensen
- · EU Lifebrain partners

HOMEPAGE

www.drcmr.dk/brain-maturation

KEY PUBLICATION

The midpoint of cortical thinning between late childhood and early adulthood differs between individuals and brain regions: Evidence from longitudinal modelling in a 12-wave neuroimaging sample. Fuhrmann D, Madsen KS, Johansen LB, Baaré WFC, Kievit RA (2022) NeuroImage 261: 119507

CLINICAL PRECISION IMAGING



Advancements in MRI are continuing to expand our possibilities for precision imaging of brain disorders, offering unprecedented insights into how a given brain disease affects the brain's structure. function, and metabolism. The DRCMR is uniquely positioned to translate these innovations into clinical applications. Our methodological research, in collaboration with the Technical University of Denmark (DTU), is pushing the frontiers of MRI data acquisition and analysis. Simultaneously, our location within a major University Hospital and the organizational integration with the Department of Radiology and Nuclear Medicine provides optimal conditions for clinical translation. Additionally, our preclinical MRI unit enables method validation in rodent models. This dynamic ecosystem makes DRCMR a critical hub for bench-to-bedside translational research, advancing MR-based Precision Medicine as a vital link between diagnostic radiology and clinical neuroscience.

Our mission is to enhance MRI's role in clinical care, empowering neurologists, neurosurgeons, and psychiatrists to tailor treatments to individual patients. We strive to identify clinically relevant MR biomarkers that assess individual disease risk, prognosis, and treatment response. Additionally, we strive to develop MRI-based brain circuit biomarkers for disabling symptoms for the evaluation and monitoring

of symptom-specific treatments. These objectives are pursued through longitudinal observational and interventional MRI studies in collaboration with our clinical partners. Integrating MRI, neuroscience, and clinical practice Our neuroimaging research spans psychiatric and neurological disorders across all life stages. We develop and validate MR-based technologies to capture risk, resilience, and disease-related changes in brain structure, function, and metabolism. Simultaneously, we advance neuroimaging data analysis to optimize clinically relevant MR "read-outs." Our studies integrate electronic health records, genomic, and biochemical ("Omics") data. Recently, we have expanded MRI protocols to assess other organs, including muscle, heart, liver, and gut, examining physiological functions to strengthen brain-body MRI mapping. This integrated approach provides novel insights into abnormal brain-body interactions in neurological, psychiatric, and systemic metabolic disorders.

Over the past three years, we have successfully developed highly sensitive multi-modal MR protocols to detect pathogenic and pathophysiologic processes. We have applied these protocols to identify pre-symptomatic MRI markers in high-risk and resilient populations for neurological disorders (e.g., Parkinson's disease), psychiatric disorders (e.g., schizophrenia), and large population cohorts.



Movement Disorders



Neuroimaging in Multiple Sclerosis



Developmental Psychiatry



Brain Body Interaction



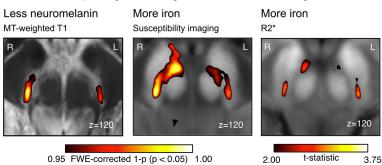
MOVEMENT DISORDERS

The Movement Disorders group bridges clinical, computational and cognitive neuroscience to advance the pathophysiological understanding of movement disorders. Our research primarily focuses on Parkinson's disease (PD) and dystonia. Current key projects are the 7-tesla PD project, the ADAPT-PD project and the OPD project. In the 7T project, we use the ultra-high field MR scanner in order to map the structural integrity of midbrain nuclei at high resolution. This allows us to investigate the relationship between the individual spatial pattern of neurodegeneration in Parkinson's disease and the patient's clinical symptoms (Madelung et al., 2022, MovDis). Novel projects are the longitudinal assessment of changes over disease progression and the mapping of midbrain changes in the prodromal stages of PD in patients with REM-sleep behavior disorder.

In the ADAPT-PD project, we investigate dysfunctional circuit dynamics in cortico-basal ganglia projections in PD with the aim to "normalize" them with brain stimulation techniques. ADAPT-PD is a collaborative international, translational and multi-modal project involving different techniques (invasive and non-invasive recordings as well as brain stimulation) in animal models and PD patients.

In the OPD project (Optimism and Pessimism in the Dopamine System in PD), we test a novel theory suggesting a hitherto unkown diversity in dopaminergic signaling and how this diversity is affected by neurodegeneration in PD. Observing which parameters of the model are changed in the disease can then lead to a mechanistic understanding of how the disease affects brain function, leading to different symptoms.

Neuromorphological Changes in the Substantia Nigra in PD



Patients with Parkinson's disease have a lower neuromelanin signal in the substantia nigra, indicative of the loss of dopaminergic neurons. They also show partially overlapping, but also spatially diverging excessive iron accumulation in this region.

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- · Research Fellow David Meder
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- · Assoc. Prof. Mattias Rickhag
- · Research Fellow Lasse Christiansen
- · Postdoc Mikkel Malling Beck
- · PhD Stud. Ditte Høier Frantzen
- · PhD Stud. Ditte Høier Frantzen
- · Stud.Assist. Jonas Laugesen
- · Res.Assist. Laura Sakalauskaitéé
- · PhD Stud. Mihai Atudorei
- PhD Stud. Birgitte Liang Chen
 Thomsen
- · PhD Stud. Christopher Fugl Madelung
- · MSc stud. Claudiu Corcea
- · Stud.Assist. Deniz Alp Tankisi
- · Neurophys.Assist. Aino L. Jensen
- · Postdoc Amin Ghaderi Kangavari
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- · Assoc. Prof. Annemette Løkkegaard
- · Prof. James Rowe
- · Prof. Ray Dolan
- · Prof. Stéphane Lehéricy
- · Research Fellow Damian M. Herz

HOMEPAGE

www.drcmr.dk/movement-disorders

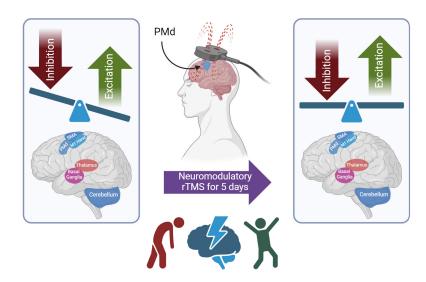
PUBLICATIONS

Low-frequency transcranial stimulation of pre-supplementary motor area alleviates levodopa-induced dyskinesia in Parkinson's disease: a randomized cross-over trial. Lohse, A., Meder, D., Nielsen, S., Lund, A.E., Herz, D.M., Løkkegaard, A., Siebner, H.R., 2020. Brain Communications 2, fcaal47.

NEUROIMAGING IN MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is a complex autoimmune-mediated, demyelinating and neurodegenerative disease, and is the leading, non-traumatic cause of neurological disability in young adults. Crucial to the diagnosis and monitoring of MS, Magnetic Resonance Imaging (MRI) allows to detect MS lesions in the brain and spinal cord. The NeuroImaging in Multiple Sclerosis (NiMS) group aims to push the frontiers of MRI to capture overall MS-related tissue damage and to uncover the pathophysiological mechanisms of MS. Our multi-modal research combines structural and quantitative MRI techniques with other brain mapping modalities, such as transcranial magnetic stimulation (TMS). Using our 7T MR scanner, our recent work revealed a link between cortical lesion volume and glutamate and GABA concentrations, suggesting an excitation-inhibition imbalance in MS. Currently, we are exploring the global contribution of diffuse cortical demyelination to disease progression in primary-progressive MS with the power of 7T MRI.

In a new project, we are testing the potential of repetitive TMS to treat fatigue in MS, a symptom that widely affects the quality of life of patients. Further human and pre-clinical 7T work aims to disentangle cell type specific morphological changes in MS pathology (C-MORPH), by combining diffusion and spectroscopic imaging properties. Finally, together with the Reader Centre and the Danish MS Centre, NiMS is coordinating DanNORMS, a large, multi-site, phase 3 Danish clinical trial assessing the non-inferiority of two treatments for relapsing MS. Here, NiMS is currently modelling the advanced diffusion MRI signal in MS lesions. To contribute to MS research and decision making on a European level, we also recently became an affiliated site of the MAGNIMS network, and we have started collaborations focused on large data analyses.



Fatigue in MS is believed to be related to a motor network dysfunction, due to an imbalance between excitatory and inhibitory signals. We are employing a novel repetitive TMS protocol to alter this network dysfunction. (created with BioRender.com)

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- · Assoc. Prof. Tim B. Dyrby
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- · PhD stud. Sofus A. Drejer Nygaard
- · Research Assistant Alec Gallo
- · Research Assistant Chiara Cabras
- · MSc stud. Ramla Abdi
- · MSc stud. Jesús Díaz Pereira
- · MSc stud. Philipp Renn
- · MSc stud. Silja Marie Patursson Vange
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- · Research Radiographer Sascha Gude
- · Research Technologist Sussi Larsen
- · Research Manager Karam Sidaros

EXTERNAL COLLABORATORS

- · Prof. Finn T. Sellebjerg
- · Consultant Jeppe Romme Christensen
- · Consultant Morten Blinkenberg
- Consultant Stephan Bramow
- · Consultant Camilla G. Madsen

HOMEPAGE

www.drcmr.dk/ neuroimaging-in-multiple-sclerosis

KEY PUBLICATION

Association of Cortical Lesions With Regional Glutamate, GABA, N-Acetylaspartate, and Myoinositol Levels in Patients With Multiple Sclerosis. Madsen MA, Považan M, Wiggermann V, Lundell H, Blinkenberg M, Romme Christensen J, Sellebjerg F, Siebner HR.Neurology. 2024 Jul;103(1):e209543.

DEVELOPMENTAL PSYCHIATRY

Most psychiatric disorders are rooted in abnormal neurodevelopment. Having a long-standing interest in neurodevelopment, our research is geared to improve the prediction and characterization of psychiatric disorders across the lifespan. We wish to contribute to the development of new personalized strategies for prevention and treatment by identifying new treatment targets. In close collaboration with our clinical partners, we employ state of the art multimodal brain imaging, and advanced modelling approaches to elucidate neurobiological and neurocognitive trajectories of brain development.

Our work is centered around two key projects, The Danish High risk and Resilience study (VIA) and the Treatment Effects of family-based Cognitive Therapy in children and adolescents with Obsessive compulsive disorder (TECTO).

TECTO combines a randomized clinical trial and longitudinal case-control design in pediatric patients with obsessive-compulsive disorder. VIA is a national longitudinal study of 522 11-year-old (VIA11) children born to parents with or without a diagnosis of either schizophrenia or bipolar disorder, now followed up at age 15 (VIA15). We have received funding to aquire yet another round of data at age 19 (VIA19), which ads to the uniqueness of the cohort, allowing longitudinal analyses. Line Korsgaard Johnsen and Valdemar Uhre successfully defended their PhD theses in 2022, as part of the VIA and TECTO studies.

Results form their PhD have been published in Schizophrenia Bulletin and Neurolmage Clinical. We have further published our results showing that children at familial high risk for schizophrenia or bipolar disorder show altered connectivity patterns, mirroring findings in schizophrenia. We have acquired funding for and recruited one PostDoc on the TECTO and two PostDocs on the VIA study in 2024.

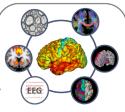
Longitudinal, interventional and cross-sectional study designs



Children and adolescents with a clinical diagnosis or at high risk for developping psychiatric problems



Clinical-, cognitive-, socialmood-, behavioral-, and physical- tests, questionnaires and interviews as well as biological markers



Anatomical and functional magnetic resonance imaging (MRI) and electroencephalography (EEG)

General study designs, assessments and outcome measures.

GROUP MEMBERS

- · Senior Researcher Kit Melissa Larsen
- · Senior researcher William F.C. Baaré
- · Prof. Hartwig Siebner
- · Senior Researcher Kathrine Skak Madsen
- · Research Fellow E. Hernández-Torres
- · Postdoc Line Korsgaard Johnsen
- · PostDoc Janine Bühler
- · PostDoc Mette Falkenberg Krantz
- · PostDoc Valdemar Uhre
- · PostDoc Maria del Lucero Pacheco Blas
- · PostDoc Vasilis loakeimidis
- · PostDoc Adam Kaminski
- · Research Assistant Miaamalie S. Jensen
- PhD Students Vytautas Labanauskas
- Students Simon Y. Jensen, Valdemar Kruse, Ditte H. Frantzen, Mathilde M. Hansen, Julia Diaz, Emilie W. Tolstrup, Karlijn Hendriks

EXTERNAL COLLABORATORS

- · Prof. Merete Noordentoft
- · Prof. Katrine Pagsberg
- · Prof. Anne Amalie Elgaard Thorup
- · Prof. Kerstin Plessen
- Prof. Ole Mors
- · Prof. Dost Ongur
- · Prof. James Blair
- · Prof. Nadia Micali
- · Prof. Rosalyn Moran

HOMEPAGE

www.drcmr.dk/developmental-psychiatry

KEY PUBLICATION

Children at familial high risk of schizophrenia and bipolar disorder exhibit altered connectivity patterns during pre-attentive processing of an auditory prediction error. Larsen KM, Madsen KS, Themaat AHVL, Thorup AE, Plessen KJ, Mors O, Nordentoft M, Siebner HR. Schizophr Bull. 2024 Jan 1;50(1):166-176.

BRAIN-BODY INTERACTION

The Brain-Body Interaction Group focuses on the interplay between the central nervous system and other organ systems of the body. Impaired central control of physiological processes lie at the core of a range of diseases, disorders and complications to these. The overarching aim is to cast light on this previously overlooked aspect using a wide range of methods.

The group was started in 2020 and the initial focus was on establishing a framework for future projects. The main project has been an investigation on complications to diabetes mellitus in cooporation with Steno Diabetes Center Copenhagen. With a focus on autonomic dysfunction and neurovascular coupling, this project investigates the brain-gut axis as well as control of cerebral perfusion. Due to significant comorbidity it is a challenging project but headway has been made; a substudy is complete, another is ongoing along with data analysis. A new project investigating autonomic control in REM sleep behavior disorder in cooporation with the Movement Disorders Group is in the planning phase.

GROUP MEMBERS

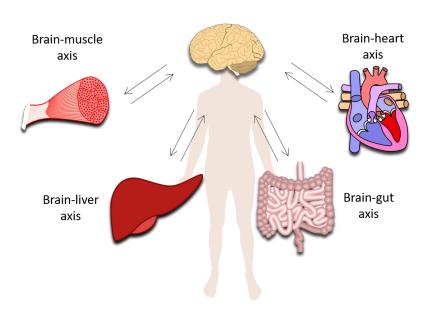
- · Head of Section Mads Barløse
- · Prof. Hartwig R. Siebner
- Head of Department Claus Leth
 Petersen
- · Postdoc Kristian Nygaard Mortensen
- · MD Thomas Siebner
- · MD Sofus Nygaard

EXTERNAL COLLABORATORS

- · Prof. Sten Madsbad
- · MD, PhD Christian Stevns Hansen

HOMEPAGE

www.drcmr.dk/brain-body-interaction



Schematic representation of the research targets of the group.

INFRASTRUCTURE

INFRASTRUCTURE



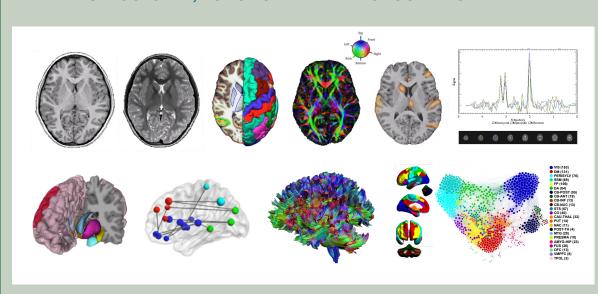
SCANNERS

1 x 7.0 tesla 1 x 7.0 tesla preclinical 4 x 3.0 tesla 1 x 1.5 tesla

LABS

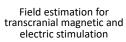
5 x Non-invasive brain stimulation & EEG 1 x Hardware 1 x Preclinical including optogenetics 1x GM-level 2 preclinical 2x Behaviour-Test Labs

STRUCTURAL, FUNCTIONAL AND NEUROCHEMICAL MRI

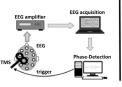


NON-INVASIVE PRECISION BRAIN STIMULATION





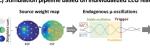








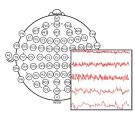
C) Stimulation pipeline based on individualized EEG features

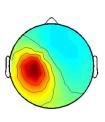


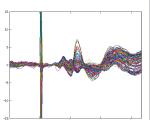


ELECTROENCEPHALOGRAPHY (EEG)









BEHAVIOURAL ASSESSMENTS









METHOD GROUPS

Overlapping and supporting the DRCMR research groups presented in the previous section, we have seven method groups that support the research infrastructure at DRCMR. These groups follow the latest developments within their respective areas of expertise and ensure that the methods used in our research are state-of-the-art. Each method group is headed by a group leader and the groups meet on a regular basis to discuss and plan their activities.

Spectroscopy

MR Methodology

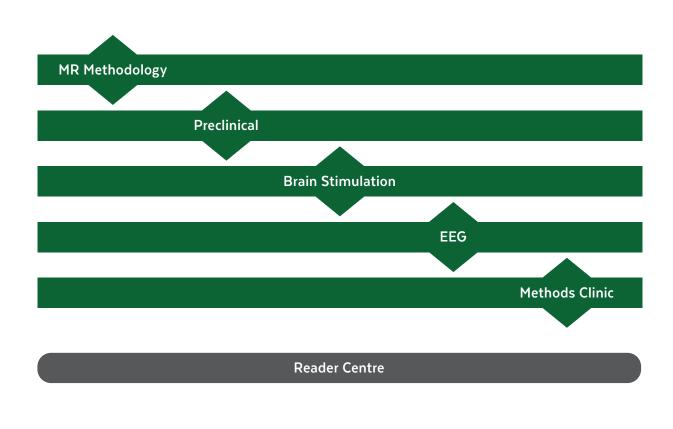
Preclinical











EEG

Brain Stimulation



Methods Clinic

Reader Centre

MR METHODOLOGY

The MR Methodology group supports the research activities that involve magnetic resonance (MR) at DRCMR. MR is a cornerstone in the research at the department and is in many projects often used in conjunction with other independent methodologies. In this group, we support the MR acquisition part of these projects.

The centre has 7 MR scanners of which four are used for both research and clinical purposes. Three 3T and one 1.5 T from Siemens serve both the clinic and research and two Philips Achieva systems (3T and 7T) are used in research only. We also have a preclinical Bruker BioSpec system (7T) used for animal research, post mortem imaging and method development on phantoms. In the MR Methodology group, we try to synchronize the data acquisition and quality, and try to maximize the potential of the different systems.

Part of this work is to pioneer new techniques, exchange sequences between our own systems and with other sites around the world. An important aspect of this work is also to monitor data quality and to plan hardware repairs and updates. Work is also done on adopting cutting edge hardware built by our collaborators or in our own workshop. Furthermore, we organize the mandatory MR safety training for all staff at DRCMR.

Standard shimming

B_o mapping

GROUP MEMBERS

- · Assoc. Professor Henrik Lundell
- Research Fellow Vanessa Wiggermann
- · Assoc. Prof. Lars G. Hanson
- Clinical Physicist Lasse Rahbek
 Søndergaard, PhD
- · Professor Tim Dyrby
- · Professor Axel Thielscher
- · Assoc. Prof. Esben Thade Petersen
- Assoc. Prof. Kristoffer Hougaard Madsen
- · Senior Researcher Nathalie Just
- · Postdoc Hans Stærkind
- · Research manager Karam Sidaros
- · Postdoc Kristian Mortensen

EXTNERAL COLLABORATORS

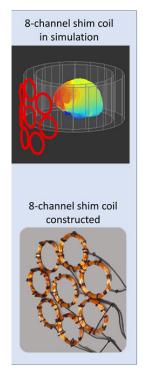
- · Paul de Bruin, PhD
- · Karen Kettless, PhD

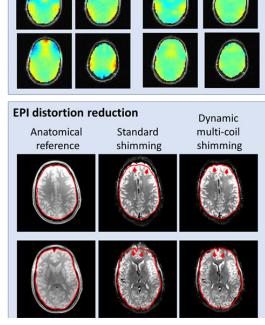
HOMEPAGE

www.drcmr.dk/mr-methods

KEY PUBLICATION

High-Field Optical Cesium Magnetometer for Magnetic Resonance Imaging Stærkind, H., Jensen, K., Müller, J. H., Boer, V. O., Polzik, E. S. & Petersen, E. T., 24 Apr 2024, In: PRX Quantum. 5, p. 1-13 13 p., 020320.





Dynamic multi-

coil shimming

In the MR Methodology group we developed an 8 channel shim coil for improved $B_{\rm 0}$ magnetic field homogeneity in the brain. This reduces image distortion for fast imaging techniques (EPI) used in high

PRECLINICAL GROUP

Our vision is to integrate our basic research with the human research in a translational forward (rodent-to-human) and backward (human-to-rodent) approach with the ultimate goal of improving the treatment and diagnosis of brain disorders. Our research spans from animal behaviour platforms to multi-modal microstructural, functional and metabolic imaging in combination with cell-type specific brain stimulation approaches (chemo- and optogenetics) and other interventions with potential therapeutic relevance. Associate professor Mattias Rickhag and Professor Tim Dyrby co-shares management of the preclinical group.

Our preclinical research facilities have been in an expansion phase with implementation of an array of new technologies. We have setup a new animal behaviour platform to probe sensorimotor modalities in rodents. In parallel, we have established cell-type specific chemogenetics for selective modulation of distinct brain circuits. Mattias Rickhag received a grant from the Michael J Fox Foundation to study the role of corticostriatal projection systems in parkinsonism. He will implement celltype specific chemogenetics and modulate corticostriatal circuit components in parkinsonian animal models. Tim Dyrby received a grant ("CoM_BraiN") from the European Research Council (ERC) to study conduction velocity in brain networks. He will implement optogenetics and electrophysiology to measure conduction velocities concomitant with MRI, and synchrotron for imaging of myelin and demyelination processes. Nathalie Just received a grant from the Lundbeck Foundation to study inhibitory processes and neurometabolic coupling using chemogenetics and functional MRI. Henrik Lundell received a grant from the European Research Council (ERC) ("C-MORPH") to develop new diffusion MRI based methods and to map temporal dynamics of glial activation in the LPS model (a model of neuroinflammation) in mice.

B C Merged NeuN NeuN Tix3 Merged NeuN NeuN NeuN Tix3

Visualization of corticostriatal intratelencephalic glutamate projections by use of the Tlx3-tdtomato mouse line demonstrates extensive axonal arborizations in striatum

GROUP MEMBERS

- · Professor Tim Dyrby
- · Associate Professor Mattias Rickhag
- · Associate Professor Henrik Lundell
- · Senior Researcher Nathalie Just
- · Post Doc Mathias Mathiasen
- · Post Doc Mariam Andersson
- · Post Doc Hanna Villa Merkle
- Post Doc Emma Thomson
- · Postdoc João Lima
- · PhD student Mihai Atudorei
- · PhD student Mario Corral Bolaños
- Research assistant Christian del Agua Villa
- · Research assistant Gustaf Olsson
- Neuroscience master student Claudiu Corcea
- · Bioanalyst Sascha Gude

HOMEPAGE

www.drcmr.dk/preclinical-research

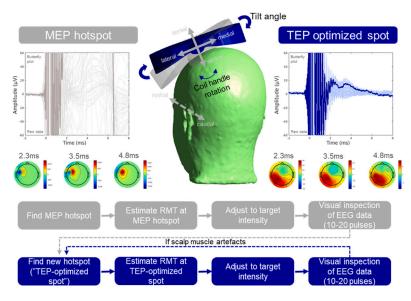
KEY PUBLICATION

Susceptibility-induced internal gradients reveal axon morphology and cause anisotropic effects in the diffusion-weighted MRI signal, S Winther, H Lundell, J Rafael-Patiño, M Andersson, JP Thiran, TB Dyrby, Scientific reports 14 (1), 29636

BRAIN STIMULATION

A range of Transcranial Brain Stimulation (TBS) techniques have emerged over the last decades. These techniques have become versatile neuroscientific tools and shown therapeutical potential to treat circuit dysfunctions in brain disorders. At DRCMR, TBS is used extensively to modulate and map brain activity both in health and disease. The Brain Stimulation Methods Group facilitates, supports, and advances all forms of transcranial brain stimulation research at DRCMR. We support ongoing research aiming at ensuring quality of the experimental work - from the design of experiments to data acquisition and analysis. We work on improving state-of-the-art stimulation protocols by taking individual brain anatomy, activation history, and neural state into account. We develop in-house protocols for combining TBS with neuroimaging in order to inform stimulation parameters and ensure both spatial and temporal precision. In 2022-2024 members of the brain stimulation methods group made a breakthrough discovery, which we expect to have transformative effects on the field of TMS-EEG (Beck, Christiansen et al., 2024, Brain Stimul). By capitalizing on ultrahigh EEG sampling frequency combined with indivualized coil positioning, we have unveiled the very early or 'immediate' TMS evoked potentials (iTEPs) in EEG activity during the first 10ms after a TMS pulse.

The group has a strong focus on education: We provide in-house teaching in all TBS techniques and organize international graduate-level workshops. In 2022, 2023, and 2024 more than 60 young scientists from across Europe, America, and Asia participated in our Copenhagen Brain Stimulation (CoBS) School. The group is headed by Senior Researcher Lasse Christiansen and meets every second Monday. We welcome all researchers at DRCMR who wish to use brain stimulation in their research.



Unveiling immediate TMS-Evoked Potentials (i-TEPs) in EEG. Left: EEG activity obscurred by artefacts with associated characteristic topoplots. Left: i-TEPs with a peri-central origin. Below: approache to minimize artefacts.

GROUP MEMBERS

- · Senior Researcher Lasse Christiansen
- · Research Fellow Leo Tomasevic
- · Research Fellow Mikkel Vinding
- · Postdoc Armita Faghani
- · Postdoc Mads A.J. Madsen
- · Postdoc Mikkel Beck
- · Postdoc Angela Mastropasqua
- · Postdoc Björn Sigurdsson
- · Postdoc Xavier Corominos
- PhD Studs. Marie Louise Liu, Maria Drakaki, Mia Kolmos, Janine Kesselheim, Vytautas Labanauskas, Sofus Nygaard, , Salvatore Bertino, Marten Nyuts, , Kora Montemagno, Annamaria Palese, Mohammed Zeroual
- · NP Assistant Aino Jensen
- RAs Nora Raaf, Laura Sakalauskaitéé,
 Ditte Haagerup, Bilal Benoma, Chiara
 Cabras, Marlene S.G. Antunes, Thomas
 T. Thomsen, Jonas Laugesen, Iman
 brahim, Ann-Charlot Rughaven
- Master Studs. Arnheidur Sveinsdottir, Naiara Calvente, Kim Kürzel, Emelie Bougelet
- Stud. Assts. Mifuyu Hori, Lea Kukovec, Louise Mejer, Deniz A. Tankisi

HOMEPAGE

www.drcmr.dk/tms-group

KEY PUBLICATION

Transcranial magnetic stimulation of primary motor cortex elicits an immediate transcranial evoked potential, Beck MM, Christiansen L, Madsen MAJ, Jadidi AF, Vinding AC, Thielscher A, Bergmann TO, Siebner HR, Tomasevic L. Brain Stimulation 17, no. 4 (2024): 802-812

ELECTROENCEPHALOGRAPHY

The Electroencephalography (EEG) group is a method group, with main role of supporting researchers at DRCMR by facilitating studies conducted at the highest scientific level. The group's tasks include training researchers in laboratory usage, providing support for planning and conducting experiments, and offering advanced data analysis methods along with guidance on their application.

Another core task of the EEG group is to develop methods tailored to specific study requirements, with a primary focus on projects involving the combination of EEG and brain stimulation techniques. For instance, in 2022–2024, the Brain Stimulation and EEG Methods Group made a pioneering contribution to the TMS-EEG field. The team leveraged ultra-high EEG sampling rates and individualized coil positioning to uncover immediate TMS-evoked potentials (iTEPs) within the initial 10 milliseconds of a TMS pulse.

In addition, the group has developed open-source, Python-based software for online visualization of EEG metrics. The EEG-based Stimulation Monitoring (EStiMo) tool enables the real-time visualization of immediate effects and potential abnormalities induced during intervals between consecutive TMS bursts.

GROUP MEMBERS

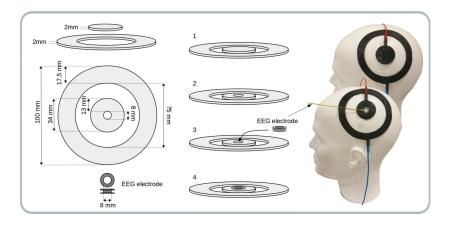
- · Research Fellow Leo Tomasevic
- · Postdoc Angela Mastropasqua
- · Postdoc Melissa Larsen
- · Research Fellow Mikkel C. Vinding
- · Postdoc Monica Biggio
- · Postdoc Mikkel Malling Beck
- · Postdoc Syoichi Tashiro
- · PhD stud. Janine Kesselheim
- · Postdoc Mads A.J. Madsen
- PhD stud. Anna Hester
 V. L. v.Themaat
- · MD Sebastian Strauss
- · Stud. Felix Schmidt
- · Stud. Albert Orero Lopez
- · Stud. Adam Ryszczuk

HOMEPAGE

www.drcmr.dk/eeg

KEY PUBLICATION

Relationship between high-frequency activity in the cortical sensory and the motor hand areas, and their myelin content, Tomasevic, L, Siebner, HR, Thielscher, A, Manganelli, F, Pontillo, G & Dubbioso, R 2022, ", Brain Stimulation, vol. 15, no. 3, 018, pp. 717-726.



The design of the hybrid electrode modified from the publication by Tashiro et al. "Probing EEG activity in the targeted cortex after focal transcranial electrical stimulation" in Brain Stimulation (2020 May-Jun;13(3):815-818).

METHODS CLINIC

We are an informal group running a biweekly clinic open to all members of DRCMR and their collaborators. Our goal is to provide assistance with almost any science-related question. We welcome inquiries from any domain (behavioral, neural, physical, etc.) and any data modality (behavioral, cognitive, MRI, fMRI, etc.). We offer help at any stage of the scientific process, including conceptualization, coding, data formatting, experimental design, analysis, and interpretation. Additionally, we assist with broader topics like responding to reviewers, writing grants and papers, and creating figures. Attendees may present a few slides outlining their questions or simply describe their queries verbally. Responses can range from brief to in-depth, taking anywhere from one to 90 minutes.

The clinic is chaired and organized by Ollie Hulme and Kristoffer Madsen, and answers are provided collectively by the group of attendees. Attendance is voluntary but encouraged based on individual research needs.

ORGANIZED BY

- · Senior Researcher Oliver Hulme
- Assoc. Prof. Kristoffer H. Madsen
 Clinic meetings are open to all members
 of DRCMR and their collaborators

HOMEPAGE

www.drcmr.dk/methods-clinic



The methods clinic in action.

READER CENTRE

Large cohort studies, clinical trials and biomedical research demand effective data management and even more specific and robust MRI techniques. The DRCMR Reader Centre takes pride in supporting such studies from idea to quality-assured results. This includes study planning, study coordination, MRI scan logistics, big data handling, ROI and lesion delineation, manual and automated data analysis, stakeholder communication and much more. All of these tasks are undertaken with a strong focus on continuous quality assurance while maintaining flexibility in regard to the needs of the individual study.

Lesion delineation and assessment is one of the focus areas of the centre, especially lesions related to multiple sclerosis and white matter hyperintensities (WMH). Drawing on the combined skills of the group and researchers at DRCMR, the Reader Centre has further refined its sensitive and reproducible algorithms to render the evaluation of lesions and lesion size more automatic and less dependent upon subjective assessment. Thus, the Reader Centre offers analysis of advanced structural MRI measures, such as brain segmentation, atrophy, lesion quantification and cortical thickness. Although most studies in the Reader Centre focus on the brain, MR images of other organs are also analysed in some studies, e.g. the spinal cord, liver and leg muscles. A major current undertaking is that the Reader Centre is co-ordinating the imaging part of the national multi-centre clinical trial DanNORMS in collaboration with the Danish Multiple Sclerosis Center. The Reader Centre is performing QA and data analyses for MR images acquired at 9 imaging sites across Denmark. The study has succesfully recruited a total of 594 MS patients that will be scanned up to 7 times each.

Restore FLAX Wast 27 FLAX Feedom See Resto 27 Feet

Cerri, Lundell et al. arXiv 2022

GROUP MEMBERS

- · Research Manager Karam Sidaros
- · Senior researcher Henrik Lundell
- Research Radiographer Jasmin
 Merhout
- · Research Technologist Sascha Gude
- Research Fellow Vanessa Wiggermann
- Research Fellow Enedino Hernández-Torres
- · Research Technologist Sussi Larsen
- · Student assistant Anastasia Weakley
- · Student assistant Carl Priisholm
- · Student assistant Nora Lill Evenstuen
- · Student assistant Olivia Christiansen

EXTERNAL COLLABORATORS

- Danish Multiple Sclerosis Center, Rigshospitalet
- Department of Clinical Medicine, Bispebjerg Hospital

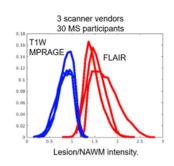
HOMEPAGE

www.drcmr.dk/reader-centre

KEY PUBLICATION

Linking lesions in sensorimotor cortex to contralateral hand function in multiple sclerosis: a 7 T MRI study, Madsen, MAJ, Wiggermann, V, Marques, MFM, Lundell, H, Cerri, S, Puonti, O, Blinkenberg, M, Christensen, JR, Sellebjerg, F & Siebner,

HR 2022, Brain, vol. 145, no. 10, pp. 3522-3535., 195



Comparison of lesion-to-normal-appearing-white-matter contrast across scanners from three difference vendors in the DanNORMS study. Lesions are automatically segmented.

MR SPECTROSCOPY

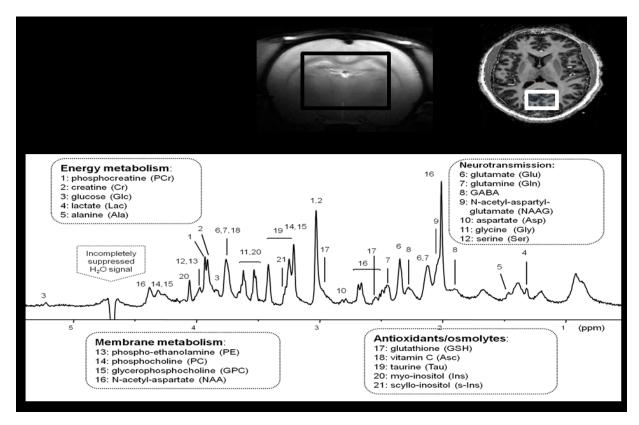
With the crucial evolution of MR Spectroscopy techniques over the past decades and the number of projects involving the measurement of metabolism both in the preclinical and clinical settings, it felt obvious that the DRCMR needed its very own MR Spectroscopy methods group, which proposes to join forces within the DRCMR for a better development and utilization of MRS acquisition, processing, analysis, and interpretation methods. We aim essentially at discussing and providing solutions to the development and use of protocols, MRS sequences, software, in-house tools etc.. We meet on a weekly basis or when somebody needs help with MRS. One of the main goals of our group is to make MRS available to all in the group. Notably, we aim to provide a platform with widely available tools and in-house developed tools. We started our very own MRS denoising challenge and efforts are on-going to be part of a very challenging but very powerful research topic.

GROUP MEMBERS

- · Senior Researcher Natalie Just
- · Senior Researcher Henrik Lundell
- · Lars Hanson
- · Vanessa Wiggermann
- · Kristin Hengel
- · Naiara Demnitz
- · Petr Bednarik
- · Alena Svatkova

HOMEPAGE

www.drcmr.dk/spectroscopy

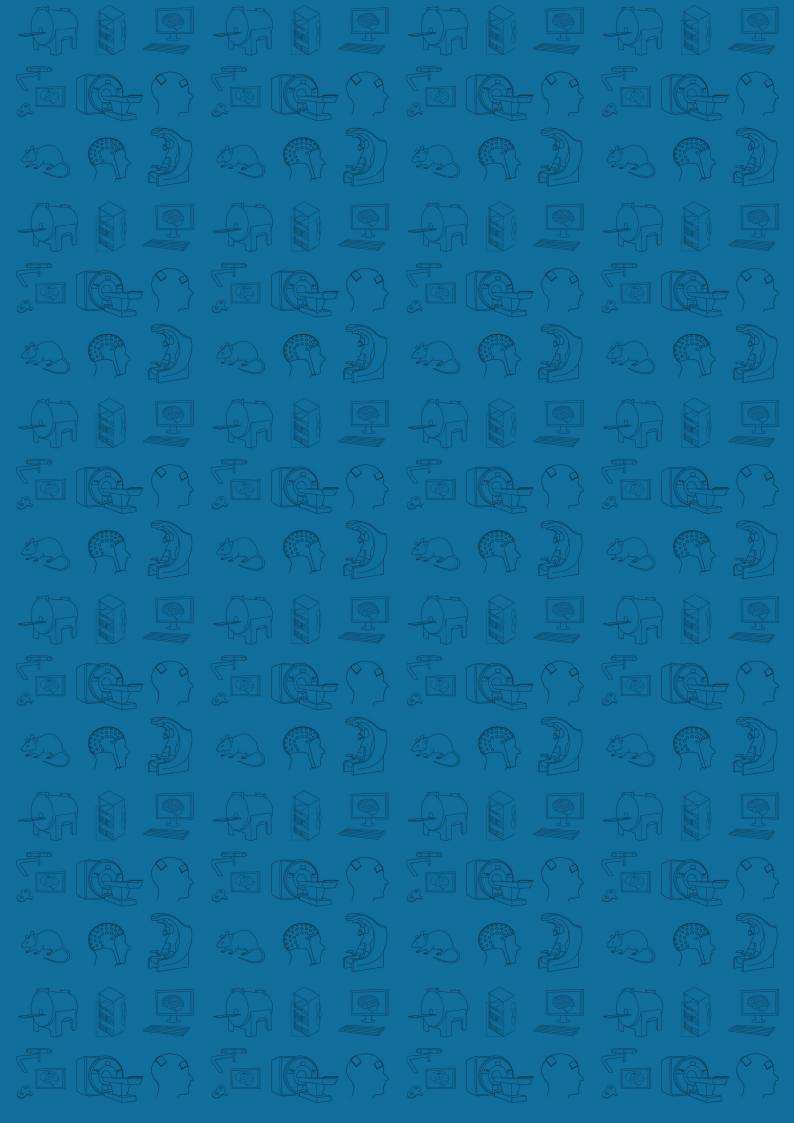


The proton neurochemical profile measured at high field strength. Up to 21 metabolite concentrations can be acquired within one 1H-MRS acquisition. These metabolites can be strong markers of disease progression.



ACTIVITIES

2022-2024 have been three dynamic years with many engaging activities and events at DRCMR. Our researchers have been extremely active, and their research results have attracted attention



ADVANCEMENTS AT THE NATIONAL 7T FACILITY

BACKGROUND

The Danish National 7 Tesla Project provides a unique platform for cutting edge imaging research open to all Danish research institutions. The first decade after the scanner's installation in 2014 identified, developed and optimized several key methodologies such as motion correction approaches. Together with the now possible fine-grained characterization of morphology and pathologies with high resolution imaging and metabolic profiling key insights into aging and neurodegenerative diseases, including multiple sclerosis and Parkinson's disease, have been obtained in smaller scale studies.

Now, the 7 Tesla Project has reached its second stage where these advancements and the built-up expertise by the users are harvested in applications in larger clinical cohorts. The implementation of standardized protocols and analysis pipelines has also lowered the threshold for starting up new projects. Despite common methodological foundations across projects, advancements in scanner hardware and software are still ongoing topics and are to a large degree integrated into specific clinical research projects.

STATUS

The current clinical research at 7T includes two large multiple sclerosis projects, a Parkinson's disease study, psychiatric cohorts with treatment evaluation in eating disorders and psychosis, and exercise interventions in healthy ageing.

A key factor for high resolution imaging is gradient performance. Integrating 'live' field measurements during the scan with the image reconstruction can immensely improve image quality and resolve noise related to motion and physiology. Hans Stærkind developed an exciting field measurement technology during his PhD project that finished in 2023. Utilizing the absorption spectrum of cesium gas, Hans built a quantum probe for measuring small gradient field perturbations on top of the static 7 tesla field. The benefit of this system is that it can be realized without any electronic components or metal parts that inevitably would interact with the scanner hardware. The project was supervised by Esben Thade Pedersen (DRCMR/DTU), Vincent Boer (DRCMR) and Prof. Eugene Polzik at the Niels Bohr Institute. In an ongoing collaboration, Hans is now

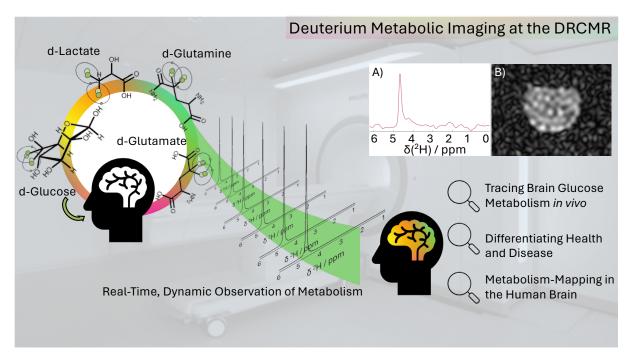
continuing the development of his probes and aims at a commercialization of his system. This endeavor is funded by Innovation Fund Denmark.

PhD student Kristin Engel is also addressing field fluctuations in experiments measuring metabolite diffusivity. Such experiments rely on strong gradient pulses but are also prone to noise in the acquisition of subtle signal components. Kristin is developing a phantom calibration framework that will be applied in upcoming clinical projects. The project is a part of the ERC funded C-MORPH project lead by Henrik Lundell.

An increasing number of projects also focus on X-nuclei spectroscopy, visualizing signal from non-hydrogen protons with MR methods. These techniques have a high specificity to certain metabolites that are otherwise masked by a large background signal from e.g. water. One interesting example is a new project on Deuterium Metabolic Imaging (DMI) initiated by Senior Researcher Petr Bednarik and funded by a grant from the Lundbeck Foundation. Heavy water or deuterated glycose can be administered to humans as a tracer and their dynamics in metabolic processes can be followed. These methodologies provide a perfect use case for 7T MRI where the high field strength is crucial for spectral sensitivity and specificity, providing a cheaper and less invasive alternative to PET.

A new line of methods is also being established by postdoc Kristian Mortensen. Kristian is translation his experience and interest in glymphatic clearance and CSF dynamics from animal research to humans in a collaborative project with Henrik Winther Schytz from the Danish Headache Center at Rigshospitalet Glostrup. Funded by a grant from the Novo Nordisk Foundation, the project is developing novel 7T methodologies to investigate CSF dynamics in patients with spontaneous intracranial hypertension, aiming at a better diagnostic and clinical management for this severe condition.

Associate professor Esben Thade Pedersen led the group from the very beginning but tragically passed away in 2023. His contributions for establishing 7T MRI research in Denmark cannot be underrated and he was an inspiring friend and colleague.



Conceptual Representation of the Deuterium Metabolic Imaging Study at DRCMR: Glucose metabolism in the brain and its changes can be a sensitive measure of brain health and disease. Administering deuterated glucose as a tracer allows us to isolate glucose metabolism in the brain and trace its conversion to metabolites such as lactate, GABA, and glutamine/glutamate. We aim to extract metabolic rates in healthy volunteers, advancing deuterium metabolic imaging as a method to reliably disentangle aerobic and anaerobic glucose metabolism pathways. A) Spectrum obtained from a phantom (spherical) B) ²H MEGE (Cocking et al., 2023) image of a phantom (spherical)

Since 2023, Research Fellow Vanessa Wiggermann and Associate professor Henrik Lundell are co-leading the group. Both are experienced 7T researchers and are well connected to both technical and clinical research projects at the department. Other 7T expertise and support have been provided by Michal Povazan and Jasmin Merhout. Since the end of 2024, after Michal moved on to other exciting opportunities in the Netherlands, the experienced MR Physicist Rasmus Hvass Hansen joined and provides now a strong support to the group.

The scanner's function is highly dependent on a good collaboration with the vendor and the support from a Philips clinical scientist. In this role, Jan Ole Pedersen was instrumental in establishing several structural imaging protocols. At the end of 2023, Paul de Bruin moved in from the Netherlands and is

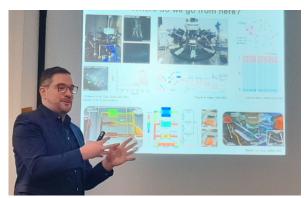
now an integral part of the local group. His general 7T expertise and his inputs into X-nuclei spectroscopy are important to a number of projects.

The ultra-high field group at DRCMR is also engaged in teaching. To share knowledge and to foster creativity in the team, a monthly session called "CRIT" (Crazy Idea Testing) is held. The sessions usually bring the whole group to the 7T scanner, when ideas that have been discussed over lunch are implemented and tested. The purpose of CRIT is manifold but includes sharing knowledge about method implementation, new research questions and provides a starting point for getting that first pilot dataset. The CRIT sessions are often preceded by journal clubs and data discussion.

BRAIN RESONANCE SEMINARS

In 2023, the DRCMR began a new seminar series: the Brain Resonance Seminars. In the Brain Resonance Seminars, external speakers are invited to DRCMR for a series of stimulating scientific talks and discussions. In addition, some talks within this series are part of the REFRESH initiative, which focuses on prominent female scientists who are invited to present their work and their career trajectories at the department. The REFRESH talks, titled "Women in Neuroscience", are supported by the Lundbeck Foundation.

The Brain Resonance Seminars are open to all interested attendees, and we hope that it will foster inspiring scientific discussions and new national and international collaborations. In 2023 and 2024, the seminars included 26 leading scientists, both nationally and internationally, spanning the fields of neurology, neuroscience, psychology, computer science and psychiatry. A full list of past speakers is given below, and a list of upcoming talks in 2025 is available on the DRCMR website.



Andreas Vlachos from University of Freiburg, presenting at the Brain Resonance Seminars

SPEAKERS IN 2023

- · Vibeke Koushede, University of Copenhagen
- · Jelena Radulovic, Aarhus University
- · Andreas Vlachos, University of Freiburg
- · Victoria Southgate, University of Copenhagen
- · Jakob Bardram, Technical University of Denmark
- · Sahil Bajaj, University of Texas
- · Micah Allen, Aarhus University
- · Angel Peterchev, Duke University
- · Warren Grill, Duke University
- Terry Jernigan, University of California San Diego
- · João Duarte, Lund University
- · Mark Schram Christensen, University of Copenhagen
- · Heidi Johansen-Berg, University of Oxford
- Gunhild Waldemar, University of Copenhagen and Rigshospitalet
- · Vibe Frøkjaer, University of Copenhagen

SPEAKERS IN 2024

- · Sâmia Joca, Aarhus University
- · Nanna MacAulay, University of Copenhagen
- · Rikke S. Møller, University of Southern Denmark, Odense
- · Per Petersson, Lund University
- · Laura Wisse, Lund University
- · Celia Kjærby University of Copenhagen
- Johanna Vannesjo, Norwegian University of Science and Technology, Trondheim
- · Peter Petersen, University of Copenhagen
- Nathalie Schaworonkow, Ernst Strüngmann Institute for Neuroscience, Frankfurt
- · Shannon Kholid, University British Columbia, Vancouver
- · Risto Kauppinen, Lund University, University of Bristol

REFRESH WORKSHOP

Achieving gender parity continues to be a challenge in Science, Technology, Engineering, and Mathematics (STEM) fields, particularly in senior and leadership positions. This also applies to the Danish Research Centre for Magnetic Resonance (DRCMR), where females are underrepresented in senior research positions despite comparable numbers of male and female PhD students and Postdocs.

The REFRESH (REtaining Female RESearcH talent at DRCMR: Supporting successful transition to senior research roles) initiative aims to tackle the gender imbalance at senior research levels at the DRCMR. The REFRESH initiative wishes to identify challenges and develop strategic initiatives for change to retain female research talent in neuroscience and promote and support female researchers' transition into senior academic roles.

REFRESH started in September 2022. We have currently had one workshop on bias awareness and have also organized a workshop for early career researchers on career development,

that took place in April 2024. All female postdocs, research fellows, and senior researchers, have been offered to participate in the mentoring program that we have initiated. We have developed a survey to identify obstacles and barriers in career development where the first round of answers have been collected. Finally, we have started our REFRESH seminar series, increasing the exposure to female role models.

The REFRESH group is working on the following topics:

- increase awareness of gender bias at the DRCMR through strategic workshop
- increase the visibility of female role models in neuroscience via a seminar series and related networking
- mentorship program for female researchers with academic career aspirations
- survey-based data collection to assess the current perception of gender bias in the department and track changes over time as a measure of the impact of the REFRESH initiative



REFRESH Workshop 2024

FOCUS ON COLLABORATION

Collaboration plays a vital role in research, especially at DRCMR. Researchers with different educational backgrounds and skills form an extremely cross-disciplinary research team, spanning medicine, psychology, physics, biology, data science and engineering. Yet, without our numerous collaborators we wouldn't be able to conduct the cutting-edge research we are currently pursuing at DRCMR! Our collaborators inspire our scientific environment and enrich our research.

STRONG TRANSLATIONAL COOPERATION

As a research centre situated at Hvidovre Hospital, our research is conducted with the objective to improve diagnosis and/or treatment of patients - or with the objective to improve prevention and promote health and wellbeing. We have strengthened our translational research by reinforcing the collaborative ties with the clinical research groups at our own hospital, Amager and Hvidovre Hospital, but also with other hospitals in the Capital Region of Denmark, especially Bispebjerg and Frederiksberg Hospital. We have strong collaborative ties with Bispebjerg and Frederiksberg Hospital thanks to Hartwig Siebner's affiliation to the Department of Neurology as Head of Research of the Movement Disorders Research Program and a collaboration on healthy aging with Prof. CJ Boraxbekk (DRCMR and Bispebjerg Hospital) and Prof. Michael Kjær's group at the Institute og Sports Medicine. We have for many years had a strong collaboration with the Danish Multiple Sclerosis Center at Rigshospitalet, led by Prof. Finn Sellebjerg and with the Mental Health Services of the Capital Region of Denmark (Profs. Anne Katrine Pagsberg, Merete Nordentoft, Poul Videbech and

Robert James Blair). But new collaborations have also been established with research groups at Herlev and Gentofte Hospital, Hillerød Hospital and Rigshopitalet.

VISITING PROFESSORSHIPS

In 2024, Professor James Rowe from The University of Cambridge revisited DRCMR for second visiting professorship. Professor James Rowe has been a close collaborator of DRCMR for many years and had a 5-month visiting professorship at DRCMR in 2019. Both stays at DRCMR were generously funded by the Lundbeck Foundation. James is a world-leading

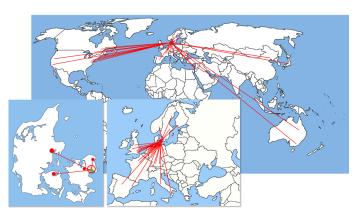
expert in frontotemporal dementia, Parkinson's disease and other neurodegenerative diseases. It was especially the movement disorders group that benefited from his engagement with ongoing projects, helpful comments and advice.

INTERNATIONAL COLLABORATIONS

We work together with many research sites all over the globe. In the field of biomedical 7T MRI, we closely collaborate with our colleagues at the Swedish 7T MR centre in Lund, and with researchers at the C.J. Gorter Center for High Field Magnetic Resonance at the Leiden University Medical Centre in the Netherlands. In 2022, we started three new Horizon Europe funded collaborative projects, CITRUS, FAMILY and TWINNIBS with collaborators in Austria, Germany, Czech Republic, The Netherlands, Latvia, Italy, Norway, Spain, USA, and Serbia. Running synergistic projects together, exchanging students, researchers, knowledge, and ideas help us to maintain a vibrant research environment. We have also strengthened our international collaborations in one of our major endeavours, the ADAPT-PD project, with Profs. Angela Cenci at Lund University and Andrea Kühn at Charité – Universitätsmedizin Berlin.

UNIVERSITIES IN THE CAPITAL REGION OF DENMARK

WWe continuously aim at enforcing our ties with our local university partners in the Capital Region of Denmark. We work together with researchers from multiple departments spanning four faculties at the University of Copenhagen. We also have a very fruitful collaboration with the Department of Technology.



nology at University College Copenhagen. Our closest regional university collaborations are with the Technical University of Denmark, where we have had strong ties with the Department of Applied Mathematics and Computer Science, and the Department of Health Technology for more than a decade. As a hospital-based research centre with a strong emphasis on biomedical technology, we offer an important hub bridging the technology-oriented research carried out at DTU with the clinically and applied research pursued at several academic hospitals in the Capital Region. The Capital Region and DTU have also initiated a more formal collaboration with the establishment of the Technical University Hospital of Greater Copenhagen (TUH) in 2024.

INDUSTRIAL COLLABORATION

We have for many years had a strong collaboration with the vendors of our MR-scanners, namely Siemens and Philips. We have close interactions with them on the latest developments and have held several joint workshops with Philips with a focus on technical optimizations at ultra-high field. Through the Innovation Fund Denmark project, Precision-BCT, we also have strong collaborations with Magventure and Localite on precision brain-circuit therapy.

ACADEMIC ALLIANCES

We encourage our researchers to have academic affiliations and to integrate their research as well as their research groups with other academic research environments. We believe that academic alliances make our researchers grow and enrich our local research environment with new possibilities, ideas and inspiration. During 2022-2024, we have two shared professorships and four shared associate professorships with DTU, one shared senior associate lectureship with University College Copenhagen (until 2023) and one professorship shared with Bispebjerg and Frederiksberg Hospital (until 2023). We have also established three new associate professorships at University of Copenhagen (Department of Neuroscience and Department of Psychology). And finally, Prof. Hartwig Siebner is professor at University of Copenhagen and also affiliated to Bispebjerg and Frederiksberg Hospital.

AXEL THIELSCHER

Prof. in neurophysics and neuroimaging

Technical University of Denmark, Department of Health Technology (DTU-HealthTech), Center for Magnetic Resonance

TIM DYRBY

Prof. in multi-modal medical image analysis

Technical University of Denmark, Department of Applied Mathematics and Computer Science (DTU-Compute), Section for Image Analysis and Computer Graphics

LARS G. HANSON

Assoc. prof. in magnetic resonance imaging

Technical University of Denmark, Department of Health Technology (DTU-HealthTech), Center for Magnetic Resonance

ESBEN THADE PETERSEN († Aug 2023)

Assoc. prof. in ultra-high field MRI

Technical University of Denmark, Department of Health Technology (DTU-HealthTech), Center for Magnetic Resonance

KRISTOFFER HOUGAARD MADSEN

Assoc. prof. in statistical machine learning for functional neuroimaging

Technical University of Denmark, Department of Applied Mathematics and Computer Science (DTU-Compute), Section for Cognitive Systems

KATHRINE SKAK MADSEN (until Mar 2023)

Senior assoc. lecturer in neuroimaging

University College Copenhagen, Department of Technology

CARL-JOHAN BORAXBEKK

Prof. of cognitive neuroscience of aging

University of Copenhagen, Faculty of Health and Medical Sciences, Institute of Clinical Medicine

And

Copenhagen University Hospital Bispebjerg and Frederiksberg, Department of Neurology

KARL MATTIAS RICKHAG

Assoc. prof. in neuropharmacology and genetics
University of Copenhagen, Department of Neuroscience

LASSE CHRISTIANSEN

Assoc. prof.

University of Copenhagen, Department of Neuroscience

OLIVER JAMES HULME

Assoc. prof.

University of Copenhagen, Department of Psychology

HARTWIG SIEBNER

Clinical Prof. with focus on precision medicine

University of Copenhagen, Faculty of Health and Medical Sciences, Institute of Clinical Medicine,

(sponsored by the Lundbeck Foundation - Grant Nr. R186-2015-2138).

And

Head of Research at Movement Disorders Research

Copenhagen University Hospital Bispebjerg and Frederiksberg, Department of Neurology

THE DRCMR IN THE NEWS!

The researchers at DRCMR and collaborators have not only been very productive during the last three years, they have also produced extremely interesting results. These results have triggered the interest of several Danish media. Below we present examples of the public engagement activities that DRCMR has contributed to in 2022-2024.

SPAGHETTI-LIKE AXONS

In an article on Videnskab.dk, part of Videnskab.dk's "Forskerne Formidler" series, postdoc Mariam Andersson and senior researcher Tim Dyrby discus groundbreaking research on the brain's communication pathways, revealing that axons, previously thought to be rigid cylinders, are actually flexible and spaghetti-like. This discovery, made using advanced 3D X-ray imaging, has significant implications for understanding and treating brain diseases such as multiple sclerosis and Alzheimer's. The research underscores the importance of accurate brain imaging for early diagnosis and personalized treatment, contributing to the advancement of neuroscience.



PUTTING CHIPS IN OUR BRAINS



An episode of the podcast series called "brainstorm" discusses the advancements and ethical considerations of brain-computer interfaces (BCIs). It focuses on Neuralink, a company founded by Elon Musk, which aims to develop brain chips enabling direct communication with digital devices. The article highlights a significant milestone where a monkey successfully played Pong using only its thoughts, showcasing the potential of BCIs. The discussion includes insights from Hartwig Siebner, head of DRCMR, and Thomas Ploug, professor at Aalborg University, emphasizing the need for ethical guidelines in BCI research.

ERC GRANT

Senior research, Tim Dyrby, received a 15 mill. DKK grant from the European Research Council in 2022. This was picked up by Dagens Medicin in an article describing the project, CoM-BraiN, which is described in a separate article in this triennial report.



Based on an article published by Dagens Medicin in March 2022.

FLIGHT OR FIGHT

In another article in Videnskab.dk's "Forskerne Formidler" series, research fellow David Meder explores new findings on Parkinson's disease. It reveals that patients with Parkinson's lose the ability to respond to surprising or frightening stimuli due to cell loss in the locus coeruleus, a small, spaghetti-like nucleus in the brain. This cell loss is linked to symptoms such as depression, apathy, and sleep problems. Using Denmark's most powerful MRI scanner, we have visualized this cell loss in living patients, providing insights into non-motor symptoms of Parkinson's. The study highlights the connection between locus coeruleus degeneration and issues like low blood pressure, emphasizing the need for further research to develop new treatments.



QUANTUM SENSING

A project led by Hans Stærkind, a postdoctoral researcher at the Niels Bohr Institute and the DRCMR, attracted considerable attention from several media. In the project Hans developed a groundbreaking magnetic field sensor that is fully compatible with MRI scanners. This innovative sensor, which uses laser light and gas, can detect errors in MRI scans without interfering with

the magnetic field. The prototype, currently housed at DRCMR, aims to improve the quality, reduce the cost, and speed up MRI scans. The research, supported by the Copenhagen Center for Biomedical Quantum Sensing, holds promise for significant advancements in MRI technology. Here are a couple of examples of the media that featured the news.

Young researcher has created a sensor that detects errors in MRI scans

QUANTUM SENSING Hvidovre Hospital has the world's first prototype of a sensor capable of detecting errors in MRI scans using laser light and gas. The new sensor, developed by a young researcher at the University of Copenhagen and Hvidovre Hospital, can thereby do what is impossible for current electrical sensors – and hopefully pave the way for MRI scans that are better, cheaper and faster.



healthcare-in-europe.com





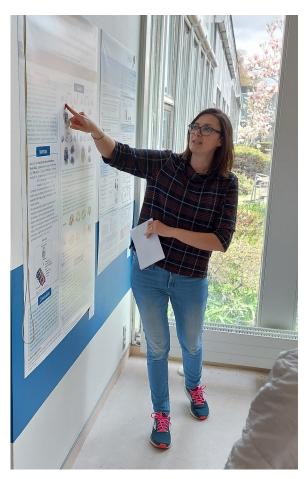
Image source: University of Copenhagen

A sensor that detects errors in MRI scans

Based on articles published by Copenhagen Univeristy (science.ku.dk) and healthcare-in-europe.com

RESEARCH DAY AT HVIDOVRE HOSPITAL

Every year, the hospital hosts a Research Day, where researchers from Amager and Hvidovre Hospital can present their work and network. The day offers talks by both senior and junior researchers, a pitch competition and poster walks. researchers from DRCMR are usually well-represented at each year's Research Day.



Postdoc Anna Plachti presenting her poster at the 2023 Research Day.

In 2022, postdoc Naiara Demnitz's abstract was 1 of 5 chosen for the yearly pitching competition out of a total of 112 abstracts accepted for the Research Day. Naiara's pitch was nicely delivered in a comprehensive language with clear slides. Her presentation was entitled "Is it all in the baseline? Trajectories of chair stands over 4-years and their association with grey matter volumes in a sample of Danish older adults" and was based on data from the LISA study. A total of 31 posters were presented by DRCMR researchers at the hospital research days during the years 2022 to 2024 with 2022 setting a record with 20 DRCMR abstracts.



Naiara Demnitz - research Pitch at AHH research day April 2022



DRCMR POSTERS AT THE ANNUAL RESEARCH DAY AT HVIDOVRE HOSPITAL 2022:

Anna Ver Loren van Themaat

Electrophysiological measures of interference control in children at familial risk for schizophrenia or bipolar disorder

Angela Mastropasqua: Probing the functional engagement of the left dorsolateral prefrontal cortex during intermittent theta burst stimulation

Anna Plachti: Multimodal brain profiles oi negative and positive emotionality traits revealed by a meta-analysis of a large brain-MRI data set shared in the EU-Life brain Consortium

Birgitte Liang Chen Thomsen: How does levodopa impact the cortex-basal ganglia circuits in patients with Parkinson's Disease?

Christian Bauer: Kardiovaskulær autonom neuropati, neurovaskulære kobling og kognitiv dysfunktion samt gastro-intestinal reaktivitet hos patienter med type 2 diabetes

Frodi Gregersen: Improving computational head models with current-induced magnetic field measurements by MRI

Lasse Christiansen: Tuning sensorimotor cortical integration by pairing digital nerve stimulation with transcranial stimulation of contralateral motor cortex

Line Korsgaard Johnsen; Interference control is more variable without a change in mean brain activity in healthy children at familial high-risk of schizophrenia or bipolar disorder

Mads Alexander Just Madsen: Linking metabolic changes in the primary sensorimotor hand area to individual motor impairment

Mariam Andersson: Delineating age effects on the microstructure of the acoustic radiation with diffusion MRI

Marie Louise Liu: Can topical application of numbing cream improve the efficacy of sham TDCS? Mattias Rickhag: Cortico-Striatal Circuit Manipulations to Evoke Parkinsonism in Mice

Mikkel Malling Beck: Characterizing dose and state dependency of early cortical responses to magnetic stimulation of the primary motor cortex using combined TMS-EEG

Naiara Demnitz: Is it all in the baseline? Trajectories of charr stands over 4-years and their association with grey matter volumes in a sample of Danish older adults

Peter August Rasmussen: Visualizing transcranial ultrasound waves With magnetic resonance - a new avenue for non-invasive brain stimulation

Sadaf Farkhani: Exploring Dynamic Brain Connectivity Through Aging Using Explainable Deep Learning

Seyedseina Hosseini: Accurate Computational Dose Modelling for Individualized Transcranial Focused Ultrasound Stimulation

Simon R. Steinkamp: A New Technique for Mapping Reward in the Brain

Søren Asp Fuglsang: Age-related changes in processing of noise sound stimuli along the auditory hierarchy: evidence from fMRI, EEG, and quantitative MRI

Vanessa Wiggermann: Characterization of the human cortex in multiple sclerosis with 7T MRI

Vytautas Labanauskas: Functional mapping of multiple brain networks with task based FMRI to delineate brain circuit dysfunction in treatment resistant depression.

VISIT FROM THR MINISTER OF ECONOMIC AFFAIRS

In October 2024, Minister for Economic Affairs Morten Bødskov visited the MRI section at Hvidovre Hospital to learn about the latest medical technology research - a quantum sensor developed by Hans Stærkind, a postdoc at the Niels Bohr Institute and the DRCMR. The new sensor, still in its prototype stage, aims to improve MRI scans by measuring and correcting the magnetic fields used in the scanning process. Although it has not yet solved specific problems, Hans Stærkind hopes that it will enhance the quality of MRI images in the future by correcting any inaccuracies in the magnetic field. During the visit, Minister Bødskov showed interest in the sensor's potential benefits for the healthcare sector and Danish industry. While it may take 5-10 years to fully develop and implement the sensor in Danish hospitals, this project represents a step forward for Danish research and health technology. The visit highlighted the hospital's ongoing efforts to advance medical technology in collaboration with leading research institutions.

The hospital management and research department leadership were present to discuss the project and its future prospects. The project underscores the hospital's commitment to improving healthcare through innovative research.



Morten Bødskov , Minister for Economic Affairs, with Hans Stærkind, a postdoc at the Niels Bohr Institute and the MRI research section at Hvidovre Hospital.

FORSKNINGSFESTIVAL CAFÉ HALGODT

In 2023 a handful of professors organized Research Festival for RegionH researchers. The event took place at café Halgodt in Skovshoved havn and was moderated by Peter Qvortrup Geisling. Each research group presented their view on future approaches to tackle the challenges in the Danish healthcare system.

At DRCMR we focused on non-invasive brain stimulation and showcased the network effects when stimulating motor cortex, and how effects are susceptible to state-changes such as increased effects on the motor system when lifting a beer. Shenanigans aside, the message stands: transcranial brain stimulation, when carried out with the sufficient precision, holds the potential to greatly mitigate neuropsychiatric and neurological symptoms. We thank the organizers for a well-planned and well-executed event.



Peter Qvortrup Geisling, the moderator at Forskningsfestival Cafe Halgodt.

OTHER SOCIAL ACTIVITES AT DRCMR

Every year, the DRCMR engages in many social activites, ranging from the annual christmas and summer partues, celebrating anniversaries of cherished employees, and participating in organised runs,. to name just a few:



25 Year Anniversary William Baaré



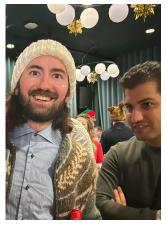
DHL Run 2024: H. Siebner, M. Novén, E. Hernández-Torres, S. Steinkamp & L. G. Hanson



The DRCMR Christmas Symposium in 2023



Christmas 2022: H. Lundell & F. Gregersen



Christmas 2024: B. Sigurðsson & A. Kangavari DRCMR Summer Party in 2022



POSITIONS OF TRUST

Hartwig Siebner:

- Editor-in-Chief (until 2022), Associate Editor (since 2023), Neuroimage Clinical (Elsevier)
- Board member, Editorial board, Brain Stimulation (Elsevier)
- Chairperson, Steering group, Danish Society for Medical Magnetic Resonance (DSMMR), until 2022
- Chairperson, Scientific Advisory Board, Danish Parkinson Association
- Vice-chairperson, Steering group member of the National Danish 7T MRI project
- Member, Steering group, National Swedish 7T MRI project
- Member, Steering group, National MR-scanner project at "Børneriget"
- Member, Steering group, NeuroGrad PhD School, Faculty of Health & Medical Sciences, Univ. of Copenhagen
- Co-speaker, Column "Motor & Pain Neuroscience", Neuroscience Academy Denmark, Column "Motor & Pain Neuroscience"
- European Society for Brain Stimulation, Board member as national representative for Denmark
- Member, Steering group, NeuroGrad PhD School, Faculty of Health & Medical Sciences, Univ. of Copenhagen
- Member, International Advisory Board, German Center for Brain Stimulation
- Member, International Scientific Advisory Board, German Parkinson Foundation
- Member, International Advisory Board, Research Training Group 2783 - Neuromodulation of Motor and Cognitive Function
- in Brain Health and disease (funded by the German Research Council), Carl von Ossietsky University, Oldenburg, Germany

Tim B. Dyrby:

- Associate Editor, Medical Image Analysis
- Coordinating Professor, The Technical University Hospital of Greater Copenhagen (TUH)
- Member of the Research Council at Copenhagen University Hospital Hvidovre
- Member of the Executive Committee of the Research Council at Copenhagen University Hospital Hvidovre
- Member, Steering group, National MR-scanner project at "Børneriget"

- Grant reviewer European Research Council, the European Synchrotron Research Facility (ESRF), Captial Region Hospital Foundation, and other international foundations.
- Organising committee, pre-conference workshop, Barcelona, Spain, The European Society for Magnetic Resonance in Medicine and Biology (ESMRMB)
- Organising committee, workshop, Microstructure by the Lake, EPLF Switzerland
- · Organizing the monthly online MicroClub talks

Carl Johan Boraxbekk:

- · Editorial Board member of Translational Sports Medicine
- Chair of the Aging theme of MIRAI (until 2022) a Japanese-Swedish research collaboration

Axel Thielscher:

- · Handling editor, Imaging Neuroscience
- · Editorial board member, Journal of Neural Engineering
- Member of the International Transcranial Ultrasonic Stimulation Safety and Standards consortium
- Grant reviewer: EU ERC, NSF (USA), NOW (Netherlands), MRC UK, DFG
- Member of PhD evaluation and scientific promotion committees at several universities (including Aalto University, Finland, KAIST, South Korea, Harvard University, Duke University)

Henrik Lundell:

- Grant reviewer: French National Research Foundation (ANR) and France and Wings for Life, Austria
- Board Member: ISMRM Nordic Chapter
- · Dutch MS Research Foundation

Vanessa Wiggermann:

- Vice-Chair of the ISMRM Nordic chapter (since 2024)
- · Board member of the ISMRM Nordic chapter
- Trainee board member of the ISMRM EMTP study group (in 2022)
- Editorial board member of Neuroimage Clinical
- Special Issue Editor Neuroimage Clinical (in 2022)
- · Grant Reviewer for the UK MS Society

Kathrine S. Madsen:

- · Grant reviewer for Duchenne Parent Project Netherlands
- · Grant reviewer for Riksbankens Jubileumsfond, Sweden

 Co-chairing the Sustainability and Advancement Committee in Fetal, Infant & Toddler Neuroimaging Group (FIT'NG) Society

Lasse Christiansen:

- Grant reviewer French National Research Foundation (ANR)
- · Grant reviewer Univeristé Grenoble Alpes

David Meder:

 Scientific Meeting Director and Board Member at Lundbeck Foundation Investigator Network

Karam Sidaros:

Member of RegionH steering committee for the implementation of electronic time recording in research projects

Leo Tomasevic:

 Board member of Associazione Ricercatori e Scienziati Italiani in Danimarca (ARSID)

Lars G. Hanson:

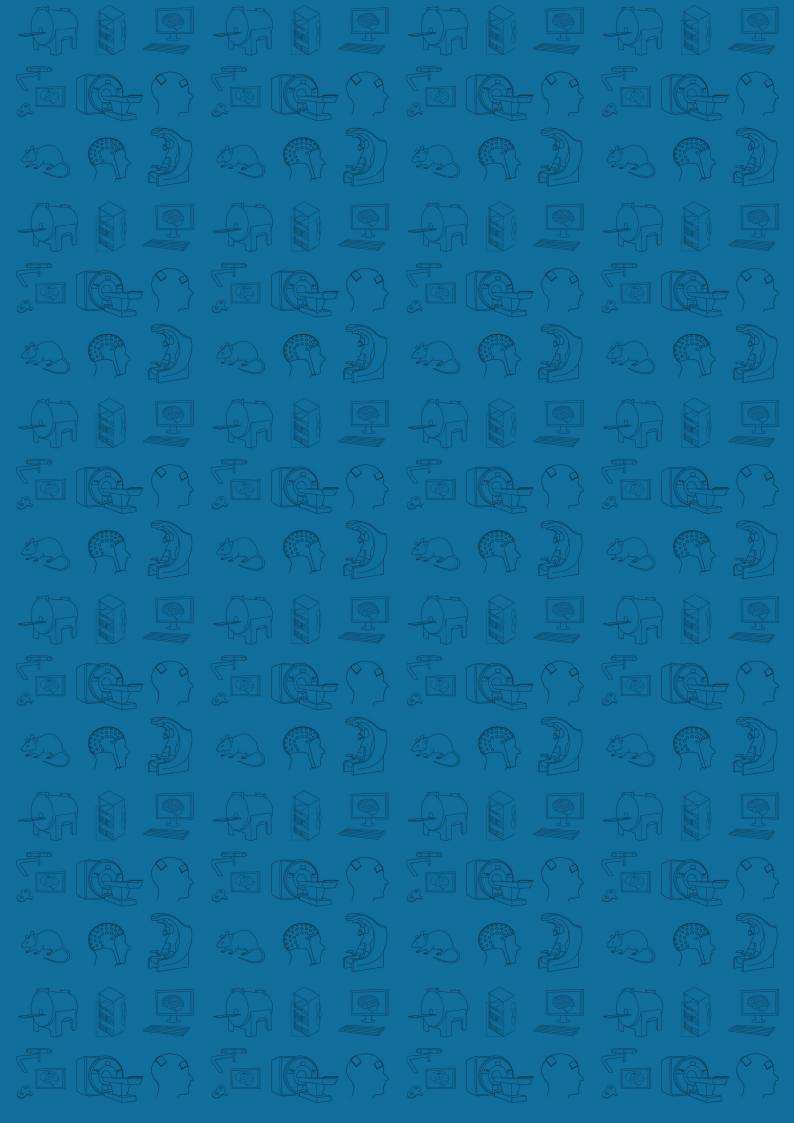
Chair of writing group for the Danish MR safety initiative on behalf of the societies DRS, DSMF, DSMMR and Radiografrådet

Mariams Andersson:

- Trainee Representative, Diffusion Study group, International Society for Magnetic Resonance in Medicine
- Co-Chairing, Gordon Research Seminar, Tissue Microstructure Imaging.

FOCUS ON EDUCATION

An education in neuroimaging is challenging for many reasons and there are a number of problems faced by most neuroimaging centres. Apart from removing ferrous-metallic objects from every possible pocket, these include issues as basic as how to understand one another. Part of the challenges is that students come from diverse backgrounds, mathematics, physics, biology, medicine, economics, psychology, and even further afield, each with their own terminologies, and the range of topics and techniques to master is often very wide. Typically, it is hard for a student to know what it is they need to know, and what it is they do not know. Our solution to this problem is to provide a wide-ranging curriculum that covers all the basic knowledge and skills necessary to follow what is going on at DRCMR and to be able to make an intellectual contribution whatever the topic. The curriculum comprises several courses and modules that most students are expected to take whilst at DRCMR.



EDUCATIONAL CURRICULUM AT DRCMR

An education in neuroimaging is challenging for many reasons and there are a number of problems faced by most neuroimaging centres. Apart from removing ferrous-metallic objects from every possible pocket, these include issues as basic as how to understand one another. Part of the challenges is that students come from diverse backgrounds: mathematics, physics, biology, medicine, economics, psychology, and even further afield, each with their own terminologies, and the range of topics and techniques to master is often very wide. Typically, it is hard for a student to know what it is they need to know, and what it is they do not know. We therefore provide a wide-ranging curriculum that covers all the basic knowledge and skills necessary to follow what is going on at DRCMR and to be able to make an intellectual contribution whatever the topic. The curriculum comprises several courses and modules that most students are expected to take whilst at DRCMR.

EDUCATIONAL CURRICULUM

At DRCMR we provide a wide-ranging curriculum that covers all the basic knowledge and skills necessary to perform the research we carry out.

DRCMR Methods Course

The internal DRCMR Methods course is a series of lectures and exercises that cover every major technique used at DRCMR as well as experimental design, data governance and neuro-anatomy.

Scanner Safety and Scanner License Courses

Scanner safety and scanner license courses are organized by the MR Methodology group. These courses give students the basic, necessary training to work in an MR environment, and the scanner license is the qualification that students need to acquire in order to autonomously operate an MR machine.

MRI Acquisition Course

Our yearly MRI acquisition course teaches the fundamental physics underlying the MR techniques employed at DRCMR. The course introduces MRI starting from a level requiring little or no MR experience. Lectures cover MR understanding, acquisition methods and parameters.



Image: Dejan Bozic © 123RF.COM

Matlab Course

Once or twice a year (depending on the need), we also have a Matlab course, which teaches the basic programming skills needed to understand and develop scripting for data analyses to students with no prior programming experience.

Copenhagen Brain Stimulation Week

Every autumn, we have our annual Copenhagen Brain Stimulation Week, which is an intensive four-day workshop providing participants with in-depth knowledge of the most common non-invasive transcranial brain stimulation techniques followed by a one-day international symposium on the latest developments within brain stimulation.

PhD Courses

Finally, our research areas organize week-long thematic PhD courses on their research in cooperation with the Graduate Programme in Neuroscience at the University of Copenhagen, Neurograd. The courses are usually arranged approximately once a year. In 2023, the Clinical Precision Imaging research area organized a course entitled Magnetic Resonance Imaging in Clinical Neuroscience: Potential & Pitfalls. The 2024 course was unfortunately postponed to 2025, where we will be organizing two courses.

PHD COURSE 2023

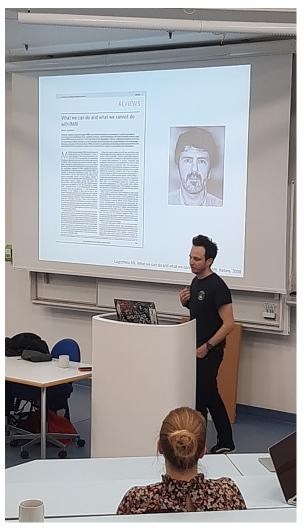
MRI-CLINICAL

In 2023, a comprehensive PhD course titled Magnetic Resonance Imaging in Clinical Neuroscience: Potential & Pitfalls was held at DRCMR, focusing on the application of MRI in clinical brain research. This course aimed to equip students with a deep understanding of MRI-based brain mapping techniques and their role in capturing brain pathology, pathogenesis, and pathophysiology. The course was originally planned for 2022, but was postponed to 2023.

By the end of the course, students were expected to gain insight into the basic principles of MR-based brain mapping techniques and understand how MRI can capture brain pathology, including neurodegeneration and neuroinflammation, as well as pathogenesis and pathophysiology such as circuit dysfunction and aberrant brain development. They were also encouraged to reflect on how decisions related to data acquisition, pre-processing, and analysis methods influence clinical outcomes obtained by MRI. Additionally, the course aimed to put into perspective key concepts of MRI-based biomarkers and precision medicine, enabling students to design, critically assess, and interpret MRI studies of brain disorders.

The course addressed the significant healthcare challenge posed by brain disorders, which are increasingly prevalent as populations age. MRI, with its unmatched resolution and versatility, is indispensable for diagnosing and managing brain disorders. The course provided a mechanism-centered and conceptual perspective on how MRI can contribute to clinical neuroscience, exploring how disease-inducing mechanisms like inflammation, degeneration, trauma, and impaired perfusion affect brain function and how these can be captured using MRI-based techniques.

Morning sessions introduced key "read-outs" of brain pathology, such as atrophy and network dysfunction, and how these can be revealed by MR-based brain mapping. Afternoon sessions focused on group work where participants applied the knowledge and concepts presented in the morning sessions. The course schedule included topics such as macrostructural brain MRI, covering atrophy, lesions, and macrostructural connectomics; microstructural brain MRI, focusing on tissue damage in the "normal-appearing" brain and tract-based struc-



Oliver Hulme presenting at the PhD Course in 2023

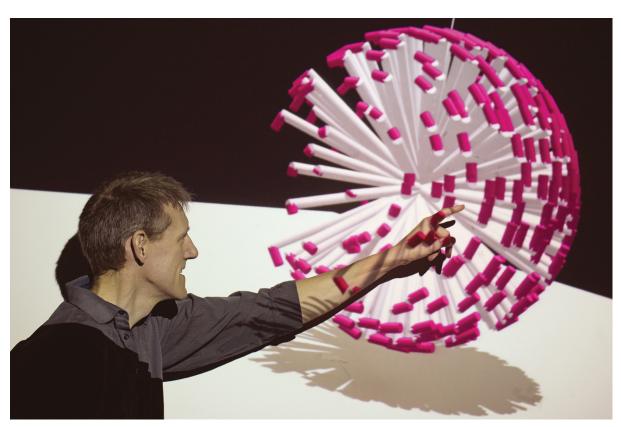
tural connectomics; functional brain MRI, probing alterations in functional brain activity and connectomics; metabolic/spectroscopic MR of the brain, involving neurometabolic profiling; and multimodal integration for multi-parametric assessment of pathology.

This course provided participants with the knowledge, skills, and competencies to effectively utilize MRI in clinical neuroscience, preparing them to design and interpret MRI studies of brain disorders with a critical and informed perspective. The course was attended by 14 PhD-students from the University of Copenhagen and the University of Aarhus.

MAGNETIC RESONANCE ACQUISITION COURSE

An educational highlight of the year is the annual DRCMR Magnetic Resonance Acquisition Course aimed at providing the participants with a solid understanding of fundamental MRI. These are both local and from other institutions where MRI is applied, not least hospitals. The course is typically given over approximately 7 afternoons in the fall, and is aimed at students of all backgrounds, new to MRI. Experienced users of MRI are often also among the participants, however.

MRI can be quite overwhelming with respect to both the vast range of applications and the interpretation of the recordings that simultaneously may reflect many tissue characteristics. The information derived from MRI may for example include shapes, volumes, molecular mobilities, chemical composition, magnetic properties, and even brain function. Measuring the parameters of interest and interpreting the results without being misled by MRI's sensitivity to other parameters, is a challenge. One ambitious goal of the teaching is that the students should become familiar with concepts, methods and terminology applied across most MR measurement techniques. Another goal is to dig deep and understand a few example applications in detail, especially contrast manipulation in structural sequences, functional imaging (fMRI) and diffusion-weighted imaging (DWI). A solid basis is both needed to perform measurements effectively, and to avoid the many pitfalls of MRI interpretation.



Demonstration of an excitation of a spin "ensemble" using self-made online MR simulation software. The MR Acquisition course is taught by Lars G. Hanson who is an Associate Professor and the Head of Biomedical Engineering MSc studies at DTU (photo: Jesper Scheel).

COPENHAGEN BRAIN STIMULATION WEEK

The 'COBS WEEK' consists of an intensive four-day workshop followed by a one-day symposium. The workshop provides trainees with in-depth knowledge of the most common non-invasive transcranial brain stimulation techniques (TMS,TES,TUS).



The week is tailored to researchers and clinicians who wish to gain extensive insight into the basics and state-of-the art application of non-invasive brain stimulation. The program covers basic physical and physi-

ological principles, electric field modelling, and a wide range of cognitive and clinical applications. We focus especially on multimodal combinations of NTBS with neuroimaging techniques such as EEG and fMRI and on the application of NTBS as precision medicine. All teaching modules are accompanied by hands-on sessions and demonstrations.

The COBS week finishes with a one-day symposium featuring talks from international experts on brain stimulation:

2022: Elsa Fouragnan, Friedhelm Hummel, Risto Ilmoniemi, Mikkel C. Vinding, Mikkel M. Beck, Marta Bortoletto, Leo Tomasevic, Christian Windischberger, Hartwig R. Siebner, Lærke Krohne, Mads A.J. Madsen

2023: Til Ole Bergmann, Miriam Klein-Flugge, Michael Nitsche, Sybren Van Hoornwewder, Axel Thielscher, Armita J. Faghani, Silvia Casarotto, Mads A.J. Madsen

2024: Laura De Herde, Jean-Francois Aubry, Rikke Kofoed, Salvatorre Bertino, Estelle Raffin, Til Ole Bergmann, Mark Hellett, Lasse Christiansen, Helen Barron, Saša Filipovic



Prof. Hartwig Siebner giving a talk at the Copenhagen Brain Stimulation Week in 2022.

METHOD GROUPS FOR RESEARCH DEVELOPMENT & TRAINING

There are several methods groups at DRCMR, each having a different set of aims and competences. There is no single template and each group is organized differently, however most groups meet on a weekly basis to discuss challenges, acute issues, new developments in the field, status of the labs, new projects, participation or organization of courses, workshops, and much else. Most groups have core members and then a large number of peripheral members attending meetings on a more ad hoc basis.

The method groups are essential for developing our research practices, as well as for ongoing methods training. Despite their diversity, the groups generally have three common aims:

1) Update and perform quality assurance on all methodology relevant for research in general and 2) Spread knowledge about innovative, upcoming methods and implement relevant novelties in an open and accessible manner for research staff and, finally, 3) Educate and support both students and researchers in methods relevant for specific experiments.



METHODS GROUPS AT DRCMR:

- MR Methodology
- · Methods Clinic
- · EEG The Electroencephalography Group
- · Brain Stimulation
- Spectroscopy
- Preclinical

Read more about the focus of each group at pp. 78-86.

STUDENT GROUP

WHO ARE WE?

The DRCMR student group consists of PhD students, research assistants, BSc and MSc students, visiting interns, and "research year" students. We meet on the last Thursday of every month to discuss topics relevant to junior researchers at DRCMR and listen to presentations from students or other colleagues.

OUR PURPOSE

We form the basis of a student network and encourage both academic and social exchanges between students at DRCMR. The talks given at the DRCMR student meetings are meant to lay the foundation for an academic toolbox that students can make use of during their studies, and to prepare students for their future careers. The presentations are given either by students themselves, or invited speakers, and are often angled towards

overarching research-related topics. For example, presentations include "How to write an article" and "How to find grants". Moreover, the student group acts as a forum for open discussion between students. The student group representatives work closely with the leadership to deliver the student consensus on various matters, in order to ensure an optimal study and work environment at DRCMR.

The student group meetings are also meant as a place where students can ask any question and receive advice from their peers. In this way, students new to DRCMR can quickly get to know their new workplace and colleagues. The student group is a place for academic growth, but also for having fun and experiencing the Danish "hygge".



Some of the members of the DRCMR student group.

TO BE OR NOT TO BE A STUDENT AT DRCMR

Every year we enroll a considerable number of students (BSc, MSc and PhD's), interns, volunteers, research year students and student assistants at DRCMR. Students are very important for our research milieu – they contribute to research and we consider it our responsibility to educate future researchers. We are keen on providing the best possible frames for the students with focus on a rich learning environment to help

them pursue their research dreams. The students normally join a research group, where they take part in theoretical and methodological discussions together with more established researchers at group meetings. Most of our students are also a valuable resource when experiments are carried out in our labs and many students even run their own experiments as part of their projects.

Christian del Agua Villa, MSc Neuroscience KU 2023 - Biomedical Engineering (BSc)

Age: 27 years old

Thesis: Acute murine models of Parkinsonism: Circuitry and behavioral insights

I am grateful to have chosen DRCMR for my master thesis. At first, the MR on DRCMR scared me, as I was not overly excited about magnetic resonance. However, I soon found that research at the DRCMR not only focused on MR, but also TMS, EEG, IT and preclinical animal research. At the DRCMR, the brain is the protagonist. My project was developed on animal models, studying the corticostriatal and nigrostriatal inputs into the basal ganglia using both an immunohistochemi-

cal and open-field murine behavioral approaches to better understand Parkinson's Disease. The

interdisciplinary nature of the DRCMR and the multiple viewpoints helped me integrate the clinical implications of my research question. As a student, being exposed to such



Mihai Atudorei, MSc Neuroscience KU 2023 - Biomedical Engineering (BSc)

Age: 31 years old

Thesis: A Chemogenetic Approach for Modulation of Excitatory Cortical Neuronal Subsets and Evoked Motor Behavior Repertoires in Mice

As part of my thesis, we worked with mice as a laboratory model, chemogenetically modulating glutamatergic cortico-striatal inputs of two distinct neuronal subpopulations: the IT-neurons (intratelencephalic) and the PT-neurons (pyramidal tract neurons). We then assessed behavioral metrics upon GPCR-ligand injection that evokes a motor response. Since the first day here at the DRCMR, I have been going to work with a smile on my face. Everyone here is astoundingly helpful, kind, and considerate. My master's thesis group was

quite small (3 people), but I can see this only as an advantage, where com-

munication is at its best and where a sense of conviviality can thrive. Socializing and asking (unending) questions was never an issue here. I enjoyed working here so much that starting a research assistant full-time position here to continue the subsequent work on my thesis was the best move I could have taken. I am deeply grateful for my supervisor.

Vlad Zalevskyi MSc - MSc student from Denmark

Age: 24 years

Study: Masters student at the Technical University of Denmark

Thesis: Synthetic Data and Contrastive Self-Suervised Training for Central Sulcus Seg-

mentation

Machine learning and deep learning are powerful and universal tools that can be applied in nearly any field. Being at the intersection of physics, medicine, image processing and DL, medical image analysis attracted me as one of the most challenging fields that can benefit from recent advances in Al and transform them into impactful solutions that affect people's lives. The Erasmus Mundus Joint Masters Degree in Medical Imaging and Applications aligned perfectly with my interests, offering a comprehensive curriculum encompassing everything from the fundamental physics of MRI to the development of state-of-the-art image analysis algorithms.

The final semester of my master's, dedicated to writing the thesis I have spent at the Danish Research Centre for Magnetic Resonance (DRCMR). My experience at DRCMR was undeniably the highlight of my master's journey, and I thor-

oughly enjoyed my time

there. I was pleasantly surprised by my colleagues' open and welcoming nature, many of whom became friends. The aspect that truly amazed me, however, was the culture of knowledge sharing, exemplified by the multiple seminars, workshops, and guest lectures held at the centre. Through this enriching environment, I gained a wealth of knowledge and skills. This experience further solidified my aspiration to pursue a career in academia, as I am excited to commence my PhD studies at the University of Lausanne later this year.

DRCMR is a perfect place to learn about the clinical and research applications of neuroimaging and I would highly recommend it to any students interested in exploring academic path in this field.

Alejandro Cortina Uribe, Intern 2023

Age: 29 years old Study: Intern

After working in the industry with radiological systems in Mexico, I wanted to dive deeper into the software for image acquisition and processing, and so I decided to come to Europe and study an Erasmus Mundus Joint Master Degree. During the master's, not only did I live around wonderful countries and meet amazing cities, but I also learned many skills regarding computer vision tasks and medical image processing.

For my thesis internship, DRCMR hosted me for 6 months to develop my thesis research focused on identifying Parkinson's Disease neurodegeneration patterns in MRI images, using artificial intelligence models. I've been beyond happy and satisfied to understand a bit more of the neuroscience

field and to learn from amazing people. I believe that anyone that is interested in applying Al tools

in the medical domain should spend some proper time with clinicians and researchers, since this field requires to find an appropriate motivation and research relevance.

I think DRCMR is the best place to involve into research as a junior, since one is constantly exposed to new topics, discussions, and state-of-the-art research, while having an excellent supporting team. I am very excited to continue working at the DRCMR for the following months as a research assistant, and work towards getting a PhD position in the future.



DISSERTATIONS

12 PhD candidates defended their theses at DRCMR in 2022—2024. Here we present selected candidates and their projects.

The PhD's where done in collaboration with The University of Copenhagen and The Technical University of Denmark.

DEVELOPING AND VALIDATING
REALISTIC HEAD MODELS FOR
FORWARD CALCULATION OF ELECTROMAGNETIC FIELDS WITH APPLICATIONS IN EEG

Jesper Duemose Nielsen

SUMMARY

Electroencephalography (EEG) is a technique that allows recording of brain activity in a non-invasive way by placing electrodes on the scalp. The temporal resolution of EEG is



very high (on the order of milliseconds), however, determining the spatial origin of the recorded signals is difficult. This is because the signals from different areas of the brain mix at each recording site (EEG sensor), a phenomenon known as "volume conduction". To reconstruct the neural generators of the recorded signal, we therefore need to "unmix" the data. This unmixing process (also known as source reconstruction) requires knowledge about various factors, e.g., the anatomy of the head, the conductivity of the different tissues, and the position of the electrodes during recording.

In this thesis, we first developed a pipeline for constructing anatomically realistic models of the head. Next, we showed how the accuracy of such a model affects our ability to model how brain signals propagate to the EEG sensor level. Finally, we explored the effect of these parameters on source reconstruction in EEG.

SUPERVISORS

Kristoffer Hougaard Madsen, DRCMR, DTU
Axel Thielscher, DRCMR, DTU
Lars Kai Hansen, DTU
Rong Xue, Chinese Academy of Sciences (CAS)

UNIVERSITY

Technical University of Denmark (DTU)

DATE OF DEFENCE

December 2nd 2022

WORKING TODAY

Postdoc at DRCMR

STIMULATION EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION ON THE CENTRAL AND PERIPHERAL NERVOUS SYSTEM: TARGET ENGAGEMENT VERSUS OFF-TARGET STIMULATION

Marie Louise Liu

SUMMARY

Transcranial Direct Current Stimulation (TDCS) is a noninvasive brain stimulation method with potential therapeutic effects. TDCS applies low-intensity DC currents through surface electrodes on the head, making it



accessible for clinical and home use. However, its therapeutic application faces challenges due to variability in outcomes among subjects and studies. Personalizing stimulation and understanding its effects on brain networks are critical. The dissertation comprises three studies on TDCS mechanisms in healthy individuals.

Study I evaluated off-target peripheral effects of bi-hemispheric MI-HAND stimulation in 30 healthy individuals using different montages. It found varied sensations aligned with the electrical current shape, affected by stimulation intensity and numbing agents. Dizziness suggested vestibular activation during TDCS. In Studies II and III, TDCS effects on cerebral blood flow (CBF) during and after stimulation were assessed using perfusion-based fMRI (ASL). Study II applied anodal TDCS of the left MI-HAND at different intensities (0.5 – 2.0 mA), but ASL showed inconsistent neuronal modulation and substantial individual variations in CBF.

SUPERVISORS

Prof. Hartwig R. Siebner, DRCMR

Prof. Axel Thielscher, DRCMR and DTU

Assoc. Prof. Kristoffer Hougaard Madsen, DRCMR and DTU Søren Asp Fuglsang, DRCMR

UNIVERSITY

University of Copenhagen

DATE OF DEFENCE

December 29th, 2023

WORKING TODAY

Resident (Neurology) at Rigshospitalet

COMING TO GRIPS WITH MOTIVATION: INTEGRATING MOTIVATIONAL CONTEXT INTO APPROACH AND AVOIDANCE BEHAVIOUR DURING GRIPPING

Sofie Nilsson

SUMMARY

People are better at approaching appetitive cues signaling reward and avoiding aversive cues signaling punishment than vice versa. This action bias has previously been shown in approach-avoidance tasks (AAT) involving flexion



(avoidance) and extension (approach) movements of the arm in response to appetitive or aversive cues. It is, however, not known whether appetitive or aversive stimuli also bias more distal dexterous actions, such as gripping and slipping, in a similar manner. Furthermore, it is not known whether these approach and avoidance actions are controlled by a common neural system that generalizes across effectors and stimuli. To this end we developed a modified version of the AAT, which required participants to grip ("approaching") or slip ("avoiding") a grip force device at the sight of appetitive and aversive stimuli. Healthy, male participants then performed the task during functional magnetic resonance imaging (fMRI). Participants were consistently faster to initiate affect-congruent actions (grip-appetitive and slip-aversive) compared to affect-incongruent ones (grip-aversive and slip-appetitive). This was present regardless of whether valence was signaled by graspable objects or faces. On a neural level, however, fMRI did not reveal brain regions where task-related changes in regional brain activation reflected affect incongruency independently of the cue category.

SUPERVISORS

Prof. Hartwig Roman Siebner, DRCMR Professor Axel Thielscher, DRCMR/DTU Research Fellow, David Meder, DRCMR

UNIVERSITY

University of Copenhagen

DATE OF DEFENCE

January 28th 2022

WORKING TODAY

Global Trial Manager, Novo Nordisk

PSYCHOLOGICAL AND NEURO-BIOLOGICAL PERSPECTIVES ON PEDIATRIC OBSESSIVE-COMPULSIVE DISORDER

Valdemar Funch Uhre

SUMMARY

My thesis aimed to evaluate the existing evidence for beneficial and harmful effects of cognitive-behavioral therapy (CBT) for pediatric obessive-compulsive disorder (OCD), and to



investigate the brain activation during inhibitory control in OCD compared with healthy controls. Results from a systematic review with meta-analysis of CBT trials suggested that CBT may be an effective treatment for pediatric OCD, but the certainty of the evidence was low for all assessed outcomes. Results from a systemativ review of fMRI studies revealed statistically significant convergence of reported case-control differences during inhibitory control in the bilateral dorsal anterior cingulate cortex (dACC). Preliminary findings from a neuroimaging study showed moderate evidence against abnormal brain activation during inhibitory control in OCD, and a positive correlation in the OCD group between symptom severity and activation of the right inferior frontal gyrus (IFG) during successful inhibition. My findings highlight a need for additional RCTs that minimize risks of bias to evaluate the effect of CBT. The bilateral dACC may be implicated in abnormal inhibitory control in OCD, and the right IFG could play a central role in the development and maintenance of OCD symptoms.

SUPERVISORS

Professor Anne Katrine Pagsberg, KU

Prof. Hartwig Siebner, DRCMR

Professor Kerstin Jessica Plessen, Lausanne University Hospital

UNIVERSITY

University of Copenhagen

DATE OF DEFENCE

June 13th 2023

WORKING TODAY

Clinical Pharmacology Specialist, Novo Nordisk A/S

ENABLING MULTIMODAL WHOLE-BRAIN INVESTIGATION FOR DRUG DISCOVERY

Johanna Perens

SUMMARY

3D imaging modalities enable preclinical brain imaging for studying disease mechanisms and developing therapies. One of the major challenges in the field has been the integration of data from in vivo MRI and ex vivo light sheet fluorescence



microscopy (LSFM). Furthermore, there is still a need for pipelines enabling unbiased analysis of LSFM-imaged whole brain volumes. This project addressed the issues by developing a multimodal mouse brain atlas and a voxel-wise statistics pipeline to facilitate the analysis and bridging of mouse brain datasets. The atlas combines MRI, LSFM, skull-derived stereotaxic coordinates, and Allen Institute's region delineations. The applicational value of these resources was demonstrated by comparing LSFM-imaged brain activity patterns induced by six body weight-lowering drugs. The screening of shared and distinct features of drug-induced activation patterns identified a set of brain regions, which may play a key role in body weight regulation. The outcomes of this project allow high-throughput, explorative investigation of complex processes as well as drug effects in mouse brains, and support anti-obesity drug discovery programs by identification of activity signatures in response to body weight-lowering drugs.

SUPERVISORS

Professor Anders Bjorholm Dahl, DTU
Professor Tim Dyrby, DRCMR and DTU
Dr. Jacob Hecksher-Sørensen, Gubra A/S
Dr. Casper Gravesen-Salinas, Gubra A/S

UNIVERSITY

Technical University of Denmark

DATE OF DEFENCE April 22nd 2022

WORKING TODAY

Research scientist at Gubra A/S

BRAIN FUNCTION CORRELATES OF INTERFERENCE CONTROL IN CHILDREN WITH FHR OF SZ OR BP

Line K. Johnsen

SUMMARY

Schizophrenia (SZ) and bipolar disorder (BP) are heritable, severe mental disorders viewed from a neurodevelopmental perspective. Limited knowledge exists about their etiology and pathogenesis. Investigating



familial high-risk (FHR) individuals can identify unbiased cognitive and biological markers. FHR individuals display cognitive impairments, notably deficits in interference control. Functional brain imaging studies reveal pre-symptomatic differences in brain function. However, neurocognitive aspects of FHR children remain elusive. This thesis aims to summarize task-related fMRI studies in FHR individuals and investigate interference control impairments in 11-year-old children at FHR of SZ or BP. Study I summarizes 19 papers, revealing no behavioral impairments but brain activation differences in working memory. Study II includes 147 children without psychiatric diagnoses, finding no overall behavioral or brain function aberrations in FHR individuals. Heterogeneity among studies impedes definitive conclusions. Future research should employ larger samples, narrower age ranges, and symmetrical recruitment criteria. Direct comparisons between FHR individuals of SZ and BP, as well as controls, could elucidate early pathogenesis stages, guiding precise treatment and prevention.

SUPERVISORS

Professor Hartwig Roman Siebner, DRCMR
Professor Merete Nordentoft, PCK
Postdocs Kit Melissa Larsen & Søren Asp Fuglsang, DRCMR
Senior Researcher Kathrine Skak Madsen, DRCMR
Senior Researcher William Frans Christiaan Baaré, DRCMR

UNIVERSITY

University of Copenhagen

DATE OF DEFENCE

January 19th 2022

WORKING TODAY

Postdoc at DRCMR

ADVANCING THE FOUNDA-TION FOR WHITE MATTER MODELING IN DMRI

Sidsel B. Winther

SUMMARY

Diffusion-weighted MRI (dMRI) is a special kind of MRI which utilises the magnetic properties of water molecules to track how these are moving inside the brain. Because the movement of the water molecules is restricted by



the nerve cells, their trajectories reflect the structure of these. However, the size of MRI voxels (volume pixels) is typically in the order of mm, while the diameters of axons are in the order of µm - about 1000 times smaller. Extracting the information entangled in the signal therefore requires intricate modeling. And this is not easy! In fact, this is the main challenge of dMRI. This PhD project has advanced the foundation for modeling the dMRI signal through two contributions. 1) By improving our understanding of how the magnetic properties of the water molecules interact with the magnetic susceptibility of the brain tissue. This interaction was known to cause a signal bias depending on the orientation between the axons and the MRI scanner. In this project, it was discovered that the orientationdependency can be utilised to reveal specific 3D structures of the nerve cells. This opens up new opportunities for the characterisation of changes to nerve cell structure inside the brain. 2) By tuning and validating a virtual brain tissue generator for the production of different realistic types of brain tissue. This enables the study of how dynamic properties of tissue impact the structures of nerve cells, and can be used to identify distinct dMRI signatures associated with specific dynamic events. These signatures can serve as novel disease biomarkers and enhance disease monitoring strategies.

SUPERVISORS

Professor Tim Dyrby, DRCMR

UNIVERSITY

Technical University of Denmark (DTU Compute)

DATE OF DEFENCE

April 10th 2024

WORKING TODAY

DeepSpin as an MRI Engineer

OPTICAL MAGNETOMETRY FOR MAGNETIC RESONANCE IMAGING

Hans Stærkind

SUMMARY

This thesis presents a novel optical magnetometer for high magnetic fields along with the first explorations of its applications in magnetic resonance imaging (MRI).



The magnetometer works by

continuously tracking a magnetic-field-dependent optical resonance in atomic cesium. A robust prototype, that can be operated in a hospital environment, has been developed and calibrated to an accuracy of a few parts-per-million. This has resulted in a novel — but still mature — technology, with specifications that compare favorably to conventional and commercially available methods for high-field magnetometry. The magnetometer has been used to map out two MRI sequences in an ultra-high-field scanner, and to detect temporal instabilities and spatial nonlinearities. This work establishes the field of optical magnetometry for MRI, with future possibilities including image corrections in e.g. error-prone sequences or MRI systems with relaxed technical requirements.

SUPERVISORS

Professor Eugene Simon Polzik, NBI

Associate Professor Esben Thade Petersen, DRCMR and DTU Research Fellow, Vincent Oltman Boer, DRCMR

UNIVERSITY

University of Copenhagen

DATE OF DEFENCE

November 28th 2023

WORKING TODAY

University of Copenhagen, Niels Bohr Institute DRCMR - Hvidovre Hospital

SHIELDED COAXIAL CABLE COILS FOR WHOLE HEAD AND NECK IMAGING AT 7T MRI

Sadri Güler

SUMMARY

Magnetic resonance imaging (MRI) is a versatile tool to image the human body. Among many of the advances achieved with MRI, one was the ability to work on the human brain and discover its functioning, as well



as helping to improve diagnostic capabilities. However, clinical MR systems in today's hospital services have a limited image quality. One way to achieve better images in MRI is to increase the static magnetic field intensity. However, a stronger magnetic field drives new challenges in the MR sensor design. One of the most commercially available sensor systems for head imaging at 7 Tesla MRI suffers from signal loss down to the neck. On the other hand, a new sensor, shielded-coaxial-cable coils (SCCs), has recently been given attention among MR researchers due to their flexibility in the placement on the human body. Although SCCs would be good candidates with their initial promise of flexible placement to extend the coverage of the head imaging at 7 Tesla MRI, researchers reported conflicting results on the working mechanism of SCCs. In this thesis, we first clarified the ambiguity in the literature and explained the working mechanism of SCCs. Then, we explored the alternative configuration setups to improve the signal quality with SCCs. Finally, we extended the coverage of a commercially available sensor system with SCCs and achieved whole head and neck imaging at 7 Tesla MRI. The new sensor is easily adaptable to research systems worldwide, and we believe it has strong potential to widen the horizon of brain research.

SUPERVISORS

Professor Axel Thielscher, DRCMR Vinvent O. Boer, DRCMR

UNIVERSITY

Technical University of Denmark (DTU)

DATE OF DEFENCE

August 29th 2024

WORKING TODAY

DeepSpin as an MRI Engineer

DYNAMIC TOMOGRAPHY IMAGING OF BIOLOGICAL STRUCTURES

Mette Bjerg Lindhøj

SUMMARY

Dynamic tomographic imaging can visualize 3D biomechanical systems in action at a very high resolution. Very few imaging techniques make this possible, which makes the modality very desirable for answering questions



about the dynamics of biological samples. However, dynamic tomographic imaging of biological samples is complex for three reasons. Firstly obtaining contrast in living soft tissue can be difficult. Secondly, the sample is exposed to ionizing radiation during imaging, which is harmful to live samples. Finally, dynamic tomographic reconstruction is complex, and the approach depends on the dynamics of the object. In this thesis, sperm cells were chosen as the sample of choice because studying their 3D tail-beating pattern is important for understanding factors related to fertility. Furthermore, sperm cells are an excellent object for probing the limits of 3D dynamic imaging systems because they are small, fast-moving and easy to come by. The main results presented are threefold. Firstly, a nontoxic labelling method based on iron-oxide nanoparticles was developed for imaging the sperm, and it is shown that labelling with nanoparticles is also practical for dynamic tomographic reconstruction. Secondly, a practical approach to assessing the functional radiation damage caused to living sperm by synchrotron radiation is presented. Finally, a high-level parallel programming approach to tomographic reconstruction was developed, which is hardware-independent and especially well suited for speeding up sparse reconstruction

SUPERVISORS

Professor Tim Dyrby, DRCMR

UNIVERSITY

University of Copenhagen

DATE OF DEFENCE

March 25th 2022

WORKING TODAY

Akutberedskabet as a Data Analyst

INVESTIGATING THE NEUROBIOLOGICAL MECHANISMS OF OPTOGENETIC STIMU-LATION OF TRANSCALLOSAL PATHWAYS USING MULTIMODAL IMAGING TECHNIQUES

Christian S. Skoven

SUMMARY

The mammal brain is comprised of cortical and subcortical gray matter regions, interconnected by densely packed white matter fiber bundles – with corpus callosum (CC) being the major commissure. The aim of this



multimodal project was to investigate the structure-function relationship of the neuronal "wires" that govern the electrochemical interhemispheric signaling in the brain. Specifically we wanted to link structure and function of the transcallosal pathway connecting the bilateral primary motor cortices (M1) in rats. The function was investigated using unilateral optogenetic stimulation in the M1 and recording the transcallosal evoked response as local field potentials with electrodes in the contralateral cortex. As optogenetics is used with varying stimulation parameters, my first study systematically investigated different parameter combinations, demonstrating a relatively invariant temporal latency of the evoked potentials within subject. The structure was then investigated using ex vivo diffusion MRI and histologically with transmission electron microscopy (TEM). My second study specifically linked the measured axon diameters (from MRI and TEM) in the projection region of CC, with the measured conduction velocity (from electrophysiology) - uniquely in the same animals.

SUPERVISORS

Prof. Hartwig R. Siebner, DRCMR
Assoc. Prof. Tim Bjørn Dyrby, DRCMR
Professor Bente Pakkenberg, Bispebjerg Hospital
Assoc. Prof. Duda Kvitsiani, DANDRITE, AU

UNIVERSITY

University of Copenhagen

DATE OF DEFENCE

August 4th, 2022

WORKING TODAY

High Field MRI group, CFIN, Aarhus University, Denmark

MULTIMODAL IMAGING OF THE SUBSTAN-TIAL SUBSTANTIA NIGRA AND LOCUS COERULEUS IN PARKINSON'S DISEASE. A NEUROIMAGING STUDY OF NEURO-MODULATORY BRAINSTEM NUCLEI ASSESSED USING ULTRA-HIGH FIELD MRI

Christopher Fugl Madelung

SUMMARY

In my thesis, I mapped two key neuromodulatory brainstem nuclei in Parkinson's disease (PD) with ultra-high field magnetic resonance imaging (MRI). The thesis consists of two studies which were carried



out at the DRCMR at Copenhagen University Hospital Amager & Hvidovre in the same cohort of patients and healthy volunteers. In my first study used neuromelanin sensitive and iron sensitive MRI to evaluate loss of dopaminergic neurons and iron accumulation in substantia nigra. Finally, I investigated correlations between these PD related structural changes in the substantia nigra and lateralized motor symptoms. Both neuromelanin loss and iron accumulation was most pronounced in a region corresponding to the dopamine-rich nigrosome-1. In my second study, I found that structural disintegration was most pronounced in the caudal part of the nucleus as opposed to the predominantly rostral disintegration seen in Alzheimer's disease. I also found a strong association between loss of LC integrity and autonomic dysfunction indexed by orthostatic change in systolic blood pressure as well as a weak but interesting association with apathy. The results show that MRI at 7T can trace the structural correlates of PD in key nuclei of the brainstem bearing great potential for longitudinal MRI studies on the course of the disease.

SUPERVISORS

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UNIVERSITY

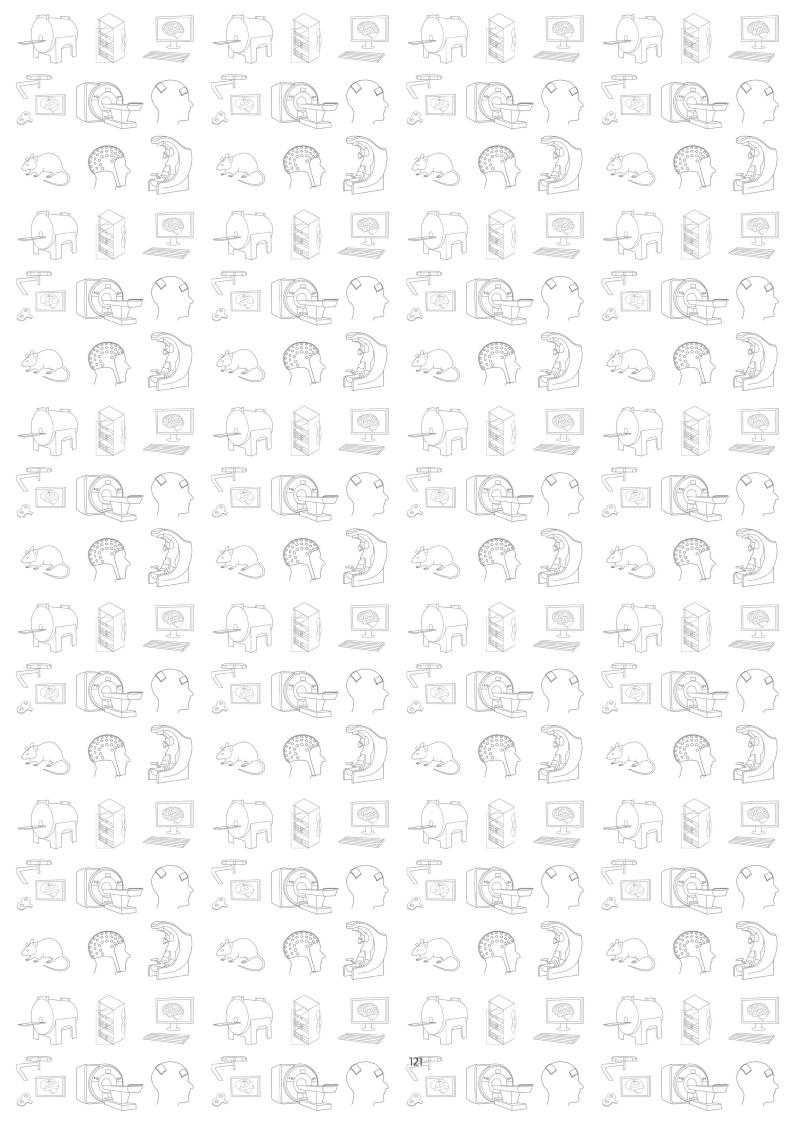
University of Copenhagen

DATE OF DEFENCE

December 2nd, 2022

WORKING TODAY

Bispebjerg Hospital as an MD, PhD



WHO WE ARE

66

Coming together is a beginning, staying together is progress, and working together is success."

- Henry Ford



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ESBEN THADE PETERSEN

10 OCTOBER 1973 - 20 AUGUST 2023

It was with great sadness that we received the news that senior researcher Esben Thade Petersen passed away in August 2023 after a seven-year battle with cancer. Esben was the 7 Tesla Group Leader at DRCMR and Associate Professor at DTU Health Technology.

Esben made numerous contributions to the MRI research field, spanning from perfusion methodology to sequence developments at ultra-high field MRI. An example of his extraordinary talent is that already as a Ph.D. student, he pioneered the so-called QUASAR arterial spin labeling technique, which allows for the simultaneous acquisition of cerebral blood flow, arterial transit time, and arterial blood volume. For this, he was awarded the I.I. Rabi Young Investigator Award by the ISMRM in 2005.

This award is an impressive accomplishment, and in Esben's case, it holds even more significance as he competed with applicants who could be five years post-completion of their Ph.D.

At DRCMR, Esben played a pivotal role in establishing and running the national 7 Tesla facility. He joined DRCMR in 2014. Esben was active in several Danish, Nordic and international MR societies, as well as MR community initiatives. At both DTU and DRCMR, Esben was a highly regarded lecturer, mentor and supervisor.

Esben was a great colleague and friend, full of warmth and care for those around him. He left us with many fond memories, and he is dearly missed. Our thoughts are still with Esben's family.



Esben Thade Petersen, PhD

COMING TO DRCMR

We have welcomed many new talents during 2022-2024. They bring valuable knowledge and experience from their previous positions and help us develop and grow.

Here we introduce the postdocs and research fellows who are new to DRCMR the past three years and a bit about their backgrounds.

Adam Kaminski

I joined DRCMR in October, 2024 as a Postdoctoral Researcher. I completed my PhD in September, 2024 in Interdisciplinary Neuroscience at Georgetown University in Washington, DC, USA. My studies focused on childhood psychiatric comorbidity by investigating a general factor



of psychopathology, or "p-factor", and its relation to individual differences in flexible cortico-cortical and striato-cortical functional connections supporting executive control behaviours. My dissertation was entitled "Transdiagnostic Alterations in Functional Connectivity Flexibility Supporting Executive Control in Childhood Psychopathology". At DRCMR, I am working on The Danish High Risk and Resilience, or VIA, study, a longitudinal study of at-risk children based on parental diagnosis of schizophrenia or bipolar disorder. The VIA study is very well-aligned with my interests in characterizing risk and protective factors of childhood psychopathology, and in particular in identifying markers of general psychiatric risk, independent of specific signs and symptoms. I will employ multimodal imaging techniques, and my first project will investigate normal and abnormal development of cortical microstructure. Future projects will employ task-based fMRI. The DRCMR is a vibrant, supportive, and highly collaborative space, and I am greatly looking forward to working with such a dynamic team.

Aino Jensen

I joined DRCMR in September 2023 as a Neurodiagnostic Technologist. My responsibilities at DRCMR is partly supporting the different treatment experiments and partly being an office manager in Center E. I previously worked at Roskilde Sygehus as a Neurodiagnostic Techonologist for 10 years and before



that, I work abroad in Saudi Arabia and the USA for 8 years. Throughout my career, my focus have been on MEP and Nerve Conduction Studies. I joined the DRCMR because I was eager to be part of developing new and precise treatments for a variety of patients groups to ease their challenges with Parkinson's, Multiple Sclerosis and Major Depression. I enjoy having moved from being part of giving patients a diagnosis to be part of finding

new and improved ways to ease their symptoms together with an excellent group of researchers from all over the world.

Alena Svatkova

I initiated my combined clinical and research position at the Radiology Department and DRCMR in April 2022. I have cultivated my clinical and research background in neuroradiology, with a particular emphasis on structural brain connectivity mapping and quantitative white matter assessment, through my



fellowship at the Brain Center Rudolf Magnus in Utrecht, the Netherlands, and subsequent postdoctoral positions at the Department of Pediatrics, University of Minnesota, and the Medical University of Vienna, Austria. My translational research work focuses on multimodal projects at both high-field (3T) and ultra-high-field (7T) human MR systems, where I integrate the latest technological advancements into clinically relevant research. Previous collaborations with accomplished translational research teams have enabled me to address the challenges associated with MRI acquisition and automated analysis in morphologically abnormal central nervous systems, commonly observed in pediatric brain diseases and adult neurological and psychiatric disorders, including Parkinson's disease, multiple sclerosis, and schizophrenia. My previous research received support from fellowship grants from the University of Pennsylvania and the University of Minnesota, as well as the Marie-Sklodowska Curie award from the European Committee. My current appointment allows me to translate my radiological expertise into clinical research projects with the aim of establishing MR markers of neurological and psychiatric disorders.

Amin Ghaderi Kangavari

I joined DRCMR in May 2023 as a Postdoctoral Researcher, working on the OPD and 7TPD projects. My primary focus in these projects has been the development of computational models for reinforcement learning, specifically hierarchical behavioral processes



in Parkinson's disease (PD) during novel probabilistic learn-

ing tasks. I aim to investigate the reasons behind impaired feedback-based learning in PD and explore whether dopaminergic treatments can modify these impairments. Recently, I also became part of an international collaboration under the ADPT-PD project, led by DRCMR. My responsibility is to analyse dynamic EEG activity and behavior during the cognitive control to understand both motor and non-motor symptoms of PD in ON and OFF dopaminergic medication states. Previously, I did research on model-based cognitive neuroscience, particularly using the hierarchical Bayesian drift-diffusion model to estimate and predict latent parameters of perceptual decision-making. I developed integrative neurocognitive models to link EEG and behavioral data at the single-trial level.

Armita Faghani Jadidi

Since my Bachelor, I have studied in the field of Biomedical Engineering and conducted projects related to neuroscience and acquired theoretical and practical skills in this field. My main interests are in neurorehabilitation techniques and biological signal processing. I have experience with several



modalities, including but not limited to EEG, TMS, and MRI, to investigate the underlying mechanism of neurological disorders and therapeutic non-invasive intervention. During my doctorate studies, I investigated the modulatory effect of novel temporal pattern of peripheral electrical stimulation on cortical and corticospinal levels, which eventually helped patients with chronic pain.

In the spring of 2022, I moved to the DRCMR as a postdoctoral researcher to expand my research towards transcranial neurostimulation techniques and joined this multidisciplinary group that develops a novel precision brain-circuit therapy (Precision-BCT) for the treatment of therapy-resistant depression. My focus within the Precision-BCT project is to advance EEG-based monitoring of the functional "target engagement" of dorsolateral high-frequency repetitive TMS (rTMS). The Danish Research Centre for Magnetic Resonance (DRCMR) is one of the leading research centers in Europe within the field of biomedical MRI. A Highly profiled research team and unparalleled DRCMR facilities in non-invasive brain stimulation modalities make it a solid fundament to continue my research. Moreover, this center has extremely strong international collaborators, which gives me the valuable opportunity to expand my network.

Björn Sigurðsson

I joined DRCMR in February 2023, right after I finished my PhD at the University of Copenhagen. My background is in computer science, and my PhD work was on imaging modalities for pre-clinical neuroscience. As a postdoc at DRCMR, I study ultrasonic brain stimulation and how to use MR images to point the



ultrasound at the right brain area. I didn't know much about brain stimulation when I started working at DRCMR but I have definitely learned a lot about it since I started. I find it fascinating that, at some point in the future, we may be able to treat patients with neuronal diseases by precisely stimulating the relevant brain area without disturbing unrelated brain areas. I spend most of my time programming and training neural networks to process MR images to make the stimulation even more precise. I enjoy my work, and I really like the people I work with. It's a very international community and people come with different experiences and expertise.

Emma Thomson

Prior to joining the DRCMR I did my PhD in Magnetic Resonance Physics at the Centre for Medical Image Computing at University College London. My work there focussed on development of novel MR sequences for in vivo contrast agent free blood brain barrier imaging. Additionally, I spent some time working as



a trainee Physicist at the National Coordinating Centre for the Physics of Mammography in Surrey, UK working on virtual clinical trials of novel imaging methodologies in X-ray mammography.

I have recently joined the DRCMR in November 2023 to work with Tim Dyrby as part of the Microstructure and Plasticity group on the eXtreme CT project. This work focuses on preclinical cytoarchitectural mapping combining information from both MR and synchrotron radiation CT images. I am excited to combine my expertise in MR physics and sequence design to explore the limits of MR and synchrotron imaging and expand our knowledge of brain microstructure.

Ikko Kimura

I joined DRCMR as a Post-doctoral Researcher in September 2024. My life goal is to develop or improve the neuromodulation and neuroimaging techniques for human applications. For that purpose, after finishing my residency, I worked on revealing the relationship between microstructural properties



revealed with diffusion MRI and repetitive Transcranial Magnetic Stimulation (rTMS) after-effect as a Ph.D. student at Osaka University. I then did a postdoc at RIKEN, Japan to improve MRI techniques.

I'm currently working at Neurophysics Group headed by Prof. Axel Thielscher. Here, I'm trying to further improve Magnetic Resonance Current Density Imaging (MRCDI) technique, which evaluates the magnetic field induced by transcranial direct current stimulation (tDCS). This technique provides a means of verifying the simulation results of tDCS to the brain. This also estimates the conductivity on each tissue for every individual, which is important not only for simulating the neuromodulation effect but also for source localisation of electro- and magneto-encephalography data. I have enjoyed working at DRCMR so far. This centre offers a wonderful working environment: excellent neuromodulation and neuroimaging facilities and opportunities for interdisciplinary work. I have benefited from researchers with different backgrounds and I firmly believe that this is the best to place to develop my scientific career. I would really love to contribute to DRCMR.

Janine Bühler

My research interests centre around the neuropathophysiological characterization of neuropsychiatric disorders using neuroimaging tools, aiming to deepen our understanding and improve treatment strategies. Furthermore, I'm particularly fascinated by the development,



maturation, and plasticity of the brain in children. I completed my PhD in Health Sciences (Neurosciences) at the University Hospital Inselspital Bern (CH), where I focused on functional neurological disorders (FND) and subsequently continued this

research line during a postdoctoral position at the University of Fribourg (CH). In July 2024, I was thrilled to join the DRCMR's Developmental Psychiatry group where I now have the opportunity to merge my interests by studying neuropsychiatric conditions such as psychosis and obsessive-compulsive disorder in children and adolescents. The DRCMR offers a unique and stimulating environment and I am enjoying the interdisciplinary collaborations and outstanding in-house expertise. I am excited to expand my skills, contribute to the team, and be part of the ongoing research ambitions in Copenhagen and at the DRCMR.

João Lima

I have a background in experimental psychology and behavioural neuroscience, with a focus on mechanisms underlying learning, memory, and altered emotionality in animal models. At the DRCMR, I am now part of Professor Tim Dyrby's ERC-funded CoMBraiN project (Conduction



velocity mapping in the brain network in health and disease) and the Microstructure and Plasticity (MaP) group. I will investigate how neurodegenerative and demyelinating diseases impact brain function by impairing the speed of neuronal communication. My approach involves manipulating brain structure and function in rodents and investigating the consequent alterations in the electrophysiological properties of the targeted neuronal populations. I will combine various techniques, including optogenetics, in vivo electrophysiology recordings, MRI, immunohistochemistry, and 3D imaging.

Kristian Nygaard Mortensen

I joined DRCMR in February 2022 as a postdoc to participate in the ETLAS2 trial, examining the effects of treating cerebral small vessel disease-patient with taladafil, a vasodilating drug, on the cerebrovascular system using arterial spin labeling and calibrated fMRI. Before joining



DRCMR, I did my PhD at the Center for Translational Neuro-

medicine, Copenhagen University. Here, I used preclinical MRI, single-photon emission tomography, and fluorescent microscopy to study the recently discovered glymphatic system, which utilizes a circulation of cerebrospinal fluid to clear the brain tissue of neurotoxic metabolic waste. Continuing this work at DRCMR, my goal is to translate the preclinical findings to humans using our 7T human MRI by developing and applying new MRI sequences to measure CSF production and exchange with brain tissue. Working at DRCMR has so far been a great experience for me. In-house, there's both broad and deep expertise in different MRI techniques which has enabled me to pursue novel and experimental MRI techniques. And the centre has an extensive network within the medical community as well as physicists and engineers, giving rise to new and exciting collaborations. The atmosphere is relaxed, fun, and driven by a multitude of diverse research interest.

Mahsa Amirrashedi

In May 2023, I joined DTU & DRCMR for my second postdoctoral position. Prior to this, I completed my PhD in Medical Physics at Tehran University of Medical Science. Throughout my PhD, my focus revolved around refining algorithms



and employing diverse quantitative correction methods—such as normalization, attenuation, scattering, novel image reconstructions, low-dose imaging, and registration—specifically tailored for a preclinical PET scanner. My journey further extended to a year-long role as a PET/MRI research physicist at Odense University Hospital, Denmark. Here, my work centered on utilizing PET/MRI for guided convection-enhanced drug delivery in large animal models. Despite this rewarding experience, my passion for Deep Learning led me to pursue an opportunity at DTU Compute and DRCMR to broaden my expertise in this domain.

Currently, I am honored to contribute to the CoM-Brain project led by Tim B. Dyrby. Within this project, my primary responsibility lies in developing a robust deep-learning pipeline to autonomously segment and detect tiny microstructures within the brain's white matter using an extremely limited training dataset. My academic interests encompass image analysis, reconstruction, registration, and multimodal imaging. However, I am particularly driven by the prospect of harnessing innova-

tive approaches like deep learning to surpass the constraints of conventional methods, which tend to be labor-intensive, tedious, and time-consuming. It fills me with great enthusiasm to collaborate with the distinguished researchers at DRCMR, leveraging their extensive knowledge and expertise in this burgeoning field.

Lucero Pacheco

I started to work at DRCMR in March 2024. I had just gotten a PhD on biomedical science in Mexico City. During that time I had worked on resting state MRI and network analysis on mainly two groups: children and teenagers with early musical training and teenagers with addiction to inhaled



substances (solvents). I wanted to acquire more knowledge on handling different kinds of MR data so I applied to a project on OCD. I feel very fortunate to have found what I was looking for and more. DRCMR is a very diverse place where people with different backgrounds meet and build science. I hope I can make the most of my stay here.

Mikael Novén

I came to DRCMR in the summer of 2022 as a postdoc in Anke Karabanov's ReScale project. I remember feeling warmly welcomed in an open, curiosity-driven, and friendly atmosphere with smart and charming colleagues which have made the bike commute from



Hovedbandegården well worth it, even in the cold, wet winter mornings. Before coming to KU/DRCMR I did a PhD in Neuro-linguistics in Sweden, focusing on neural correlates of language learning capabilities and phonological cues. In my research at DRCMR, I will investigate how functional and structural brain networks, measured using MRI, change with learning a bimanual fine motor skill and how these changes interact with ageing.

Petr Bednarik

I joined our radiology department and DRCMR in January 2022. My scientific background includes 7-year work experience at the Center for Magnetic Resonance Research and the Department of Endocrinology and Diabetes at the University of Minnesota. I advanced



functional MRS utilizing a semi-LASER sequence on 7T. Furthermore, I published several methodological MRS papers and studies in patients with T1 diabetes. After obtaining my PhD, I joined the team at the High Field MR Center at the Medical University of Vienna. Our collaboration resulted in a new paper entitled "1H magnetic resonance spectroscopic imaging of deuterated glucose and of neurotransmitter metabolism at 7 T in the human brain", which has just been published in the prestigious journal Nature Biomedical Engineering. My latest research has pioneered an innovative method for imaging brain metabolism. I have managed to develop a technique that allows us to measure brain glucose metabolism without the need for radioactive substances. This has the potential to revolutionize the diagnosis and treatment of many common conditions, such as Alzheimer's, depression, diabetes, and cancer. I will continue developing this work here at the DRCMR, thanks to the support from the Lundbeck Foundation and Hvidovre Hospital. My current appointment allows me to combine my clinical expertise in radiology with research experience in clinical research projects. My goal is to bring novel metabolic imaging techniques to clinical practice.

Piyush Swami

I am a Postdoc with the Microstructure and Plasticity Group at the Danish Research Centre for Magnetic Resonance (DRCMR), jointly affiliated with the Visual Computing Group at the Department of Applied Mathematics and Computer Science, Technical University of Denmark (DTU Compute). Previously, I was an



ERCIM Fellow at the Department of Computer Science, Norwegian University of Science & Technology in Trondheim, where I collaborated with the AI Lab and the Motion Capture & Visualization Lab, focusing on virtual reality-based experimental

design. During my doctoral studies at the Indian Institute of Technology – Delhi (IITD), my thesis was on "Intelligent System for Automated Diagnosis of Epilepsy using Brain Signals," leading to an Indian patent for an epilepsy diagnosis device. My research benefited from my affiliation with the All India Institute of Medical Sciences – Delhi (AIIMS–D). My current affiliations with DRCMR and DTU provides me a similarly rich interdisciplinary setting to expand my knowledgebase in both healthcare and engineering aspects. My current research focus includes 3D microscopy data analysis of animal models, high-performance computing, and big-data analysis. I am passionate about neuroscience, healthcare data science, signal and image analysis, and I aspire to advance welfare technologies and mentor future leaders in these fields.

Vasilis loakeimidis

I began as a postdoctoral researcher at DRCMR in October 2024, working on the VIA project, which focuses on longitudinal brain imaging analysis in children at familial risk for schizophrenia and bipolar disorder. Before this, I completed a postdoc at CUBRIC, where

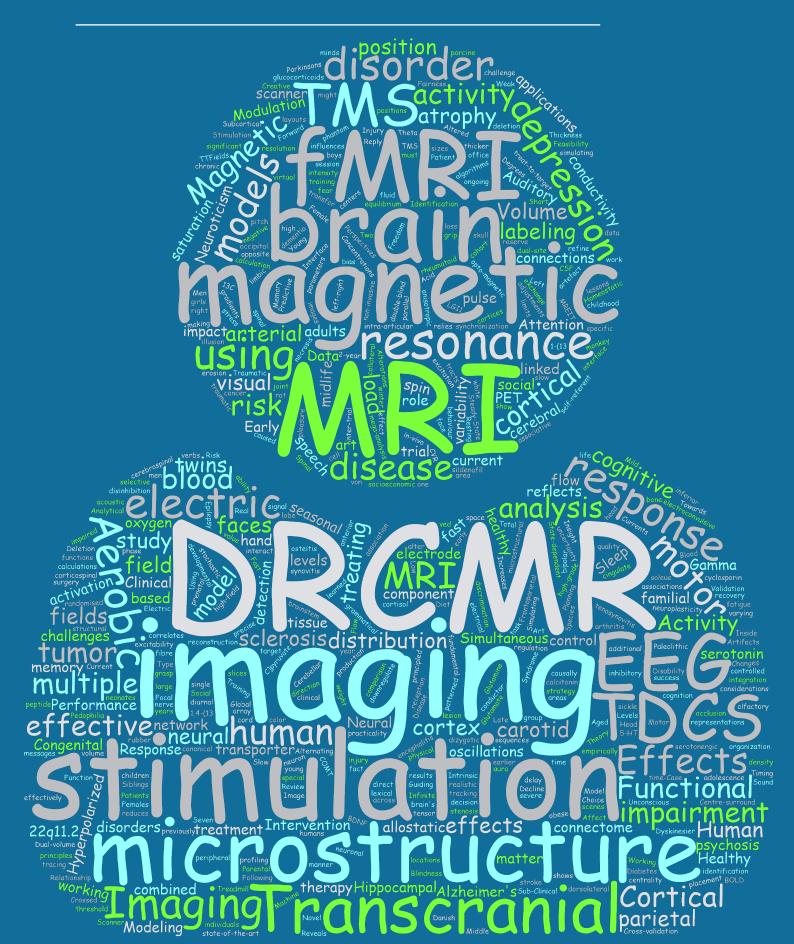


I used the Connectome scanner for multi-shell high-angular resolution diffusion imaging in individuals with Huntington's disease, and applied novel biophysical models of diffusion. Prior to that, I served as a teaching fellow and visiting lecturer at Goldsmiths and City, University of London. I earned both my master's and PhD from City, University of London, where I researched neurodevelopment and risk factors for schizophrenia using fMRI and EEG, following a bachelor's degree in biology at the University of Crete. I'm very excited to be part of DRCMR and the VIA project, with its potential to link brain connectivity maturation trajectories to mental health risk factors and resilience.

Lina Klintberg

I am a chief consultant at the DRCMR working in the leadership team to help keep organisational topics on track and helo with the day to day management of DRCMR. I have a PhD in physics from the University of Cambridge where I was also a junior research fellow before moving on to industry. I have a decade of experiene in project management as well as in leadership and general management at large international companies like BOSCH and Leica.

PUBLICATIONS



JOURNAL ARTICLES

2024

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