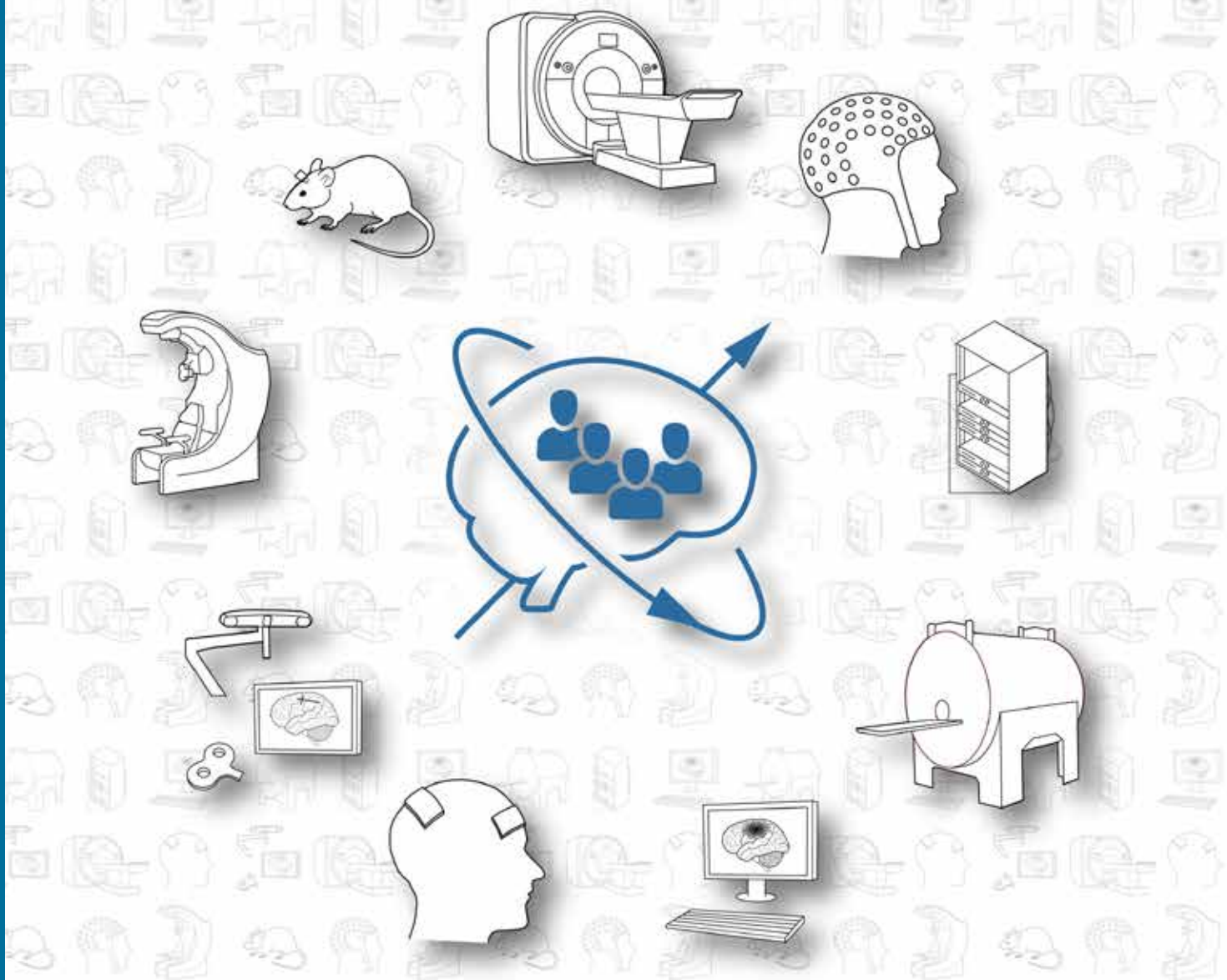
DRCMR

DANISH RESEARCH CENTRE FOR MAGNETIC RESONANCE

Biennial Report 2017–2018



Hvidovre Hospital

DANISH RESEARCH CENTRE FOR MAGNETIC RESONANCE

GLOBAL EXCELLENCE IN HEALTH

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PREFACE

Professor Hartwig Siebner, Head of Research at DRCMR. Photo: Joachim Rode.

The Danish Research Centre for Magnetic Resonance continues to evolve as new research areas come into focus and new research groups mature. An ongoing inflow of researchers and students from Denmark and around the globe secure a truly international and interdisciplinary environment that fosters innovative translational research in the field of biomedical MR-based imaging with a strong focus on the brain and its diseases.

In 2017-18 we have had an increasing focus within all of our research areas towards conducting research with a clinical perspective, helping us becoming even better at developing methods for our new focus area: Precision imaging.

As a translational research centre based at a large university hospital, we are committed to conduct innovative research at the highest level with clinical improvements for patients as the ultimate goal. My new professorship in clinical precision imaging marks our new focus on individualized brain diagnostics and therapy in a wide range of brain disorders.

This biennial report 2017-18 gives you an overview of our work the past two years and our future plans. This is also a good time to express our gratitude towards the many foundations and institutions that believe in us and our research and thus make it possible for us to pursue cutting-edge research. We also wish to thank all researchers and students who have joined us at DRCMR for their great contributions which greatly enrich our research environment and inspire our research.

Hartwig Siebner

Researchers, students and support staff at the DRCMR.

HIGHLIGHTS AND MILESTONES 2017–2018

PRECISION MEDICINE AND TWO PROFESSORSHIPS

During the last two years we have increased our focus on precision medicine. Magnetic resonance imaging (MRI) has great potential in precision medicine because many modalities can be integrated to characterize how the brain's structure, function, and metabolism are affected in a single patient. Likewise, advances in non-invasive brain stimulations provide unique, yet underexplored possibilities for personalized precision treatment of dysfunctional brain circuits. In 2018, we hosted the first International Workshop on Stimulation Precision Medicine of Brain Disorders with speakers from all over the world. Our aim was to bring together world-leading experts to discuss the potential of stimulation-based precision therapies of brain disorders. The workshop was a huge success, giving researchers a possibility to discuss their ideas, findings and hopes.

The workshop was held to mark the appointment of Hartwig Siebner as full professor with special focus on precision medicine at the Faculty of Health and Medical Sciences at the University of Copenhagen in a five-year professorship generously sponsored by the Lundbeck Foundation. The appointment and the funding which came along gives us a unique chance to focus even more on precision medicine in the years to come.

DRCMR Prof. Boraxbekk when he received his professor-diploma from the Vice-Chancellor of Umeå University.

Prof. Hartwig Siebner at the first International Workshop on Stimulation precision medicine of Brain Disorders.

In September 2017, another DRCMR Senior researcher, Carl-Johan Boraxbekk, was appointed full professor of Cognitive Neuroscience of Aging at Center for Demographic and Aging Research (CEDAR), Faculty of Social Science and Umeå Center for Functional Brain Imaging (UFBI), Faculty of Medicine, Umeå University, Sweden. CJ Boraxbekk aims to provide unique insights into neural plasticity and improved brain function after interventions and into training across the lifespan in both healthy participants and patient groups.

GLOBAL EXCELLENCE

We work hard to ensure that our research is of the highest quality. Therefore, we are extremely proud that the Capital Region of Denmark renewed the Global Excellence award in 2017. The renewal acknowledges the excellence and increases the visibility of our research. The award is a great incentive for us to constantly generate new knowledge which can ensure better diagnostics and treatment for patients in the Capital Region of Denmark and in the rest of Denmark.

INCREASING NUMBER OF COLLABORATIONS

The past two years have also led to increased national and international cooperation. We think that collaborations give us the best conditions for conducting cutting-edge, innovative and interdisciplinary research, and for carrying out large studies with great results and considerable impact. The collaborations also ensure the possibilities of integrating results quickly in the clinic, thus providing more rapid benefits for our end-users; the patients.

The collaborations are both international and national. Examples of new international collaborations are STIPED, an EU Horizon 2020 project; the JPND working group ASAP SYNTAU: Alignment and standardization of Neuroimaging Methods in Atypical Parkinsonism, specifically synucleinopathies and Tauopathies; and Lifebrain which is another EU Horizon 2020 funded project. Examples of new national collaborations are two Novo Nordisk Foundation funded Synergy grants: Uheal and BioQ where DRCMR/Hartwig Siebner is co-PI. Another example is the national longitudinal study VIA 11, the Danish High Risk and Resilience Study.

7T SYMPOSIUM

In April 2018, DRCMR hosted the first Danish national 7T MR project symposium. Approximately 100 guests came all the way to Hvidovre Hospital to hear about our experiences with the new 7T magnet and to listen to international speakers coming from Europe, America and Asia. The day was a great opportunity for researchers and guests to exchange know-how and ideas. The symposium was supported by the Lundbeck Foundation.

7T Symposium at Hvidovre Hospital.

DANISH TELEVISION AND THE MEDIA

DRCMR researchers have been invited to participate in several programs in Danish Television; in "Din geniale krop" [Your ingenious body], the mysteries of the human body were explored, and in "The experiment", we stepped into the gray zone of a field, which we still need to explore further to find out what excessive use of cell phones, tablets and laptops actually do to us. Our researchers have also been interviewed by the national radio and several newspapers on everything from smart choices, homeground advantage in football, white lies, and how to maintain a healthy brain. Dissemination and communicating our results to the public is essential since we conduct research of great public relevance and a large portion of our research is funded by taxpayers. Our increased focus on dissemination also led to an interesting collaboration with Videnskab.dk. 16 of our researchers did a course on media appearances and completed by producing a video-pitch on their research (the pitches can be seen under the individual staff at www.DRCMR.dk).

David Meder was interviewed three times by Danish Radio P1, P3 and P4 about home ground advantages and he also participated as an expert on how the brain reacts to love in Danish television.

EDUCATION AND RECOGNITION

We have a strong focus on thorough in-house education to provide young scientists with necessary knowledge and skills to conduct cutting-edge research. We aim at fostering an inspiring international and multi-disciplinary research environment through openness and respect to unfold the scientific potential and secure the wellbeing of each member of staff. A special focus is on the researchers of the future and therefore we are also very proud when our young researchers achieve grants and awards or when Danish media show an interest in our results. Cihan Göksu, Postdoc at DRCMR and DTU Elektro, was awarded with "The ISMRM Magna Cum Laude Merit Award" at ISMRM 2018 for his power pitch and e-poster entitled "Human In-vivo Brain MR Current Density Imaging (MRCDI) based on Steady-state Free Precession Free Induction Decay (SSFP-FID)". The work is about the measurement of very weak electrical currents inside the human brain with MRI.

PhD Stud. Allan Lohse won the yearly pitch competition at the Research Day at Amager and Hvidovre Hospital. His abstract on "Presupplementary Motor Area Controls Risk Taking Behavior Exclusively in Novel Situations" was 1 of 5 chosen for the competition out of a total of 84 abstracts sent in for the Research Day.

PhD Stud. Allan Lohse after winning the yearly pitch competition at AHH Research Day 2018. Photo: Communication AHH.

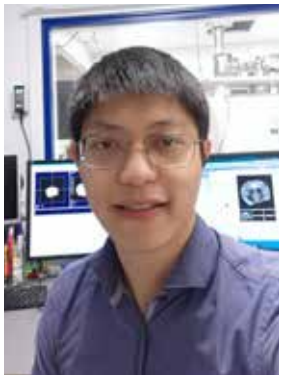
GRANT FROM EUROPEAN RESEARCH COUNCIL

Focusing on education is a long tradition at DRCMR – and in 2018 we had another proof of why also long-term investment in the most talented young researchers is worthwhile. Our rising star, now Senior researcher Henrik Lundell, engineer and PhD, who has been affiliated to DRCMR for more than 10 years (since 2007), has been acknowledged with a prestigious "Starting Grant" from the European Research Council (ERC). The award comes with 1.5 million € to support his project called C-MORPH. Lundell has over the last years worked hard to push the boundaries for precision imaging with MRI. Conventional MRI has a limited image resolution and cannot image structures smaller than about 1 mm in size. However, many aspects of the function of the brain in health and disease are determined by the structure and configuration of cells that are smaller than one tenth of the thickness of a hair. Henrik's approach to this problem has been to create hybrids of multiple techniques to tease out the geometry of specific cell types, information previously only available through tissue destructive microscopy. The project name C-MORPH stands for **C**ell-specific *in vivo* **MORPHO**metry (C-MORPH) and aims to create maps of the structure of the individual cell types that make up the brain.

Senior researcher Henrik Lundell. Photo: Communication AHH.

INTERNATIONAL TALENTS

Our talented postdocs, Chinese Yi He and Turkish Cihan Göksu, both received a Postdoc grant from the Lundbeck Foundation in the fall 2018. While drafting the biennial report, Yi He also added an individual Marie Curie fellowship to his CV. We are very proud on behalf of both researchers. Their success once again showed us how important it is to attract talent not only from Denmark but from all over the world.



Postdoc Yi He and Postdoc Cihan Göksu.

RESEARCHERS AND STUDENTS

An absolute highlight of the past two years is our staff. Researchers, students and administrative staff have once again made DRCMR an incredible place to work. Everybody is working hard to achieve the best and most innovative results, but nobody seems to forget their colleagues and the fact that collaboration is key to greatness. At the coffee machine, the 7T scanner, our labs, the kitchen, offices – all over DRCMR, engaged staff seems to discuss everything from lunch to new brain stimulation methods.

Thus, we can look back at two exciting, prosperous years, boding well for the future research work at DRCMR.

Vikings at the DRCMR Christmas party 2017.

TWO PROFESSORSHIPS IN 2017

CARL-JOHAN BORAXBEKK – PROFESSOR OF COGNITIVE NEUROSCIENCE OF AGING

The aspiration of newly appointed Prof. Carl-Johan Boraxbekk is to help us understand the aging brain. His research focuses on providing unique insights into brain aging by designing and testing novel interventions to improve brain health. In 2017, Boraxbekk was appointed full professor of cognitive neuroscience of aging at the Center for Demographic and Aging Research (CEDAR) and Umeå Center for Functional Brain Imaging (UFBI), Faculty of Social Science, Umeå University, Sweden. Carl-Johan Boraxbekk joined the DRCMR as visiting professor already in 2016, thanks to a 6-months visiting professorship sponsored by the Lundbeck Foundation. The visiting professorship developed into a 50% position at DRCMR, and Boraxbekk has continued to divide his time equally between Sweden and Denmark, also as a Prof. of cognitive neuroscience of Aging. Boraxbekk explains: "In the age of data sharing and big data efforts, I find it stimulating to bridge two of Europe's strongest brain imaging centers".

By combining interventions with advanced brain mapping techniques and extensive behavioural testing, Carl-Johan Boraxbekk and his collaborators have provided some unique insights into the neuro-cognitive mechanisms of brain and cognitive aging. A major focus in the past has been on pinpointing the effects of physical exercise on brain structure, function and chemistry. As professor of Cognitive Neuroscience of Aging Boraxbekk will continue to apply multi-modal brain imaging in his aging research. He firmly believes that combining different brain mapping modalities with innovative interventions in sophisticated ways will not only help to delineate the neural underpinnings of cognitive aging but will also unveil brain targets for interventions designed to mitigate brain aging. Exercise for brain health will continue to be a prioritized research topic for Boraxbekk's Healthy Aging group at DRCMR. In the future, Boraxbekk also plans to continue engaging in projects that require a multi-professional work team as can be found at DRCRM, since he finds it rewarding to work towards a common research goal.

"Training of new scientists is essential for any research field. At DRCMR, we have many brilliant young researchers at all levels; master students, PhD-students, postdocs, and senior researchers that are in the process of building up their own groups. I find it extremely motivating to work with young, talented researchers and hope - in my role as newly appointed professor - to inspire these talented people and provide support and education to help foster the next generation of brain imaging scientists", says Prof. Boraxbekk.

ABOUT THE PROFESSORSHIP

Faculty position as full Professor of Cognitive Neuroscience of Aging, Center for demographic and aging research (CEDAR), Faculty of Social Science and Umeå Center for Functional Brain Imaging (UFBI), Faculty of Medicine, Umeå University, Sweden.

HARTWIG SIEBNER – PROFESSOR WITH SPECIAL FOCUS ON PRECISION MEDICINE

In 2017, Hartwig Siebner was appointed as clinical professor with special focus on Precision Medicine at the Institute of Clinical Medicine by the Faculty of Health and Medical Sciences, University of Copenhagen. The clinical professorship has been sponsored by the Lundbeck Foundation. The central goal of Hartwig Siebner is to establish MRI-based Precision Medicine as an interface between diagnostic radiology and the clinical neurosciences to find the key to diagnosis and treatment with the help of advanced imaging of the brain – a key which exactly fits the individual patient. Hartwig Siebner's vision is to develop novel personalized diagnostic and therapeutic approaches that can be applied to a wide range of brain diseases. He strives to achieve this vision by merging multimodal precision brain imaging, advanced data processing and precision neurostimulation of the human brain. The professorship is extremely motivating and Hartwig Siebner is looking forward to acting out his research plans together with his colleagues at DRCMR.

"Each individual patient has his or her unique version of a brain disease. Even when patients resemble each other with respect to their symptoms, the disease-related changes are not identical. The disease has a specific fingerprint in the affected brain circuits. Combining state-of-the-art methods for brain imaging, it is possible for us to map how the disease affects a single brain and its circuits. In other words, we can draw a patient-specific 'circuit profile' of the disease and using that as a mean to adjust the treatment to the individual patient. I am convinced that imaging the brain is the key to precision medicine, because it gives us the 'fingerprint' of the disease in the brain. On the other hand, precision stimulation techniques of the human brain are rapidly advancing. By advancing these precision stimulation, tools I envision that patient-specific circuit dysfunction can be precisely targeted – opening up exciting opportunities for personalized stimulation medicine".

ABOUT THE PROFESSORSHIP

Clinical Professorship in Precision Medicine within the field: Disease-related MRI brain research & non-invasive transcranial brain stimulation.

University of Copenhagen and Hvidovre Hospital, Danish Research Centre for Magnetic Resonance (DRCMR)

Time period: 2017–2022

Sponsored by a grant from the Lundbeck Foundation: DKK 6.25 million.

FOCUS AREA: PRECISION MEDICINE

Precision Medicine has gained momentum within health science for some years now and has triggered a number of national and international initiatives. Governments and organisations have emphasized the need for a personalized precise approach to advance understanding of disease and to provide tailored effective treatments. Magnetic resonance imaging (MRI) offers powerful methodology for non-invasive brain mapping that can be repeated over time and continue to advance in precision. MRI spans many modalities which can be integrated to characterize how the brain's structure, function, and metabolism are affected in the individual patient. These integrated MRI precision tools bear enormous potential for guiding precision medicine of brain diseases. Precision fingerprinting of brain diseases with clinically applicable multimodal MRI protocols is increasingly coming into focus at DRCMR where we have seen the enormous possibilities of the personalised and precise MRI approaches from the very beginning. Precision MRI-based Medicine is central to our long-term research strategy.
Precision Medicine is often about genetics and chromosomes. However, fingerprinting of brain diseases with MRI plays a very fundamental role which is presently somehow underrated in the emerging field of Precision Medicine. This is especially the case for brain diseases, where it is the individual dysfunction of specific brain circuits that determines which symptoms a patient will have and how severe they are. Capturing disease-induced circuit abnormalities at the individual level will help to identify individual "circuit fingerprints" that can be targeted with personalised treatment regimes, for instance personalized brain stimulation or personalized training interventions. Similar considerations apply for Precision Medicine in other areas as well, for instance using MRI-based techniques to personalize radiation therapy or other oncologic therapies to treat cancer.
To be able to carry out Precision Medicine, it is important to work across disciplines, integrating the knowledge from Genetics, Molecular Biology, MRI physics and Data Science to find patterns which can lead to better diagnostics and treatment. However, a large amount of knowledge and data contributes to both new opportunities and new challenges. It is not enough to be able to measure almost anything, but we also need to figure out what it means and how the information can be used – therefore the challenge is to figure out what markers are relevant for what and choose the appropriate ones. Focusing on brain diseases, we will increase our efforts to push the field of Precision Medicine in the years to come.

AN EXAMPLE ON PRECISION IMAGING

"In patients with Parkinson's disease, we can see the amount of tissue loss and infection in the brain with MRI. This is not possible to see in a blood test. So, we can actually look into the brain and read something about the individual patient and his or her individual disease. And from there, we can estimate which kind of treatment would fit this specific patient. Therefore, smart scanning of the brain is a fundamental element when dealing with tailored diagnostics and treatments", says Prof. Hartwig Siebner.

Else Smith, Deputy Director, Hvidovre and Amager Hospital at the Precision Medicine workshop.

Sarah H. Lisanby, National Institute of Mental Health, Bethesda (MD), USA, as key note speaker at the workshop on Precision Medicine.

INTERNATIONAL WORKSHOP ON STIMULATION PRECISION MEDICINE OF BRAIN DISORDERS

The strategic work with Precision Medicine as focus area resulted in Hartwig Siebner being nominated as Prof. in Precision Imaging in 2017. The nomination was a perfect kick-off for the implementation of the Precision Medicine as focus area. In September 2018, Hartwig Siebner marked the new professorship and Precision Medicine as focus area at DRCMR with an international workshop in Copenhagen, where world-leading experts discussed the potential and challenges of *stimulation precision medicine of brain disorders*. The workshop was a big success and we plan on repeating it every 1-2 years.

Word-leading experts on ***Stimulation precision medicine of brain disorders***.

SPEAKERS AND CHAIRS AT THE WORKSHOP

E. Smith
Deputy Director, Hvidovre and Amager Hospital

H.R. Siebner
University of Copenhagen, Copenhagen, Denmark

A.M. Engel
Head of Talent & Career Programmes,
The Lundbeck Foundation

C. Kruuse
University of Copenhagen

C. J. Boraxbekk
Umeå University, Umeå, Sweden

S. H. Lisanby
National Institute of Mental Health, Bethesda (MD), USA

C. Stagg
University of Oxford, Oxford, UK

R. Ilmoniemi
Aalto University School of Science, Espoo, Finland

A. Thielscher
Technical University of Denmark, Kgs. Lyngby, Denmark

N. Grossmann
Imperial College, London, UK

A.N. Karabanov
Copenhagen University Hospital Hvidovre

G. Schlaug
Beth Israel Deaconess Medical Center and
Harvard Medical School, Boston (MA), USA

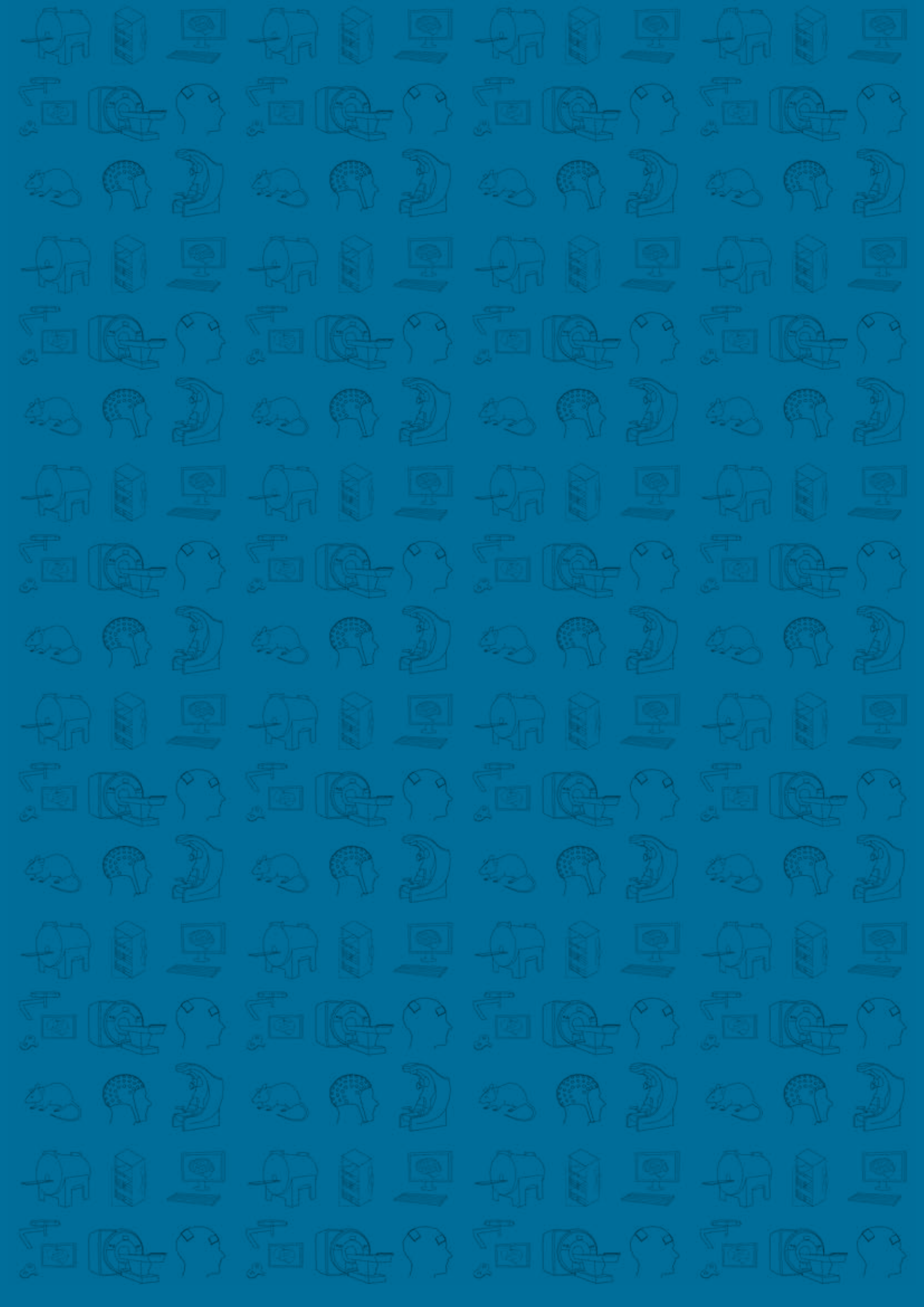
F. Padberg
Ludwig Maximilian University, Munich, Germany

D. Antonenko
Greifswald University, Greifswald, Germany

D.M. Herz
Copenhagen University Hospital Bispebjerg,
Copenhagen, Denmark

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 2017–2018.



BASICS

BIOPHYSICALLY **A**DJUSTED **S**TATE-INFORMED **C**ORTEX **S**TIMULATION

... pushes custom noninvasive brain stimulation: The BASICS of precision brain-circuit therapies

The BASICS project is an interdisciplinary research endeavor pursued jointly by DRCMR, DTU Compute and DTU Electro. The main goal is to synergistically combine non-invasive transcranial brain stimulation (NTBS), brain mapping, electric field modeling and machine learning to advance the potential of NTBS to shape human brain networks.

The vision of BASICS is to design efficient and novel brain stimulation applications through the synergistic combination of noninvasive brain stimulation, functional brain mapping, electrical field modeling, and machine learning. The BASICS project is fully funded by the Novo Nordisk Foundation.

THE INTERDISCIPLINARY NATURE OF THE PROJECT IS REFLECTED BY THE FOUR WORK PACKAGES (WP):

WP1 — BIOPHYSICAL MODELING, DTU-Elektro

WP-leader: Axel Thielscher

The WP pushes the methods for realistic field estimates to where they can reliably inform non-invasive brain stimulation. WP1 builds advanced solutions for personalised head models that can deal with structural changes in disease populations (e.g chronic stroke patients) and develops novel targeting approaches that enable optimal stimulation and "dose estimation".

WP2 — MACHINE LEARNING, DTU Compute

WP-leader: Lars Kai Hansen

The WP optimizes advanced machine learning methods that can detect individual brain states and generates models that can predict the brain reaction to stimulation protocols and allow for optimized stimulation planning for non-invasive brain stimulation.

WP3 — Modulation of the healthy brain, DRCMR

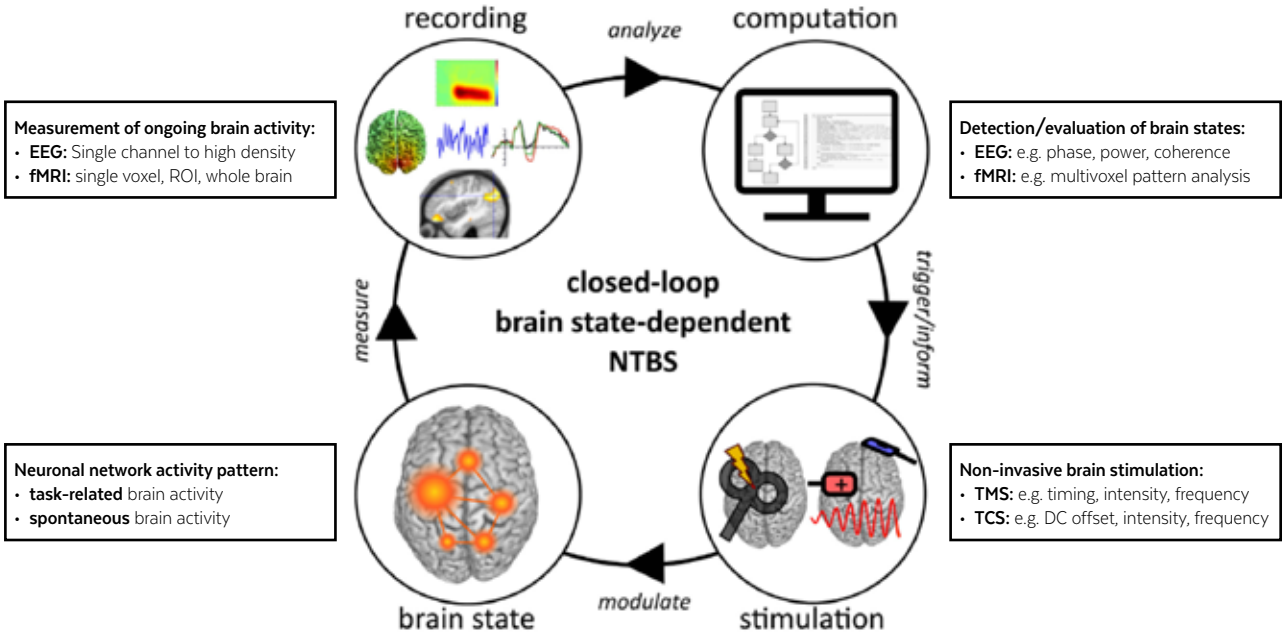
WP-leader: Hartwig Siebner

This WP establishes biophysically precise, state-informed brain stimulation in healthy individuals by harvesting the methodological developments made by earlier work packages and by experimentally testing a variety of stimulation patterns resembling natural task-related activity and connectivity patterns.

WP4 — Clinical applications, DRCMR

WP-leader: Hartwig Siebner in collaboration with clinical partners

The advances of the previous work packages will be translated into proof-of-efficacy studies in patients with movement disorders.

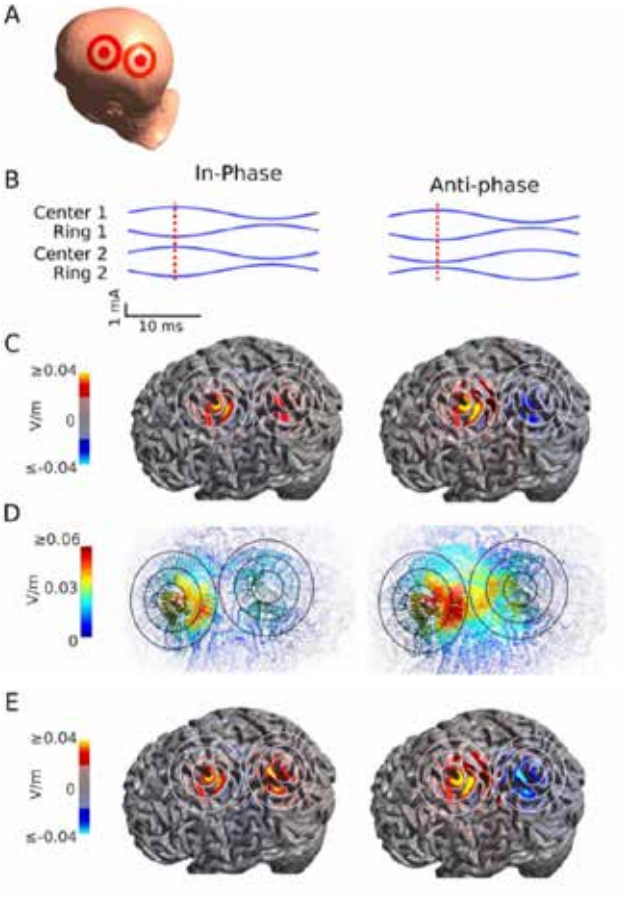


Schematic visualization of our real-time systems for brain-state-dependent stimulation. Figure Adapted from Bergmann, Karabanov, Hartwigsen, Thielscher, Siebner, 2016.

Throughout 2017-2018, the BASICS team has made significant progress towards biophysically adjusted and state-informed NTBS as represented by the many publications that the team has published over the last two years. On the technical side, progress in 2017-18 has included improvement of individualized models for healthy and diseased populations and the development of targeting approaches that enable optimal stimulation settings (37, 108) (WP 1). The BASICS' team has also further developed Bayesian machine learning algorithms to detect complex EEG-based brain-states that will improve robustness of spatial-temporal targeting in non-invasive brain stimulation (WP2). Leveraging the methodologies developed by work-packages 1 and 2, we established one of the first real-time EEG-TMS systems for EEG-informed brain-state- targeting worldwide. The system is able to adapt stimulation-based individual EEG-determined brain-states. We were able to demonstrate the feasibility of our EEG-TMS system in a proof-of-concept study in which we targeted specific phases of the peri-central mu-rhythm in healthy non-preselected individuals. In close collaboration with WP1, we have also made significant progress on technical aspects relating both stimulation artifacts and the spatial and temporal precision of state-informed transcranial brain stimulation (52). Harvesting the methodological and experimental developments of the last years has allowed us to launch a first proof-of-principle study in patients with Parkinson's disease suffering from dyskinesia (WP4).

International Network:

The research project is imbedded in a strong international network with collaborators in Europe, America and Asia. Our team of collaborators includes medical doctors, engineers and neuroscientists who closely contribute to and interact with our group.



An example for model based, optimized stimulation planning. Adapted from Saturnino et al. (2017, NeuroImage).

IMPACT

BASICS improves precision of neurostimulation by tailoring stimulation to the dynamics of targeted brain networks and by ensuring target engagement through reliable estimation of induced electric fields. Our proof-of-concept studies in healthy individuals have established a precision stimulation framework that is now being translated into therapeutic neurostimulation therapies in many neuropsychiatric disorders such as Parkinson´s disease, stroke and depression. The precision stimulation framework will effectively target affected brain circuits and hopefully result in substantial clinical improvement.

FACTS

Grant Recipients:	Hartwig Siebner (main), Lars-Kai Hansen & Axel Thielscher
Grant Size:	DKK 15 million
Funding Period:	June 2015 – May 2019
Funding Agency:	Novo Nordisk Foundation Inter-disciplinary Synergy Program
Grant Number:	NNF14OC0011413

THE LISA STUDY

FROM MUSCLE POWER TO BRAIN HEALTH

Physical activity has been suggested as one key ingredient to keep your brain healthy while aging. Considering the many beneficial effects on health in general from staying physically active, it is appealing to learn whether this also translates into a healthy mind. When it comes to exercise and brain health, the majority of previous studies have focused on cardiovascular fitness. Less is known about whether positive effects on brain health can also be achieved from muscular fitness. In the LISA study (LIve active Successful Ageing), DRCMR is part of the largest randomized controlled trial performed so far, where strength training and its effects on skeletal muscle, overall function, and brain health are being explored.

The primary aim with the LISA study is to compare immediate and long-term effects (2-10 years) of two different 1-year resistance training interventions (high intensity vs. moderate intensity), with a non-exercising control group. The recruitment of 450 home dwelling, independent men and women between the ages of 62-70 started in 2014, and the inclusion continued for 3 years. In July 2018, we marked an important milestone when the 1-year intervention part of this large trial was completed. After months of quality control and data handling, we are now ready to start looking at the immediate effects of resistance training for this age group. As with any longitudinal study, and intervention in particular, a critical issue is to get people to continue to be part of the study. In LISA, we have so far only experienced a dropout rate of around 7%. This is encouraging because it allows us to have sufficient power in our subsequent analyses. Currently, 400 of the 450 have undergone a 2-year visit and around 6 persons have reached a 4-year visit.

HEAPS OF DATA, FROM MUSCLE TO BRAIN

Data collection takes three days to complete for each time point and participant. It starts with medical examinations, blood samples and anthropometrics. This is followed by a set of physical tests, mainly focusing on power and strength, but also gait speed. General cognitive abilities are also estimated as well as questionnaires about quality of life, personality and mental distress. On the last day, we perform brain imaging at the DRCMR. The brain imaging data includes high resolution multimodal MRI, covering anatomy, tissue microstructure, functional connectivity and perfusion aspects of brain aging. Also, a unique feature of the LISA-study is that we perform MRI of the thigh muscle (both legs). With this rich data set we will be able to explore the link all the way from muscle morphology to brain structure and function.

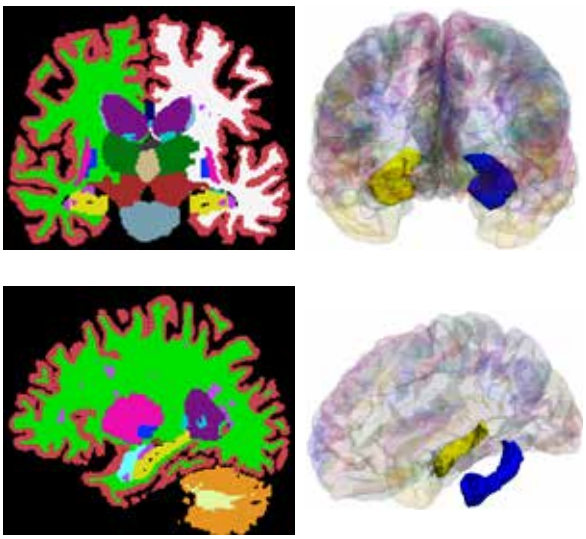
Significantly, the LISA study is three times larger than the only previously performed randomized controlled study on strength training and brain health. Another exceptional aspect of the LISA study is the long-term follow-up, where data collection will continue for 10 years. So, even though we are currently excited about starting to analyze the immediate effects of the intervention, we also have much to look forward to in the future. After all, the LISA-study is only in its beginning phase.

FACTS

The LISA study is overall led by Professor Michael Kjær at the Institute of Sports Medicine, Bispebjerg Hospital. It is funded by the Nordea Foundation and the Center for Healthy Aging, University of Copenhagen. It is also a collaboration with Professor Erik Lykke Mortensen, department of Public Health, University of Copenhagen. Carl Johan Boraxbekk is responsible for the brain imaging at DRCMR.

IMPACT

To meet future societal demands of a larger proportion of older individuals, we need to find ways to promote healthy brain aging. The results from the LISA study have the potential of influencing a large part of our population and will provide recommendations to policy makers and clinicians on how to take care of our growing older population.



In the LISA-study, the goal is to understand how strength training influences the brain structure and function. We use Freesurfer (left panel) to segment the brain structure. A particular region of interest is the hippocampus (right panel), a structure important to preserve for healthy brain aging.

LIFEMABS: DANISH REGISTERS

A UNIQUE SOURCE FOR BRAIN AGING RESEARCH

Population neuroscience is a hot research topic around the world. The ultimate goal is to explain the trajectories of individual brain development across the life course, and make predictions about who will have a healthy brain aging and who is at risk for an unhealthy aging. A dream for any scientist in this field would be to have longitudinal data starting at childhood, all the way to adulthood. Because of the unique resources offered by the Danish registers, this is made possible with the LifeMabs study.

WHO WAS INVITED TO LIFEMABS?

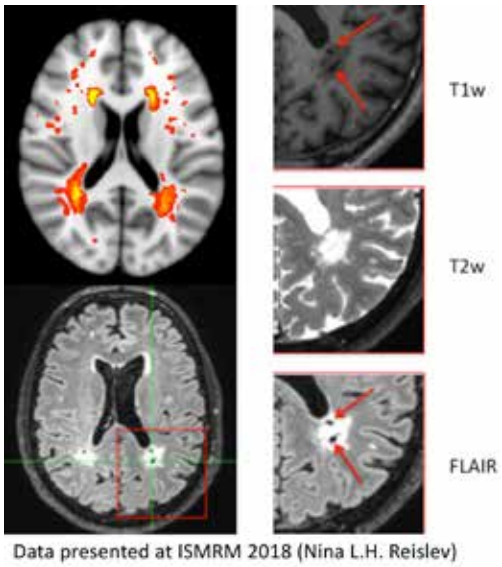
To be part of the LifeMabs study, the participants must have been part of the Copenhagen Perinatal Cohort (CPC), which is a cohort of children that were born at Rigshospitalet, Copenhagen, between the years of 1959-61. In addition, the participants must also have been part of the Prenatal Development Project, which was a follow-up of the CPC cohort in 1982-94 and the Copenhagen Aging and Midlife Biobank study, which took place in 2009-11. Thus, the participants in LifeMabs are a well characterized group of people with longitudinal data from childbirth to present time. When they entered the LifeMabs study, the participants were in their mid-50s . In total, 285 people underwent brain imaging, and the last day of scanning was 26 March 2018.

DATA IN LIFEMABS

In LifeMabs, multiple tests of cognitive functions, personality questionnaires, and information about parental and adult socioeconomic position, collected during three time points throughout the life course, create unique longitudinal lifespan trajectories. Multimodal MRI was then collected at DRCMR to address the questions about how life course development, of e.g. cognitive functions, also may influence brain health when we age. The MRI contains high resolution structural, functional and perfusion sequences. Multimodal imaging of brain aging is arguably a strong asset in this study, and we believe that this also will inform theoretical views on brain aging because not all modalities may show a similar brain pattern.

NEXT STEP

Several important pieces of information have already been obtained from this cohort, for example that early life biomedical and social factors influence allostatic load in midlife. Now the aim is to link these lifespan associations also to brain health, using the multimodal MRI protocol. Understanding the different trajectories in aging, whether it is towards normal or pathological, will provide important knowledge regarding how precise interventions, tailored specifically for certain negative trajectories, can be used to provide opportunities for healthy brain aging. It will also provide answers to the timing of such interventions, perhaps some things need to be accomplished already early in life. When we age, we age with large interindividual variability. Some people appear to cope well with aging, whereas others do not. With the life course trajectories provided in the LifeMabs study, we hope to come one step closer to understanding factors that predict these individual differences.



Data presented at ISMRM 2018 (Nina L.H. Reislev)

FACTS

LifeMabs is overall led by Professor Erik Lykke Mortensen, department of Public Health, Copenhagen University. The study was initiated by Professor Mortensen and Associate Professor Ellen Garde, and has been supported by a grant from Nordea Foundation to Center for Healthy Aging, Copenhagen University.

IMPACT

With LifeMabs, some truly unique information about the transition from birth to midlife and its impact on brain health will be revealed. This has the potential for huge public health impact and may guide clinicians and policy makers for early interventions to promote healthy brain aging.

We are using a multimodal approach tounderstand white matter lesions. Based on different imaging modalities, T1, T2, Flair, a goal is to provide a better marker of tissuedegeneration. In combination with the uniquelongitudinal information in the LifeMabs study, the origin as well as the consequences of white matter lesions can be addressed.

OMNISAM

THE OMNIBUS SATIETY METRIC PROJECT

Designing food and beverages that maximizes satiety has long been the ambition of industry and public health. Foods that fill faster and for longer are desirable for weight management and for public health programs designed to prevent obesity. Insofar as progressive satiety metrics, they have done so primarily along two frontiers. The first frontier employs subjective measures, quantified using standardized scales, such as the visual analogue scale or category scales. The second frontier entails measuring biomarkers of satiety, either neural or hormonal. There is a wealth of evidence that several hormones and several brain regions correlate with, or causally affect, appetite and food consumption. Such advances, however, are not yet at the stage of developing or validating explicit metrics. To date, no metric has more than 25% of the variance in next meal energy consumption, and no metric has been shown to have predictive accuracy for real world consumption. The projects main objective is to develop a multi-modal-based metric of satiety that is predictive of future energy consumption that surpasses the performance of existing benchmark metrics, and acts as a proof-of-concept for its use in industrial R&D. The overreaching strategy is to develop a multi-modal metric that targets the spectrum of processes underlying the satiety cascade comprising brain, blood and behavioural (BBB) data. Subjects undergo a pre-load – ad libitum intake paradigm comparing milk-based products differing in levels of calories and protein to carbohydrate ratio. Extracting the temporal dynamics of the BBB data, we will compute a metric for predicting next meal energy consumption. Our framework is premised on two central conjectures:

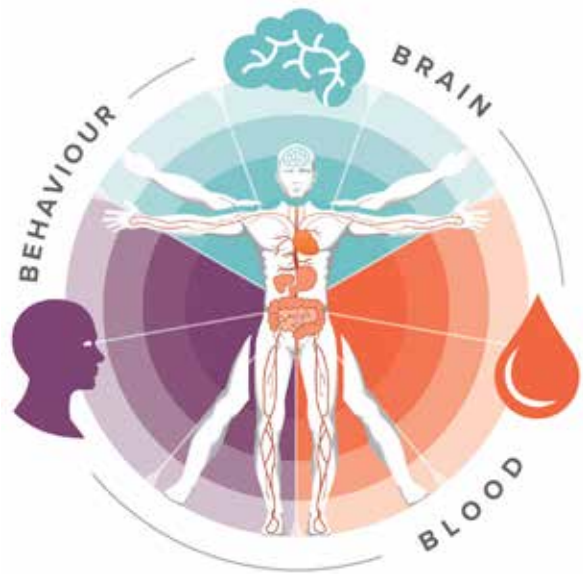
Multimodality

Satiety metrics that exploit the three modalities of blood, brain and behaviour, will be more powerful than existing single-modality metrics.

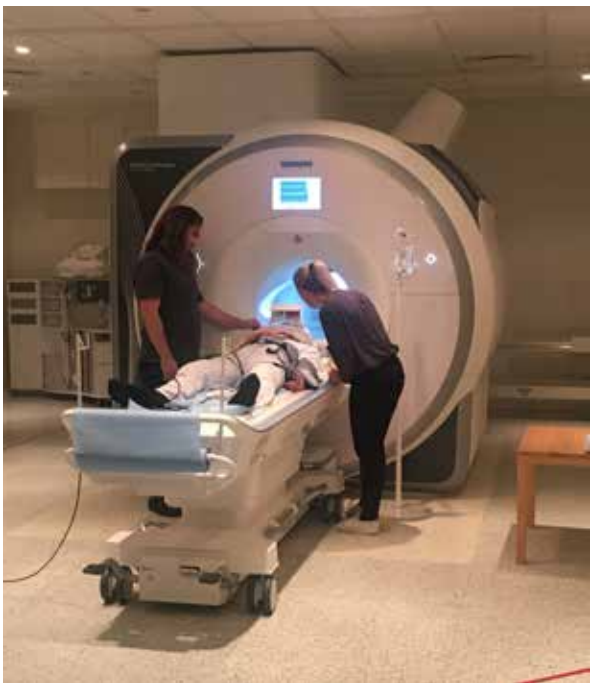
Dynamics

Existing satiety metrics are weak because they do not extract information from the dynamics of states as they unfold over time. Satiety metrics that explicitly compute dynamics will be more powerful than static measures.

We propose to overcome this deficiency in developing the Omnibus Satiety Metric (OmniSaM). The project spans the three modalities: Brain data, Blood data and Behavioural data



An overarching schematic that depicts our aim to combine data from brains, blood and behaviour to understand and predict satiety.



The experiment in action. The participant is lying on the bed about to go into the scanner, where they will respond to images of food. Periodically, we stop the scanner to perform questionnaires and to sample their blood.

THE SET-UP

Brain data

WP leader: Hartwig Siebner, University of Copenhagen, Danish Research Centre for Magnetic Resonance

Central to Work Package #1 is:

1. To provide a neural metric based on the distributed activity of the hypothalamus
2. To test the predictive efficacy of hypothalamic activity as the satiety cascade unfolds in time, from cephalic, to gastric, to absorptive phases,
3. To infer to the full temporal profile is a better predictor of next-meal energy consumption.

We use specific imaging protocols aimed at measuring activity of the hypothalamus and its sub nuclei. Preload milk drinks is given orally via infusion pump and gustatory manifold whilst acquiring functional Magnetic Resonance Imaging data. We analyse the data using standard multiple linear regression techniques as well as multivariate Bayesian (MVB) decoding methods. We use MVB to decode from the hypothalamic nuclei at the time of preload onto the future energy consumption of the ad libitum meal.

Blood data

WP leader: Sten Madsbad, University of Copenhagen, Department of Endocrinology, Hvidovre Hospital. Kjeld Hermansen, Aarhus University Hospital, Department of Endocrinology.

Central to Work Package #2 is:

1. To provide a comprehensive assay of all relevant hormones and metabolite signals and their temporal evolution
2. To address how the dynamics of these signals and their interactions are predictive of next-meal energy consumption.

Blood samples are collected at regular intervals throughout the experiment from preload to ad libitum meal. They are performed according to standard procedures and assayed for satiety hormones and metabolite composition using an explorative approach. We model the dynamics of the hormonal cascades, computing temporal derivatives, as well as fitting basis functions to the time series.

Behavioural data

WP leader: Barbara V. Andersen, Aarhus University, Department of Food Science

Central for Work Package #3 is:

1. To test the span of a subset of pre-loads
2. To provide a benchmark for the satiety metric; subjective data of appetite-related sensations and intake of ad libitum meal on the basis of the preload paradigm, and
3. To identify behavioural indicators of satiation and satiety.

From a sensory perspective, central questions are additionally:

4. Differences in desire, sensation and satiation dynamics based on load related to satiety capacity, and
5. Which key sensory indicators of satiation and satiety can be identified.

Reports are acquired at regular time intervals throughout the full duration of the experiment. Subjects will report using a computerized VAS scales measuring desires, expectations, appetite, physical and psychological well-being sensations. Energy of food consumed is key behavioural outcome for validating the metric.

Multi-modal metric

Central for Work Package #4 is

1. to develop and test the performance of the multi-modal metric incorporating data from the three WP's: Brain, Blood and Behaviour.

Data on dynamics in neural activity, hormonal and metabolite status, behaviour and subjective sensations contribute to the multi-modal metric. We (use dimensional reduction methods to identify the principle components within each data modality that express the largest variance. Taking the highest ranked components for each modality for each time point, we regress these components onto the target variable or ad libitum meal energy consumption for all subjects in a random effects regression analysis. This provides modality and time-specific statistics of interest, such that the predictive value of each data modality can be evaluated at each time point. From this regression analysis, we expect to be able to extract the weightings of the multimodal data that best predict energy consumption.

FACTS

Project homepage: www.omnisam.au.dk

Funding:	DKK 5.4 million from Arla Food for Health
Periode:	2016-2019
Awarded to:	Hartwig Siebner at DRCMR Sten Madsbad at Department of Endocrinology, Hvidovre Hospital, and
Project leader:	Derek V. Byrne from the group "Food, Quality Perception & Society" at Aarhus University, Department of Food Science

IMPACT

The work of the OmniSaM project is intended to have broader impact in the long term. Firstly, it offers to develop a foundational insight into how satiety works that will be vital for understanding how satiety mechanisms can go wrong in metabolic disorders that either involve over- or under-eating. Secondly, by improving satiety measurement, it is hoped that it will be possible to design food and beverages to maximise satiety, as a healthier means of helping people control their dietary intake that relies less on self-control.

THE DANISH HIGH RISK AND RESILIENCE STUDY

Schizophrenia and bipolar disorder are severe heritable psychiatric disorders that partially overlap genetically. Disturbances occurring early in brain development play a critical role in the aetiology of these diseases. Developmental deficits or delays in motor, emotional, social, and cognitive functioning can already be observed at a young age, before the onset of a psychotic disorder. Children of parents with schizophrenia or bipolar disorder are at an increased risk of developing a mental illness themselves and 55% of these children may experience some kind of mental illness during their lives.

The Danish High Risk and Resilience Study – VIA 11 is the first follow-up study of a Danish cohort of 522 children, 11 years of age, born to parents with or without a diagnosis of either schizophrenia (N=202) or bipolar disorder (N=120). The cohort was assessed for the first time at age 7 in VIA 7. "VIA" is the Latin word for road and describes the overall purpose of the project to investigate the developmental path of children with vulnerabilities. VIA 7 and VIA 11 involve several centres across the country (for more information, see http://via11undersoegelsen.dk/).

Results from the VIA 7 baseline study indicate that the children at high risk show motor function impairments, widespread neurocognitive impairments, and a higher level of psychopathology already at age 7. In general, these impairments were more pronounced in children of parents with schizophrenia than in children of parents with bipolar disorder.

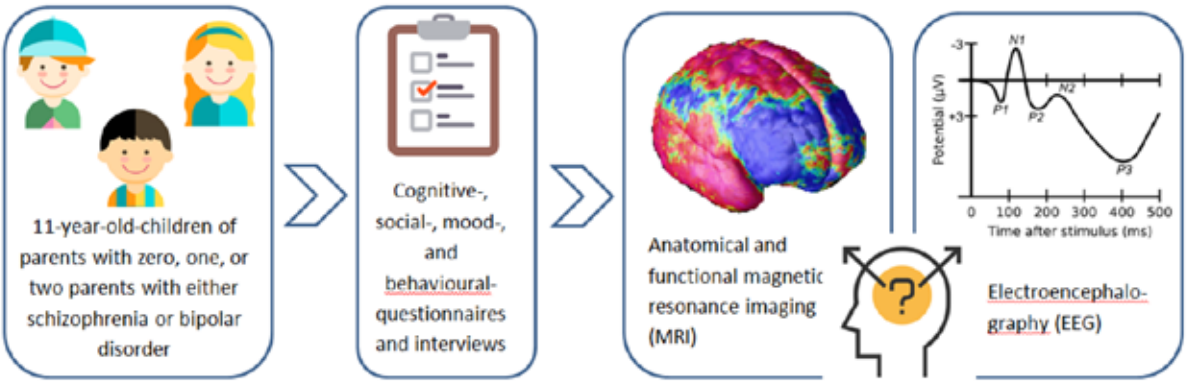
VIA11 STUDY DESIGN

The entire VIA 7 cohort has been invited to participate again in VIA 11. Follow-up assessments and questionnaires of social, cognitive, emotional, and motor functioning are currently conducted at Gentofte Hospital, Copenhagen, or Aarhus University hospital, Skejby, as well as in the children's home.

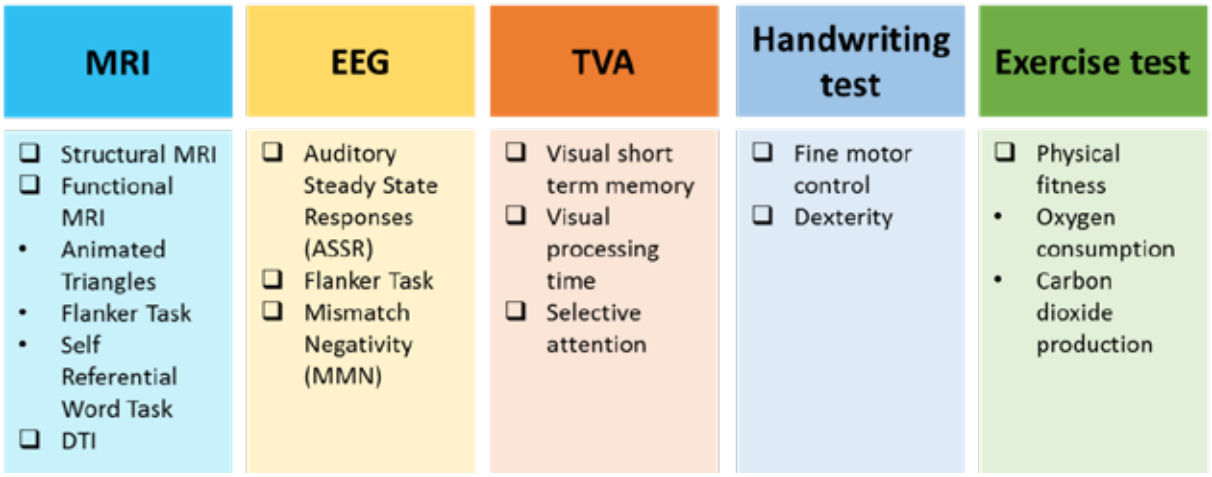
In addition to the assessments that were undertaken in VIA 7, children in VIA 11 also undergo magnetic resonance imaging (MRI) of the brain and electroencephalography (EEG) (see Figure 1): VIA 11 Brainmap. Structural and functional images of the brain are acquired at DRCMR and at the Center of Functionally Integrative Neuroscience (CFIN), Aarhus University, each scanning half of the VIA 11 cohort. EEG is only acquired at DRCMR.

VIA 11 BRAINMAP

The aim of VIA 11 Brainmap is to provide new insights into brain-behaviour relationships in children at familial high risk of developing schizophrenia or bipolar disorder as compared with children at low risk. Importantly, children are scanned at an age where few will have developed manifest psychopathological symptoms. This enables us to elucidate possible early patterns of atypical brain-behaviour relationships that can either reflect an increased risk of developing mental health problems later in life, or an increased level of resilience, protecting high risk children from developing mental health problems. We hope to re-assess the children again at age 16. This would



The VIA 11 study assesses the same cognitive, social, mood, clinical and behavioral measures as in in the baseline VIA 7 study. After the clinical part, the children visit DRCMR and CFIN, where they undergo structural and functional MRI, as well as EEG (DRCMR only).



At DRCMR, children first undergo MRI imaging followed by EEG, with a lunch break in between. Finally, children perform the TVA, handwriting test, and physical exercise test.

allow us to test the predictive value of observed brain-behaviour patterns and to investigate developmental changes in these patterns over time.

Structural brain images are acquired to measure global and regional cortical thickness and area, brain tissue volumes, and degree of myelination. Additionally, functional MRI is used to measure the children's brain activity while performing three behavioural paradigms: First, a flanker task to assess their ability to control and suppress inappropriate responses (i.e. inhibition). Second, an animated triangle task to measure social cognition, and third, a self-referential task to measure the children's ability to reflect on their own and others' feelings and knowledge. Findings from previous studies indicate that patients with schizophrenia and bipolar disorder show behavioural deficits in performing such tasks, and that task performance is predictive of onset and severity of the diseases. Finally, diffusion weighted images are acquired to measure grey and white matter microstructure and structural brain connectivity.

Next to MRI, children undergo several other assessments at DRCMR (see Figure 2). EEG is used to investigate electrical brain activity in terms of neural oscillations and event-related potentials while children perform an auditory steady-state task (ASSR), a modified flanker-test (similar to the one used in fMRI), and a mismatch negativity task (MMN). The ASSR and MMN tasks respectively, measure to which degree children automatically synchronize neural activity and detect defiant (auditory) stimuli. Both of these abilities are important for efficient higher order cognitive processing. These tasks will thus give us a more basic understanding of cognitive impairments in high risk-children.

Finally, we assess basic visual processing abilities using the Theory of Visual Attention (TVA) test, fine motor control and dexterity using a digitized drawing pad, and children's physical fitness by recording oxygen consumption and carbon dioxide production during an all-out exercise bout on a bike ergometer.

CURRENT STATUS OF VIA 11 BRAINMAP AT DRCMR

Since March 2017, 241 children have been successfully re-assessed in VIA 11. At DRCMR, we have studied 128 children. Data collection is planned to continue until mid-2020. Currently, pipelines for processing imaging and electrophysiological data are being developed and tested next to the regular data quality assessments. In addition, we are in the process of writing up manuscripts for publication concerning a meta-analysis on structural imaging in children with familial high risk for schizophrenia or bipolar disorder and the VIA 11 EEG protocol.

FACTS

VIA 11 started 01.03.2017 and is led by Prof. Merete Nordentoft from the Research Unit, Mental Health Center Copenhagen, University of Copenhagen. The VIA 11 research group involves multiple clinical and research centres across Denmark. VIA 11 received funding from the Lundbeck Foundation Initiative for Integrative Psychiatric Research (iPSYCH), the Mental Health Services of the Capital Region of Denmark, the Research Fund in Capital Region of Denmark, The Independent Research Fund Denmark and Innovation Fund Denmark.

IMPACT

The combination of a multidimensional assessment of cognition, physical activity, environment, and genetics with multimodal imaging in VIA 11 allow to differentiate factors that veer children on paths to health or to illness. The VIA 11 Brainmap study allows to identify brain risk and resilience markers which may help to develop targeted treatments that prevent the transition to these disorders.

LIFEBRAIN A PROJECT ON OPTIMISING THE USE OF EUROPEAN BRAIN IMAGING COHORTS – HEALTHY MINDS FOR 0-100 YEARS

DRCMR is partner in the EU Horizon 2020-funded Lifebrain project (www.lifebrain.uio.no). Lifebrain integrates 11 longitudinal and seven cross-sectional, mostly population-based, European cohort studies from eight research centres, investigating cognitive and mental health across the lifespan.

The main goal of Lifebrain is to identify determinants of brain, cognitive and mental health at different stages of life, and to establish a solid foundation of knowledge for understanding how brain, cognitive and mental health can be optimized through the lifespan.

Lifebrain intends to link existing cohorts to national registries, biobanks and data from other large studies, and enrich them with a new online data collection. By working with stakeholders and health authorities, the project strives to provide the evidence base for (personalised) policy strategies for prevention and intervention, improving clinical practice and public health policy for brain, cognitive and mental health.

LIFEBRAIN ACHIEVEMENTS

Lifebrain is characterized by a focused, smooth and productive collaboration across partners and has made great progress in the first two years of its existence and delivered on all project milestones. These include the development of a data storage, management and analysis infrastructure, categorization of all available data across Lifebrain data sites, initiation of online data enrichment, development of dried blood spot kits to measure specific biomarkers of interest, development of standardised brain image analyses pipelines, development of statistical tools for analysing multidimensional longitudinal and multicentre data, and stake-holder engagement and outreach.

The online data enrichment, in which an estimated number of 4,700 participants will take part, allows maximizing data comparability across Lifebrain sites. Assessed data categories will include among other things demographics, information on physical activity, alcohol use and smoking habits, personality, and mental health. The Dried Blood Spots home kits that have been developed and distributed by VITAS will measure specific biomarkers of interest within Lifebrain, such as vitamin D, proinflammatory cytokines, lipids and stress hormones.

In the first year of Lifebrain, a small group of persons travelled across Europe in order to be scanned in all the scanners that have been used by the different Lifebrain partners to acquire brain imaging data. Getting images from the same person on different scanners allows us to develop algorithms to correct for potential differences in brain image intensity profiles across scanners. Furthermore, to improve comparability across sites, all imaging data within Lifebrain will be (re)-processed using uniform imaging analysis streams.

Novel longitudinal statistical tools have been developed to exploit the potential of the large Lifebrain cohort. Among these, a statistical framework to estimate reliability and to identify sources of measurement error in order to improve future study designs with respect to precision of measurement.

Lifebrain organized a number of stakeholder engagement activities, including workshops, and public lectures. Moreover, information was collected in a sub-study regarding the views and perceptions of healthy adults participating in brain research studies on brain health and personalized brain health prevention. The Lifebrain website (http://www.lifebrain.uio.no/), Facebook page (www.facebook.com/lifebrain.h2020/) and a monthly e-newsletter allow disseminating information about current research results, publications, events and deliverables. Stakeholder workshops in Barcelona and Oslo, that attracted clinicians, policy-makers and patient-organisations, provided the foundation for directing upcoming Lifebrain results into

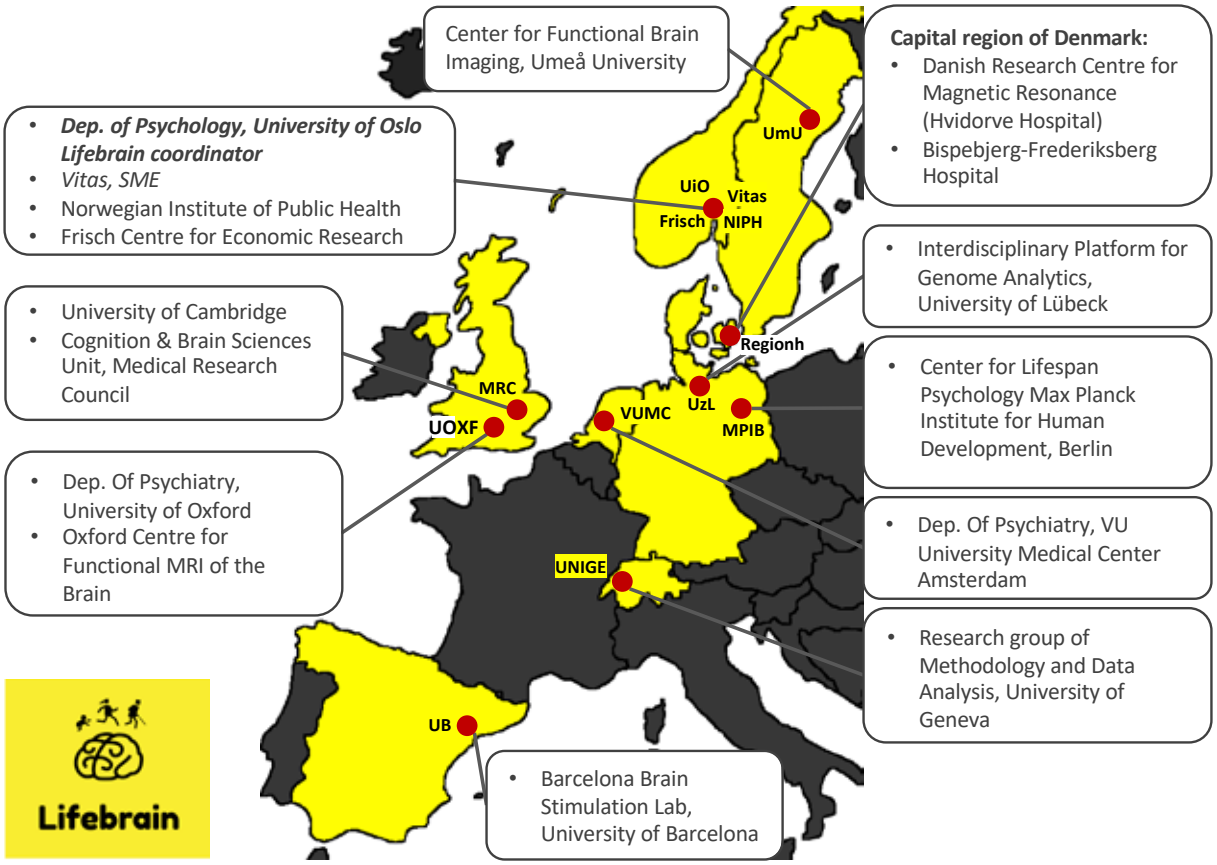
FACTS

The funding period runs for 5 years starting from 1 January 2017.

Lifebrain is funded by the EU Horizon 2020 framework with Euro 10 million.

Lifebrain coordinator is Prof. Kristine Walhovd, Centre for Lifespan Changes in Brain and Cognition, University of Oslo, Norway and is realized through a close collaboration between major European brain research centres and VITAS (a SME) specialized in measuring biomarkers in dried blood spots (see figure).

Lifebrain is organized in seven work packages (https://www.lifebrain.uio.no/lifebrain-project/). Senior researcher William Baaré from DRCMR is work package leader of work package 2: Data management and integration.



European Lifebrain partners and the Lifebrain logo.

clinical practice and health policy. A policy review is currently being conducted on European policies to explore how project results could be relevant and how these results could lead to the promotion of personalized health policies.

CURRENT STATUS OF LIFEBRAIN

The second phase of Lifebrain will focus on harvesting the rich data available in Lifebrain. Several studies have been initiated and are in progress. A key study investigates the role of social economic status and cognitive abilities on structural brain measures using a meta-analytic framework. Other studies focus on e.g. memory, depression, personality, and sleep. Furthermore, Lifebrain data sites are continuing to populate the Lifebrain database and restructuring and reprocessing brain image data using uniform pipelines.

IMPACT

Lifebrain will make major conceptual, methodological and analytical contributions towards large integrative cohorts and their efficient exploitation. Moreover, Lifebrain will provide novel information on brain, cognitive and mental health maintenance as well as onset and course of brain, cognitive and mental disorders. This will pave the way for earlier diagnosis of brain disorders, aberrant development and decline of brain, cognitive and mental health, as well as future preventive and therapeutic strategies. Lifebrain will closely work with stakeholders and health authorities to promote personalised policy strategies for prevention and intervention and improving clinical practices. Finally, Lifebrain will promote public health policies for brain, cognitive and mental health.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 732592.

MAX4 IMAGERS

INTRODUCTION

In the outskirts of Lund in the southern part of Sweden, a major research facility has been established consisting of two circular-shaped buildings having diameters of 528 and 96 meters, respectively. These buildings house the MAX IV synchrotron, one of the world's most powerful x-ray source and equipment. The synchrotron opens a new horizon in medical imaging because it is possible to obtain 3D tomographic scanning of anatomical structures at such a high image resolution not possible with any other existing imaging technology.

The facility is a big boost for the scientific infrastructure in the Øresund Region, and it is expected to reveal new insights for research and can change the way we today think of diagnosis and treatment of patients - if only we can learn how to utilize the facility!

You see, synchrotron imaging is challenging. There is a lot of know-how in how to prepare samples and scan them. The images are typically huge (hundreds of gigabytes) and data analysis is a substantial challenge. Finally, one needs to be able to translate the ultrafine anatomical and physiological findings into new knowledge relevant to clinical/pre-clinical applications. Successful usage is truly an interdisciplinary endeavor, and the MAX4 Imagers project aims to establish the expertise amongst the universities and major hospitals in the region. This involves the development of algorithms to assist data analysis. An equally important goal is to disseminate the possibilities to other clinical researchers, so that they too can harness the powerful opportunities and thus bolster the scientific output of the region. Four pilot projects have been selected to showcase the broad range of possibilities that synchrotrons provide.

FOUR DEMONSTRATION PROJECTS

The researchers will investigate and demonstrate how to derive the full potential of synchrotron imaging in healthcare for better disease understanding and diagnostics. This will be applied in four demonstration projects that cover a wide spectrum of tissue types from the A) microstructure of the brain, B) sperm cells, C) pathological mechanisms in muscle contractures, and D) in tooth bone microstructure.

A. The microstructure of brain in health and disease

We use synchrotron imaging to investigate the 3D microstructure of healthy and diseased brain tissue, including cells, blood vessels and axons - the nerve fibres which are responsible for communication in the brain. The morphology of important structures such as axons is related to their function, i.e. an axon with a larger diameter will relay information faster than one with a smaller diameter. Any damage to the axons will affect the transfer of information and disturb the brain network. Several neurodegenerative diseases, such as Multiple Sclerosis, manifest as microstructural changes in the brain. Diffusion MRI can be used clinically to detect these changes, but due to limited prior knowledge of what the 3D microstructural environment in the brain looks like, it is unable to identify what kind of changes have occurred. By imaging brain tissue in 3D with super high resolution synchrotron radiation, we gain a better understanding of the true anatomy and also further insight into the mechanisms behind diseases. With this information, we can tailor the diffusion MRI technique to better describe the microstructural environment and potentially identify new biomarkers for disease.

As part of the MAX4 Imagers aim, we develop algorithms to segment and characterise anatomical features of interest from the synchrotron data we acquire. In the example of the axons, this entails: finding them in the data, extracting their shapes and analysing their morphologies, i.e. axon diameter variations along the axon, axonal trajectories, etc.

B. Pathological mechanisms in muscle contractures

Muscle contractures are a frequent complication in patients with Central Nervous System (CNS) lesions. The aim of this project is to elucidate whether the composition and the amount of connective tissue is changed in muscle tissue with a contracture using synchrotron imaging. The results of this project are of crucial importance for patients with CNS lesions, since a clarification of the arising of muscle contractures can create a base for an effective preventative treatment of patients with CNS lesions.

FACTS

PI is Tim B. Dyrby, DRCMR, Hvidovre Hospital

Partners are Rigshospitalet, University of Copenhagen, Technical University of Denmark (DTU) and international partners at MAXIV, Lund University, Sweden.

Funded by a DKK 4.5 million grant from the Capital Region Research Fund for Healthcare as part of their strategic focus area on the potentials of synchrotron imaging in the Capital Region of Denmark.

Funding period: 2017-2021

C. Sperm cell tail beating

Sperm cells are highly specialized cells responsible for delivery of a haploid paternal genome into the egg. In order to do so, the sperm cell has shut off unnecessary functions, packed the genome tightly into the head and is equipped with a huge beating flagellum. The flagella beating frequency is fast (up to 30 Hz) but to penetrate the tight mucus layer surrounding the egg, the sperm cell needs to be hyperactivated, which entails high amplitude flagellar bending, a reduction in beat frequency, and side-to-side yawing.

Poor sperm motility and inadequate hyperactivation can lead to infertility. However, sperm cells have never been investigated with the power of synchrotron beams. We want to study super-resolution 3D sperm tail beating patterns using synchrotron imaging. This can leverage new vital information on both mechanistic and molecular function of sperm motility.

D. Bone microstructure and Evaluation of Peri-implant Hard Tissues

Bone microarchitecture is an interconnected network of plate- and rod-like structures. Tooth loss is associated with bone loss. In this project, a goat model has been used to mimic a critical sized defect used for evaluation of osseointegration and peri-implant hard tissue in the mandible after immediate vertical bone augmentation. The purpose of this study was to perform a standardized histological method to be compared with synchrotron imaging for evaluation of peri-implant bone and bone microarchitecture. Synchrotron data has been collected at the European Synchrotron Radiation Facility (ESRF) in Grenoble, France.

IMPACT

Our novel 3D anatomical insights from synchrotron imaging - combined with the development of algorithms to analyse the huge amounts of data produced - will lay the ground for:

Improved knowledge of the 3D microstructure in different tissues

Understanding of disease mechanisms

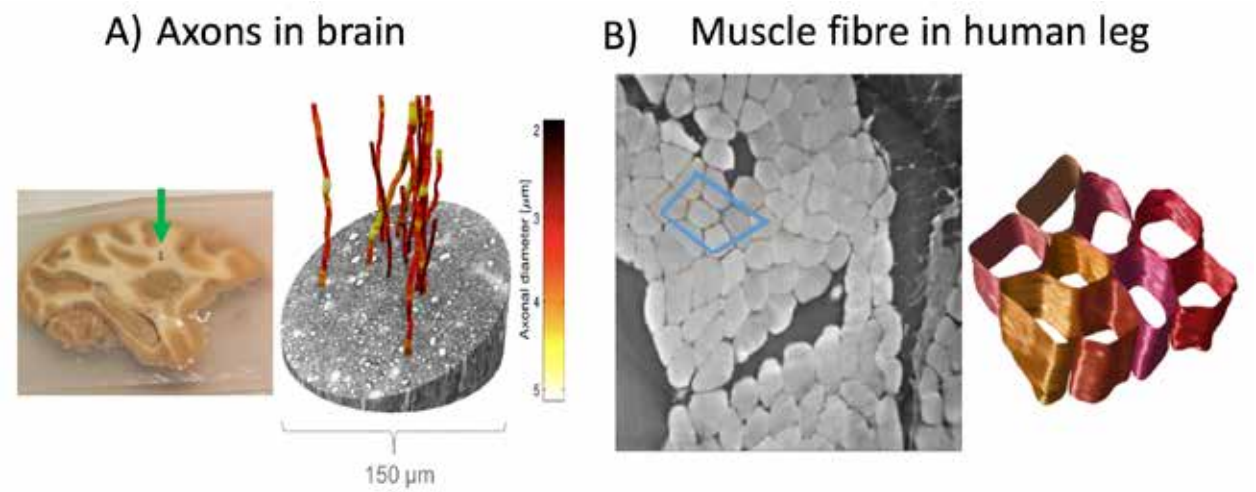
New imaging biomarkers for disease

Improvement of the imaging methods currently used in the clinic for diagnosis e.g. MRI

It is our vision to establish an internationally leading competence centre on synchrotron imaging and its application to health science centered at the hospitals in the Capital Region of Denmark together with its regional university partners.

We wish:

- To establish know-how on the use of synchrotron imaging and its application in health sciences to obtain novel 3D anatomical and physiological insights.
- To design new algorithms that can handle, process and analyse BIG synchrotron imaging data sets.



The figure shows the first results of our synchrotron imaging data and algorithms to segment anatomical features from these very big and high image resolution data sets. A) Left: a slice of a post-mortem monkey brain from which small tissue samples were extracted (arrow). Right: A synchrotron imaged tissue block is shown in grey scale, and a few axons have been segmented in 3D. The colour represents their diameter in micro-meters. The axons are clearly not having the same diameter along their projections as have been thought. B) Left: One slice of synchrotron data from muscle tissue punctured from the leg of a healthy human. Right: 3D segmentation of a few muscle cells indicated in the blue square region in synchrotron image (left).

TECTO BRAIN IMAGING

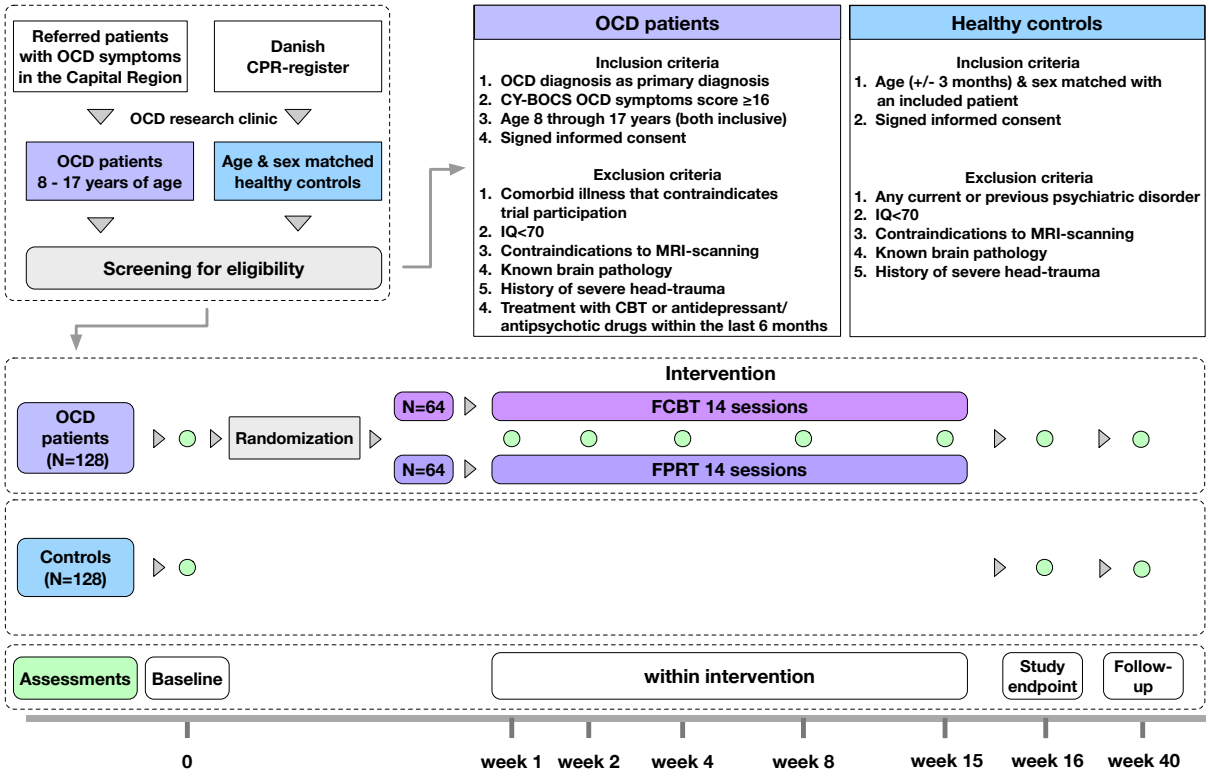
TREATMENT EFFECTS OF FAMILY-BASED COGNITIVE THERAPY IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE COMPULSIVE DISORDER

Cognitive behavioral therapy (CBT) with exposure and response prevention (ERP) is the recommended first-line treatment for children and adolescents with obsessive-compulsive disorder (OCD). However, more than 40% of the patients do not or only partially benefit from CBT.

TECTO is a large collaborative study with national and international partners led by Anne Katrine Pagsberg. TECTO combines a randomized clinical trial (RCT) and longitudinal case-control design with the aim of elucidating how neural, cognitive, emotional, and neuroendocrine factors moderate and mediate the response to family-based cognitive behavioral therapy (FCBT) with ERP, in pediatric patients with OCD. TECTO is the first large RCT in pediatric OCD to include neuroimaging. Characterizing the neural underpinnings of response to FCBT is essential for improving treatment efficacy and identifying potential new treatment targets.

TECTO STUDY DESIGN

At baseline, 128 pediatric OCD patients will be compared to 128 healthy control participants to map neurobiological, cognitive, and emotional markers of OCD. After baseline assessments, patients are randomly assigned to 16 weeks of either FCBT with ERP or an active control treatment with family-based psychoeducation and relaxation training (FPRT, see figure).



Overall TECTO design. OCD: Obsessive-Compulsive Disorder. FCBT: Family-based Cognitive Behavioral Therapy, with exposure and response prevention. FPRT: Family-based Psychoeducation and Relaxation Training. All participants undergo comprehensive clinical and cognitive assessments and will undergo brain imaging at baseline and in week 16 at the end of treatment. The TECTO study is registered on ClinicalTrials.gov (https://clinicaltrials.gov/ct2/show/NCT03595098).

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.

The TECTO brain imaging efforts will take place at the DRCMR. We will gather structural and functional brain images of all participants at baseline and at end-of-treatment. We aim to determine structural and functional brain profiles of pediatric OCD and elucidate profiles that predict and mediate FCBT response, using magnetic resonance imaging (MRI). Previous functional MRI (fMRI) studies of OCD patients indicate abnormal response-inhibition-related and task-switching-related activity in specific areas of cortico-striato-thalamo-cortical circuits. Changes in the activation of these areas during treatment might predict treatment outcome.

CURRENT STATUS OF TECTO BRAIN IMAGING

The enrollment of participant only started in September 2018, therefore, analyses are still to come.

TECTO RESEARCH ENVIRONMENT

Neuroimaging is done at DRCMR, Hvidovre Hospital, and is performed by PhD stud. Valdemar Uhre under supervision of Prof. Hartwig Siebner, Senior researcher William Baaré and Postdoc Kasper Winther Andersen. Assoc. Prof. Signe Vangkilde, Dept Psychology, UC, will supervise cognitive tests and analyses. Prof. Kerstin Plessen, Univ. of Lausanne, CH (TECTO initiator) will supervise emotion regulation assessments. Dr. Nicole Lønfeldt, with expertise in oxytocin's roles in emotional disorders and parenting behavior, will supervise the neuroendocrinological sub-study. Prof. Niklas Rye Jørgensen at the Clinical Biochemical Dept, Rigshospitalet, will conduct immunoassays of oxytocin with training and supervision of an expert in extracting oxytocin from saliva, Assoc. Prof. Eli Lebowitz, Yale University. Data integration will be performed in collaboration with Assoc. Prof. Line Clemmensen from the Technical University of Denmark (DTU) and Assoc. Prof. Kristoffer Madsen (DRCMR & DTU).

TECTO's steering committee and advisory board include national and international experts.

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.

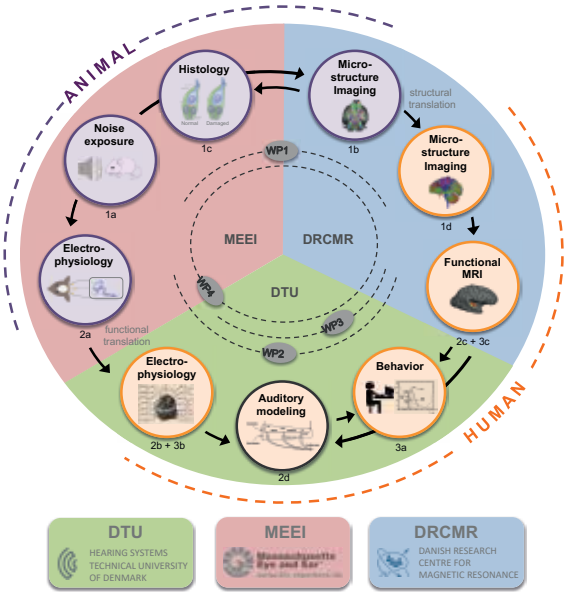
For a video presentation of the TECTO trail see: bit.ly/2OrqyZv

UPCOMING KEY PROJECTS

During 2017 and 2018 several researchers at DRCMR received major funding for new prestigious projects. The projects are now starting up and will be carried out during the coming years at DRCMR and at partner institutions.
Read about some of the projects here

UHEAL: UNCOVERING HIDDEN HEARING LOSS

UHeal is a synergy project supported by the Novo Nordisk Foundation and coordinated by Prof. Torsten Dau, DTU. The synergy project combines cellular physiology of the ear (Harvard Medical School), clinical audiology (DTU), and non-invasive MR imaging (DRCMR) to tackle the challenge of hidden hearing loss. Exposure to noise over longer periods can cause damage to synapses in the inner ear, which affects people's ability to understand speech in noisy environments. This type of synaptic nerve damage cannot be measured with standard audiometry in humans and is not detected by the clinical hearing tests used today. Such "hidden" hearing loss is presumably widespread, even among younger people. The synergy project will develop imaging techniques to detect cell damage in the ear and examine how this affects the bran networks involved in hearing. The project will yield diagnostic tools that will enable diagnosis for this hearing disorder and thereby offer better opportunities for treatment.



From DRCMR: **Prof. Hartwig Siebner**, Senior researcher Jens Hjortkjær (also DTU-Elektro), Assoc. Prof. Tim Dyrby (also DTU-Compute), Postdoc Søren Asp Fuglsang and Postdoc James Breen-Norris.

C-MORPH – NONINVASIVE CELL SPECIFIC MORPHOMETRY IN NEUROINFLAMMATION AND DEGENERATION

C-MORPH is funded by an ERC (European Research Council) starting grant given to Senior Researcher Henrik Lundell who will use MR imaging and spectroscopy as a tool to identify specific fingerprints of underlying disease processes. The project builds on two independent spectroscopic MR methods already developed by Henrik Lundell: The first MR method is called *Powder averaged diffusion weighted spectroscopy (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 will leverage these innovations for MR-based precision medicine and advance PADWS and STGT methodology on state-of-the-art MR hardware. Henrik Lundell will harvest the synergy of these methods to realize **C**ell-specific *in vivo* **MORPH**ometry of the living human brain. The ability of the novel MR-based methods and analyses to derive cell-type specific tissue properties in the healthy and diseased brain will be validated with the help of a strong translational experimental framework, including histological examinations. Once validated, the experimental methods and analyses will be streamlined and transformed into clinically applicable tools. The **C-MORPH** project will push the frontiers of MR-based personalized medicine, guiding therapeutic decisions by providing sensitive probes of cell-specific microstructural changes caused by inflammation, neurodegeneration or treatment response.

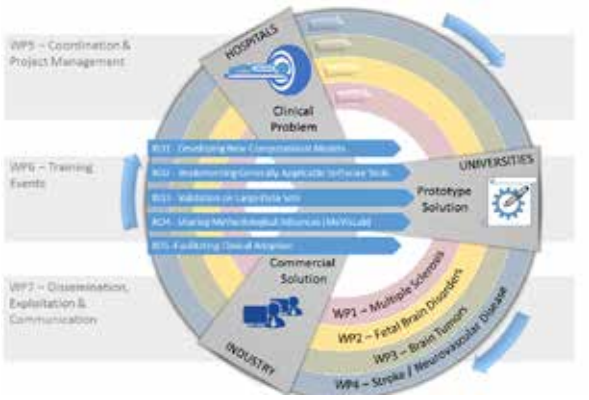
From DRCMR: The **C-MORPH** project is spearheaded by **Senior researcher Henrik Lundell** and additional staff to be recruited.

This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement No 804746).

European Research Council
Established by the European Commission

TRANSLATIONAL BRAIN IMAGING TRAINING NETWORK (TRABIT)

TRABIT is a Marie Skłodowska-Curie Innovative Training Network (ITN) financed by H2020 with partners from all over Europe coordinated by Koen Van Leemput, DTU and started in 2017. The project aims to train a new generation of innovative and entrepreneurial early-stage researchers (ESRs) that will bring quantitative image computing methods into the clinic, enabling improved healthcare delivery to patients with brain disease. In recent decades, medical imaging techniques such as computed tomography, ultrasound, and especially magnetic resonance imaging have gained a central role in the clinical management of disorders of the brain. In total, 15 PhD students from all participating sites, including one at DRCMR, will work on translating the wealth of information contained in medical images into optimized patient care by improving computational tools to help analyze and quantify the torrent of acquired imaging data. These innovative computational tools will help clinicians to better diagnose and treat patients with brain disease.



From DRCMR: **Assoc. Prof. Tim Dyrb**y (also DTU-Compute), PhD stud. Carmen Moreno Genis, Prof. Hartwig Siebner and PhD stud. Stefano Cerri.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 765148.

"TESTING THE EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION AT MULTIPLE LEVELS IN THE HUMAN BRAIN: ESTABLISHING THE DOSE-RESPONSE RELATIONSHIP BETWEEN THE INJECTED ELECTRIC FIELD AND THE PHYSIOLOGICAL AND BEHAVIOURAL EFFECTS"

The project is funded by the Lundbeck Foundation as part of the foundation's NIH & LF Brain Initiative. The initiative provides funding to researchers at Danish research institutions who are interested in participating in NIH BRAIN Initiative funded projects to enable Danish researchers to participate in an ongoing NIH project. DRCMR has received LF funding for collaboration on a project that is pursued by Gottfried Schlaug at the Beth Israel Deaconess Medical Center, Harvard Medical School, on *Imaging the Neural Effects of Transcranial Direct Current Stimulation* (NIH 1R01MH111874-01).

The project focuses on a widely used method for non-invasive brain stimulation, called Transcranial Direct Current Stimulation (TDCS). During TDCS, weak electric currents are injected into the brain through skin electrodes attached to the head. TDCS does not excite neurons in the brain but modulates their spontaneous activity. These neuromodulatory effects can outlast the time of TDCS and cause long-lasting improvements of brain function. Promising initial results show that TDCS has the potential to become a valuable add-on therapy for neuropsychiatric disorders. However, its effects are still highly variable across individuals, which is a major obstacle that hampers the development of TDCS into a standard therapy. Together with researchers from Harvard Medical School, DRCMR will develop a method to select the best individual stimulation strength for each participant or patient. To this end, we want to elucidate how the effects of TDCS on brain activity and behaviour depend on the electric current flow in the targeted brain area. The project represents a critical step for transcranial brain stimulation, moving away from an insufficient "one-size-fits-all" approach towards systematic dosage control of TDCS. It is anticipated that this will minimize inter-individual variability of the treatment outcome, removing a major hurdle for the use of TDCS as treatment of brain disorders such as stroke and depression.

From DRCMR: **Assoc. Prof. Axel Thielscher** (also DTU-Elektro), Prof. Hartwig Siebner and Senior researcher Anke Karabanov.

STIMULATION IN CHILDREN AND ADOLESCENTS (STIPED)

STIPED is an EU Horizon 2020 financed project with partners from all over Europe. The main ambition of the **STIPED** project is to introduce TDCS to children and adolescents with Chronic pediatric neuropsychiatric disorders as a novel and alternative treatment option. At the end of the project, a new technological solution for personalized treatment that can be well integrated into the health care system will be established. The main vision of this project is to introduce TDCS as an innovative, alternative treatment option for pediatric neuropsychiatric disorders and to study the effect size of disorder-specific stimulation protocols combined with disorder-specific cognitive tasks on core behavioral and neurocognitive symptoms. Efficacy, safety, tolerability and acceptability of TDCS in Attention Deficit Hyperactivity Disorder and Autism Spectrum Disorder will also be clarified.

From DRCMR: **Assoc. Prof. Axel Thielscher** (also DTU-Elektro) and Postdoc Oula Puonti.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 731827.

INTERFACING EMERGING QUANTUM TECHNOLOGY WITH BIOLOGY AND NEUROPHYSIOLOGY (BIOQ).

BioQ is funded by a Novo Nordisk Foundation Synergy Grant. The collaboration is led by Professor Ulrik Andersen (DTU Physics) and brings together a dedicated team of quantum physicists and neurophysiologists from DTU Physics, DTU Electrical Engineering, Copenhagen University's Department of Neuroscience and DRCMR.

The objective of **BioQ** is to achieve extraordinary sensitivity in imaging with resolutions from millimeter to nanometer-scale. The vision is to realize room-temperature brain imaging at the whole-brain level with millimeter resolution, at the brain circuitry level with sub-micron resolution and at the synapse level with molecular nanometer resolution. This is well beyond the limits of today and will bring the quantum sensing technology to real-life applications in bio-medical imaging.

From DRCMR: **Assoc. Prof. Axel Thielscher** (also DTU-Elektro) and Prof. Hartwig Siebner.

RAY DOLAN AS VISITING PROFESSOR

Professor Ray Dolan from Max Plank Centre for Computational Psychiatry, University College London, will be visiting the DRCMR for 6 months in the second half of 2019. The visit is financed by a Visiting Professor grant from the Lundbeck Foundation.

Ray Dolan will be working on "How the brain constructs models of the world to enable planning and decision-making". The flexibility of human decision-making is thought to arise from "cognitive maps". Such maps enable agents to establish relationships between isolated experiences and to generalize knowledge to new situations. This has been extensively studied in the context of spatial navigation in rodents, where an important neural signature has been found, in which past trajectories are replayed from memory. Despite advances in animal models, there has been little attempt to study this process in humans, in part because of the difficulty in accessing such neural signatures. In unpublished work, Ray Dolan's group has shown that they can now obtain a reliable measure of replay from Magnetoencephalographic recordings, and that this replay is subjected to constraints imposed by the agent's cognitive map. During his visiting professorship, the ideas will be developed further in collaboration with colleagues at DRCMR and from other Danish research institutions.

From DRCMR: Prof. Hartwig Siebner, Senior Researcher Oliver Hulme and Postdoc David Meder.

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

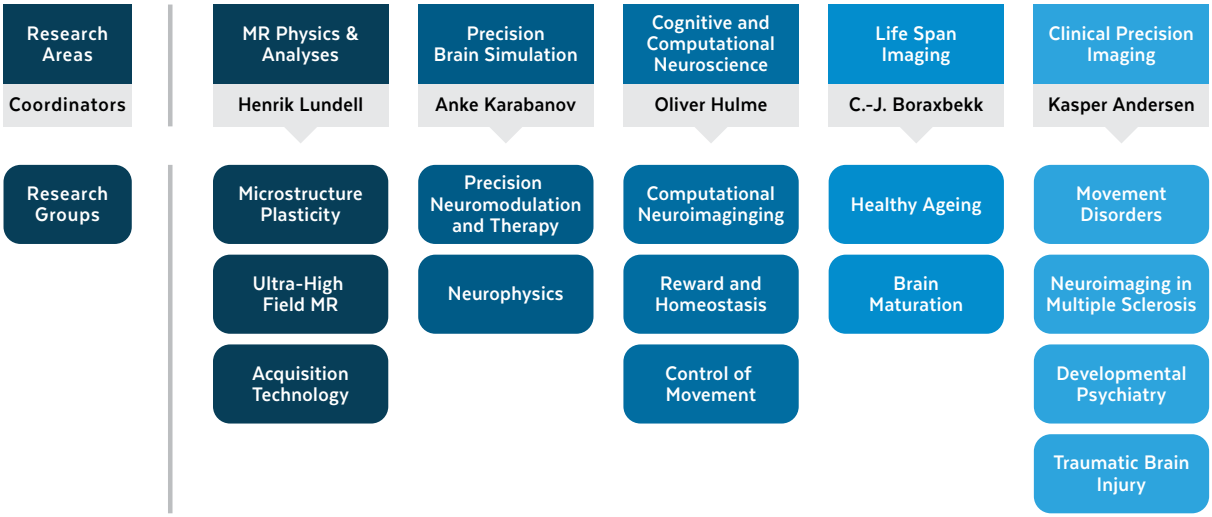
We use brain mapping to unravel causal dynamics in the human brain.

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.


Research Areas
Coordinators
Research Groups
MR Physics & Analyses
Henrik Lundell
Microstructure Plasticity
Ultra-High Field MR
Acquisition Technology
Precision Brain Simulation
Anke Karabanov
Precision Neuromodulation and Therapy
Neurophysics
Cognitive and Computational Neuroscience
Oliver Hulme
Computational Neuroimaginging
Reward and Homeostasis
Control of Movement
Life Span Imaging
C.-J. Boraxbekk
Healthy Ageing
Brain Maturation
Clinical Precision Imaging
Kasper Andersen
Movement Disorders
Neuroimaging in Multiple Sclerosis
Developmental Psychiatry
Traumatic Brain Injury

MR PHYSICS AND ANALYSES

The reasearch at DRCMR involves a growing toolbox of different advanced methods, but MR-based techniques and analysis are central in most projects. MRI offers a broad range of methods and contrasts to study brain anatomy at high resolution, different aspects of tissue composition, and dynamics following neuronal activation or other physiological processes. The rapid technical development within MRI enables new research questions to be investigated. An important part of the research activities at DRCMR are therefore to adopt and advance the latest developments within the field and its validation to support and strengthen our neuroscientific and clinical research.

Ultra-high field MRI is crucial for innovation in experimental and clinical research integration of multimodal approaches during the scanning session. Additionally, translation of experimental methods to clinical scanners for routine work is also vital in our research. Therefore, we embrace new insights in MR physics in terms of both hardware development and refinement of acquisition software and sequences.

The main MRI modalities of interest are diffusion, perfusion and spectroscopy. By keeping at the forefront with the latest MRI technologies and by combining the information from other modalities, such as non-invasive transcranial brain stimulation, we enable high-level basic science and foster research synergies among internal research groups, external collaborators, and the clinic.

Assoc. Prof. Tim Dyrby has coordinated the strategic interacton between the technologically driven research groups at DRCMR from 2016-2018.

In 2018, he handed over the coordinating role of MR Physics and Analyses to Senior researcher Henrik Lundell.

Microstructure & Plasticity

Ultra-High Field MR

Acquisition Technology

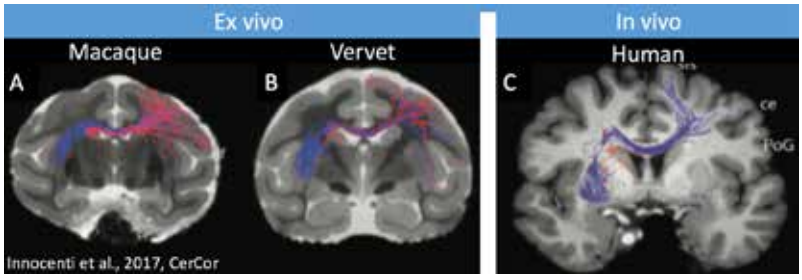
MICROSTRUCTURE AND PLASTICITY

Our vision is to link non-invasive microstructural imaging technologies to infer the underlying brain physiology in health and disease. Taking a basic-science perspective, we map brain structure and its plasticity from isolated tissue compartments (i.e. microstructure as cellular spaces, neuron, cell membranes) to whole-brain connectivity and relate the microstructural features to physiology.

In 2017-18, the group has been succesfull in finding funding, and we have continued to expand our technological tools for validation to include electrophysiology, optogenetic brain stimulation and synchrotron imaging. To conduct synchroton imaging a large scale research facility is needed , we use the MAX IV synchrotron in Lund as part of our MAX4Imagers project supported by the Capital Region Research foundation (PI: Tim Dyrby) – see page 26. Synchrotron imaging creates BIG data as it enables unique 3D insight into microstructural environments of cells and axons at nanometer image resolution. Mariam Andersson, Martin Kjer and collaborators have established a data processing pipeline for handling the BIG data and algorithms to analyse both cell sizes and axon distributions - (see figure page 27 for MAX4Imager project).

Tim Dyrby and collaborators successfully arranged the first fully booked workshop on axon diameter estimation with invited international speakers in connection with the ISMRM 2018 conference in Paris.

Henrik Lundell and Tim Dyrby together with collaborators in Lund introduced new patent-pending sequence designs that combine time-dependent matching of multidimensional diffusion encoding to better disentangle size and anisotropy contrast mechanisms in tissue. In 2018, Henrik Lundell was awarded the prestigeous ERC starting grant to further develop his research on biomarkers for neuroinflammation and degeneration.



Translational research together with collaborators: Demonstrating the existence of cortical projections to contralateral striatum originate from frontal areas. Ex vivo tractography in macaque (A) and vervet (B) monkeys, and in vivo humans (D).

GROUP MEMBERS

- **Assoc. Prof. Tim B. Dyrby**
- Senior researcher Henrik Lundell
- Postdoc Kasper W. Andersen
- Postdoc Martin Kjer
- Postdoc Yi He
- Postdoc Tram Nguyen
- Postdoc James Breen-Norris
- Postdoc Nina Rieslev
- PhD stud. David Romascano
- PhD stud. Carmen Genis
- PhD stud. Sara Andreasen
- PhD stud. Mette Bjerg Lindhøj
- PhD stud. Mariam Andersson
- PhD stud. Christian Skoven
- PhD stud. Christian Bauer
- PhD stud. Johanna Perens
- Stud. Inês Mexia Rodrigues

EXTERNAL COLLABORATORS

- Prof. Daniel Alexander
- Assoc. Prof. Markus Nilsson
- Dr. Samo Lasic
- Prof. Daniel Topgaard
- Senior researcher Kristian Almsgård
- Assoc. Prof. Martin Bech
- Assoc. Prof. Simon Eskildsen
- Assoc. Prof. Morten Mørup
- Prof. Jean-Philippe Thiran
- Prof. Giorgio Innocenti
- Prof. Bente Pakkenberg
- Asst. Prof. Jessica Pingel
- Assoc. Prof. Itamar Ronen
- Prof. Anders Dahl
- Prof. Maurice Ptito
- Prof. Jon Sporring

HOMEPAGE

www.drcmr.dk/map

PUBLICATIONS

2, 8, 22, 32, 34, 49, 50, 65, 66, 68, 79, 98, 107, 115, 120

ULTRA-HIGH FIELD MR

The vision of the Ultra-High Field MR group is to provide state-of-the-art sequences and protocols for early and accurate diagnostics in tomorrow's precision medicine by taking full advantage of the 7T system available at DRCMR. However, a series of technical challenges arises when working on MR systems operating at ultra-high fields of 7 tesla or above. Therefore, we work on both software and hardware solutions in order to achieve our goals. Topics include advanced motion correction and reacquisition schemes crucial for achieving the extreme high-resolution images, especially in patients that may move during the scan session. We push the borders by developing faster and smarter sequences such as GABA spectroscopic imaging, which allow the investigation of neural activity processes in the brain. Novel RF and coil designs help improve the homogeneity of the acquired images, thereby improving speed and image quality even further. We strive to make these technical innovations, made by the group, available to all clinical studies performed on the system. The group's clinical interest ranges from high-resolution structural, functional and quantitative imaging to advanced spectroscopy editing and imaging. We apply these techniques to aging studies, studies of neurodegenerative diseases, in particular Parkinsonism and multiple sclerosis, but also for investigating the natural aging processes. The hope is to find robust imaging biomarkers that at an early stage separate healthy aging from unhealthy aging and in the long run be able to contribute to the development of methods to early prediction of disease (e.g. dementia and Parkinsonism).

GROUP MEMBERS

- **Assoc. Prof. Esben Thade Petersen**
- Postdoc Vincent Boer
- Postdoc Anouk Marsman
- MR Clinical Scientist Jan Ole Pedersen
- Senior researcher Henrik Lundell
- Senior researcher Peter Magnusson
- Assoc. Prof. Lars G. Hanson
- Postdoc David Meder
- PhD stud. Hans Christian Stærkind
- PhD stud. Anna Lind Hansen
- PhD stud. Mads A. Just Madsen
- PhD stud. Christopher Fugl Madelung
- Phd stud. Kyong Min Nam
- Research asst. Nam Gyun Lee

EXTERNAL COLLABORATORS

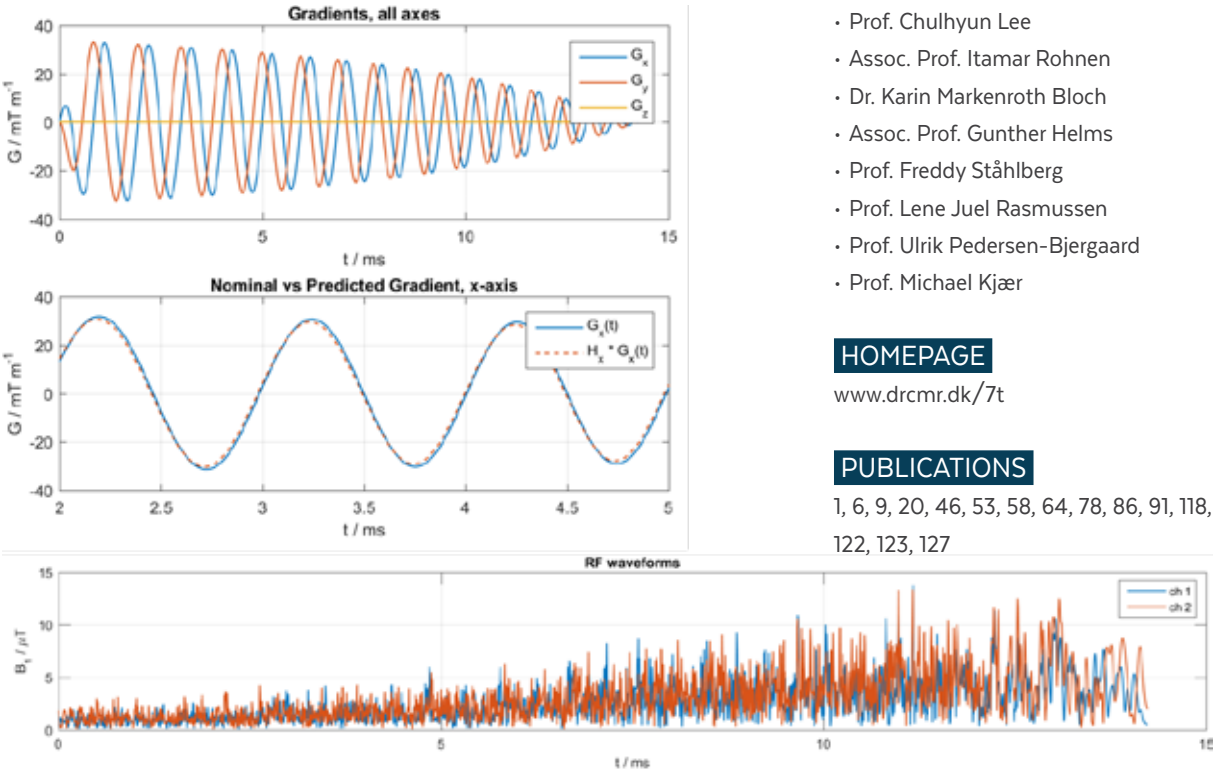
- Prof. Jeroen Hendrikse
- Prof. Dennis Klomp
- Prof. Andrew Webb
- Prof. Matthias van Osch
- Prof. Chulhyun Lee
- Assoc. Prof. Itamar Rohnen
- Dr. Karin Markenroth Bloch
- Assoc. Prof. Gunther Helms
- Prof. Freddy Ståhlberg
- Prof. Lene Juel Rasmussen
- Prof. Ulrik Pedersen-Bjergaard
- Prof. Michael Kjær

HOMEPAGE

www.drcmr.dk/7t

PUBLICATIONS

1, 6, 9, 20, 46, 53, 58, 64, 78, 86, 91, 118, 122, 123, 127



Unleashing the full potential of 7 tesla MRI requires advanced RF designs due to larger field inhomogeneity and increased specific-absorption-rate experienced at higher field strength. An example of selective exitation in shape of our center logo.

ACQUISITION TECHNOLOGY

Research focus:

- Motion and artifacts
- Multi-modal data acquisition
- Spectroscopy and spectroscopic imaging
- Fundamentals and education

The members of the Acquisition Technology Group do research improving MR scanning, e.g. with respect to speed, robustness, sensitivity or specificity, often in collaboration with other research groups. The employed methods range from fundamental physics to advanced data processing techniques needed to extract important physiological parameters from the measurements. The targets of development include imaging, spectroscopy, and multi-modal acquisition. This benefits, for example, the department's neurophysics and high-field research groups, and collaborations with these have led to recent development of novel methods for Magnetic Resonance Current Density Imaging (MRCDI) and fast spectroscopic imaging. Another highlight of 2017-2018 is the development of open source hardware for real-time processing and encoding of non-MR signals in MR-data, www.drcmr.dk/MagstripeEncoding, done in connection with the PhD study of Jan Ole Pedersen who finished May 2018. Two new students, Malte Laustsen and Fróði Gregersen, got funding from Sino-Danish Center for Education and Research for research in motion artifact correction and MRCDI, respectively.

The group also contributes to research projects, e.g. concerning sequence choices and sensitivity consideration, and provide education in MRI safety, physics and techniques at the DRCMR, the DTU and elsewhere. Educational material and software is made available free of chargw, and is used widely internationally (more than 150,000 YouTube views, 1,000 app downloads, and countless downloads of teaching material - see www.drcmr.dk/MR).

GROUP MEMBERS

- **Senior researcher Lars G. Hanson**
- PhD stud. Frodi Gregersen
- Senior researcher Axel Thielscher
- PhD stud. Malte Laustsen
- PhD stud. Jan Ole Pedersen
- Senior researcher Kristoffer H. Madsen
- Senior researcher Peter Magnusson
- Senior researcher Esben Pedersen
- Postdoc Cihan Göksu
- Postdoc Vincent Boer

EXTERNAL COLLABORATORS

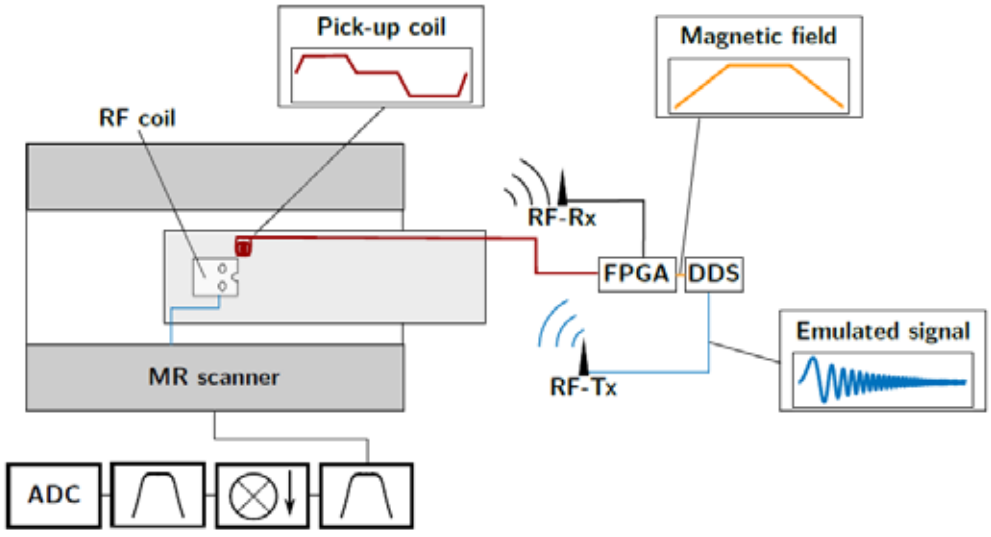
- Prof. Rong Xue
- Philips Healthcare
- MR Clinical Scientist Mads Andersen
- Prof. Jan Henrik Ardenkjær-Larsen
- Christian G. Hanson
- Prof. Klaus Scheffler

HOMEPAGE

www.drcmr.dk/acquisition

PUBLICATIONS

80, 83, 84, 112, 125, 138



Electronic phantom developed in connection with PhD work of Jan Ole Pedersen. The programmable device responds to magnetic fields in a way that mimics a small MR sample. This is useful for hardware characterization and method development.

PRECISION BRAIN STIMULATION

The brain concurrently integrates millions of neural signals in complex networks, producing thought, feeling, and action. Magnetic resonance imaging and other brain mapping techniques offer unique possibilities to study the dynamics in functional brain networks. However, these techniques are correlative in nature and render it difficult to obtain causal insights into the brain´s network dynamics. Non-invasive Transcranial Brain Stimulation (TBS) techniques directly interact with intrinsic brain activity and can induce long-lasting effects on human brain function. Yet, current applications often lack specificity and are hampered by a substantial interindividual and intraindividual variability in their outcome.

We strive to advance TBS as a unique interventional tool to study causal brain dynamics and enhance cognitive and motor function in health and disease. We aim to overcome current limitations through innovative applications that shape electrical signaling in the brain with unprecedented spatial, temporal, and functional precision. 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.
We adopt a "triple M" approach which integrates TBS-induced brain Modulation with neuroimaging-based brain Mapping and biophysical brain Modeling to decipher the underlying physiological and biophysical mechanisms needed to improve the effects of TBS.

The DRCMR houses a unique infrastructure, including 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-loop and closed-loop applications and with neuro-navigated TMS-fMRI on a state-of-the-art 3T MR system. One laboratory is equipped with the first robotic TMS-system in Scandinavia. The robot is used for investigator-independent, automated transcranial magnetic stimulation.

Senior researcher Anke Karabanov coordinates the research area.

Precision Neuromodulation and Therapy

Neurophysics

PRECISION NEUROMODULATION AND THERAPY

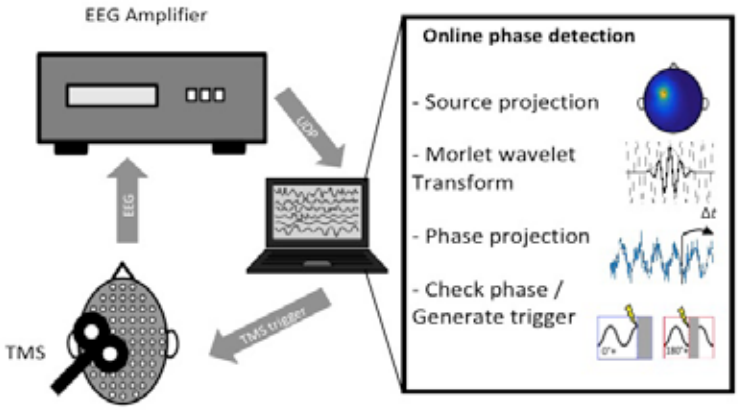
Many brain diseases are caused by dysfunction of brain circuits. Transcranial brain stimulation (TBS) is uniquely suited to individually target specific brain circuits but current therapeutic interventions lack specificity and ignore inter-individual variations. In the Presicion Neuromodulation and Therapy group, we develop TBS-based treatments that effectively target the individual circuit dysfunction at high functional precision.

In order to design circuit interventions with high individual presicion, we merge basic and clinical research with state-of-the art brain mapping and focus on three main research pilars:

TARGET ENGAGEMENT: To capture the neurophysiological effects of TBS, we use electrophysiological (MEP, EEG) and advanced brain mapping techniques (MRI, MRS) and relate physiological changes to TBS effects at the behavioral level. In 2018, we provided new insights in the physiology of use-dependent plasticity in the brain by characterizing the synergistic interplay between motor training and motor immobilization using this approach.

BIOLOGICALLY INSPIRED TBS: To enhance the efficacy and reliability of TBS, we draw inspiration from the natural activity patterns (motifs) which are generated by the brain itself. In 2018 we have contributed to the development of more precise cortical TBS markers by separating the cortical response to TBS from peripherally induced response to the sensory aspects of stimulation.

CLOSING-THE-LOOP TBS: To individualize stimulation we capture the ongoing expression of functional brain states with neurophysiological methods and use this information to inform the timing and pattern of TBS. In 2018, we succeded in providing proof-of-concept for the technical feasibility of closed-loop TBS.



Example of a brain-state informed TMS-EEG setup for the online detection of EEG-state markers. Taken from Madsen, Karabanov et al 2018.

GROUP MEMBERS

- **Prof. Hartwig Roman Siebner**
- Senior researcher Anke Karabanov
- Postdoc Leo Tomasevic
- Postdoc David Meder
- Postdoc Syoichi Tashiro
- PhD stud. Janine Kesselheim
- PhD stud. Allan Lohse
- PhD stud. Lærke Krohne
- PhD stud. Mads Just Madsen
- PhD stud. Sofie Nilsson
- PhD stud. Christian Skoven
- Research asst. Marie Louise Liu
- Research asst. Marjolein Piek
- Stud. Felix Schmidt

EXTERNAL COLLABORATORS

- Senior researcher Estelle Raffin
- Assoc. Prof. Annemette Løkkegaard
- Assoc. Prof. Christina Kruuse
- Research fellow Mitsuaki Takemi
- Senior researcher Raffaele Dubbioso
- Prof. Angelo Quartarone
- Senior researcher Til Ole Bergmann
- Research fellow Virginia Conde

HOMEPAGE

www.drcmr.dk/neurophysiology

PUBLICATIONS

3, 13, 14, 25, 56, 60, 62, 90, 113

NEUROPHYSICS

Our primary research foci are the optimization of the spatial, temporal and neural specificity of non-invasive transcranial brain stimulation (TBS) methods and the development of novel TBS approaches. Our vision is to boost the efficiency of TBS so that it becomes a relevant therapy option for neuropsychiatric diseases. In addition, we aim to provide basic neuroscience research with precise interventional tools to demonstrate causally the link from brain activity to behaviour.

Existing TBS methods induce electric currents into superficial brain areas to modulate and shape neural activity. We develop and apply new biophysical models to reveal and optimize the current flow patterns in the brain and to estimate their impact on neural activity (www.simnibs.org; Fig. A&B). To validate the predictions of the biophysical models, we have successfully implemented novel MR methods to measure the current flow patterns induced by TBS (MR current density imaging; Fig. C). We are further establishing low-intensity ultrasound stimulation in our lab, which is a novel method with improved spatial precision compared to TBS methods using electric currents.

We complement our research on new biophysical methods by translational research that aims to demonstrate the predictive value of our methods in estimating the physiological brain responses to TBS. We perform this research in several internal and international collaborations.

In addition to our TBS research, we contribute to an exciting new project on highly sensitive measurements of the magnetic fields of neurons based on nitrogen-vacancy centers in diamond, driven by our collaborator Ulrik Lund Andersen (DTU Physics). We provide highly realistic simulations of the neuronal magnetic fields to guide methods development.

GROUP MEMBERS

- **Assoc. Prof. Axel Thielscher**
- Postdoc Oula Puonti
- Postdoc Cihan Göksu
- PhD stud. Guilherme Bicalho Saturnino
- PhD stud. Cristina Pasquinelli
- PhD stud. Mürsel Karadas
- PhD stud. Maria Drakaki
- PhD stud. Frodi Gregersen
- Stud. Jonas Auernheimer

EXTERNAL COLLABORATORS

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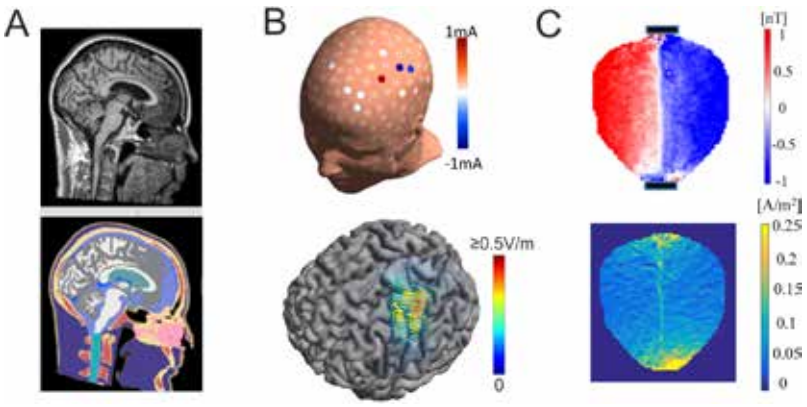
- Prof. Agnes Flöel
- Prof. Thomas Knösche
- Prof. Gottfried Schlaug
- Franz Bødker, PhD

HOMEPAGE

www.drcmr.dk/neurophysics

PUBLICATIONS

10, 26, 29, 30, 37, 52, 67, 70, 76, 83, 84, 92, 94, 96, 108, 110, 129



A Automatic accurate new whole-head segmentation method.
B New automatic optimization method for focal multi-channnel transcranial electric stimulation (TES).
C Highly sensitive imaging of the currents induced by TES in the brain.

COGNITIVE AND COMPUTATIONAL NEUROSCIENCE

Cognition includes a spectrum of faculties that we all take for granted. Learning, decision-making, attention, reasoning, memory, language, and motor control are all part of our mental toolkit. Cognitive Neuroscience is the subfield of neurobiology charged with elucidating 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. Both cognitive and computational neurosciences constitute major research themes here at DRCMR.

Our long-term vision is to pioneer new methods for bridging computational modelling of cognition and neuroimaging, and to use this to understand brain function. Principal among these efforts is to develop advanced multi-modal methods for fitting computational models in parallel to individual neural elements; an approach that will allow us to change the way we ask questions about how computational variables are encoded in the brain.

We have several groups of researchers pursuing research along a diversity of frontiers: There are decision neuroscientists, who are attempting to dissect the neural architectures underlying risk-sensitive choice in dynamic sequential gambling environments, foraging games, and in games involving large and real financial losses. The Reward and Homeostasis group seeks to build fundamental theories of reward value that are grounded in our physiology and evolutionary history. Regarding the auditory system, researchers are using detailed anatomical functional mapping procedures and multivariate, computational methods, to map its functional architecture; on the somatosensory system researchers are using multi-modal imaging techniques to trace the sensori-motor consequences of electrical stimulation of the skin. The Control of Movement group is investigating how the brain engages in motoric control of its body, skill-learning, and optimizing motor action. Finally, the Computational Neuroimaging group engages in machine learning research that aims to improve the modeling and analysis of neuroimaging data from EEG, to fMRI, as well as diffusion & structural data.

Senior researcher Oliver Hulme coordinates this research area.

Computational Neuroimaginging

Reward and Homeostasis

Control of Movement

COMPUTATIONAL NEUROIMAGING

The Computational Neuroimaging group focuses on application of sophisticated modelling and machine learning methodology to improve the sensitivity and interpretability of brain imaging data. Recently, there has been a lot of focus on the use of machine learning to extract early biomarkers for early diagnosis based on neuroimaging data. In particular in the field of psychiatry, this is a challenging endeavor mainly due to the high dimensionality of neuroimaging data and typical scarce availability of training data. Therefore, methods to efficiently extract features and thereby reduce the dimensionality of the input data are very important. To this end, we investigate methods to reliably extract predictive features based on multivariate modelling, where one focus area is multi-way extensions of methods that can estimate and quantify functional connectivity patterns across trials, sessions, subjects and modalities while appropriately taking variability into account. Recently, we have been investigating properties of multivariate decomposition techniques for early prediction of individuals at risk of developing schizophrenia.

Other recent research includes the development of tools for online analysis of neuroimaging data enabling state-dependent stimulation and brain-computer interfaces. We develop software capable of estimating phase and coherence properties of EEG with minimal latency and investigate how reliabel these properties can be estimated based on realistic simulations.

GROUP MEMBERS

- **Assoc. Kristoffer H. Madsen**
- PhD stud. Lærke G. Krohne
- PhD stud. Guilherme B. Saturnino
- Postdoc Oula Puonti
- Stud. Xinlu Cai
- Stud. Patrick Niekrenz
- Stud. Qiang Li
- Stud. Andrea S. Frederiksen
- Stud. Laura Rose
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- Stud. Johannes Kruse
- Stud. Jesper L. Hinrich
- Stud. Agla Harðardóttir
- Stud. Søren F. V. Nielsen

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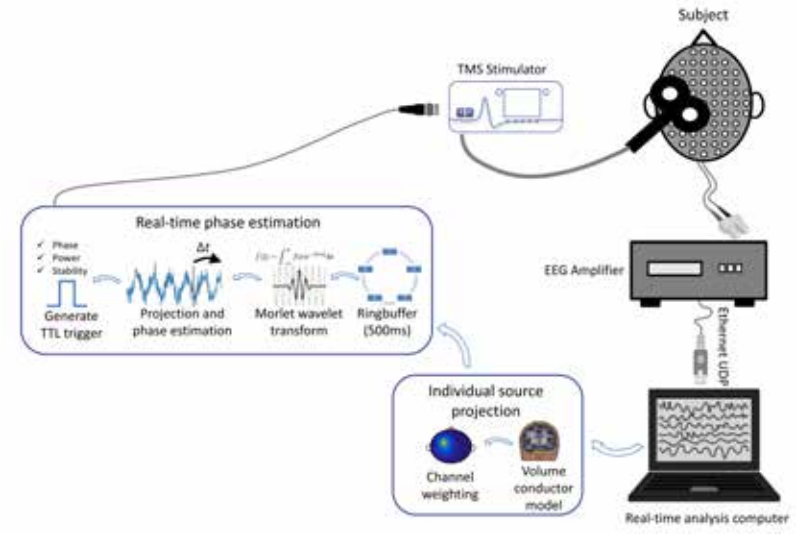
- Prof. Lars Kai Hansen
- Prof. Rong Xue
- Prof. Raymond Chan
- Prof. Liang Wang
- Prof. Tülay Adali
- Postdoc Nathan Churchill
- Assoc. Prof. Torben Lund

HOMEPAGE

www.drcmr.dk/modelling

PUBLICATIONS

19, 32, 45, 51, 52, 87, 100, 106, 108



Real-time TMS-EEG phase targeting: Setup used to perform EEG phase dependent TMS stimulation. EEG is streamed for real-time analysis with low latency. If the stimulation criteria are met a TMS trigger signal is generated.

REWARD AND HOMEOSTASIS

The Reward and Homeostasis group aims to address some simple but difficult problems. Ultimately, these follow from one overarching question: How does the brain compute value, and why? We generally try to address this problem by stepping outside of neuroscience to think about what constraints should be imposed on the functions of a reward system, and then test these ideas by stepping back into neuroscience via experiments that combine neuroimaging, behavioral testing, and physiological recordings.

We consider the constraints imposed by evolution, whereby the homeostatic states of the body (such as energy, hydration, and temperature) confer different chances of survival. As such reward computations should be, at least in principle, calibrated to assign value to the homeostatic dynamics that defend long-run survival. This attempts to provide a unifying explanation of a number of decision-making phenomena such as risk and loss aversion from first principles. This line of work is primarily theoretical, though it informs our experimental questions.

We also consider constraints imposed by economics, for how the reward system evaluates monetary outcomes and how this impacts on decision-making under risk. By thinking about what is an optimal decision strategy for making one's wealth grow, and how that should change under different dynamic settings, one can look at how the brain's valuation computations should systematically change under these different dynamics. This line of work is experimental and combines high-stakes gambling games with functional neuroimaging.

Finally, we consider constraints imposed by physiology, in particular endocrinology, for how the reward system evaluates food. We are interested in how hunger and satiety modulate the reward system, and how this is mediated by the metabolites and hormones that cascade following consumption.

GROUP MEMBERS

- **Senior researcher Oliver Hulme**
- Postdoc Barbara Vad Andersen
- Postdoc David Meder
- PhD stud. Tobias Dahle-Morville
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- Research asst. Magnus Koudal
- Stud. Cornelia Rudolph

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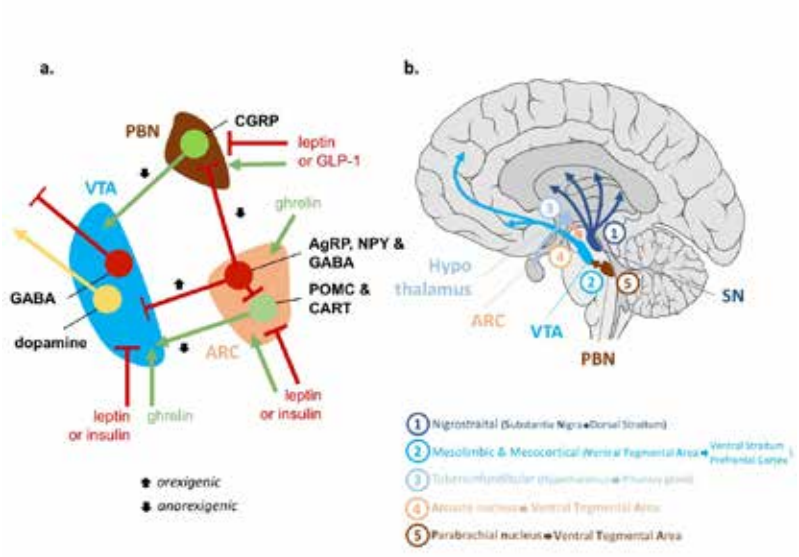
- Prof. Karl Friston
- Prof. Denis Burdakov
- Prof. Alexander Sebald
- Dr. Edward Webb

HOMEPAGE

www.drcmr.dk/reward-and-homeostasis

PUBLICATIONS

16, 35, 73, 85



An illustration of what can be called a homeostatic reinforcement interface, subsystems of the brain where homeostatic control interfaces and thus interacts with the reward value computations.

CONTROL OF MOVEMENT

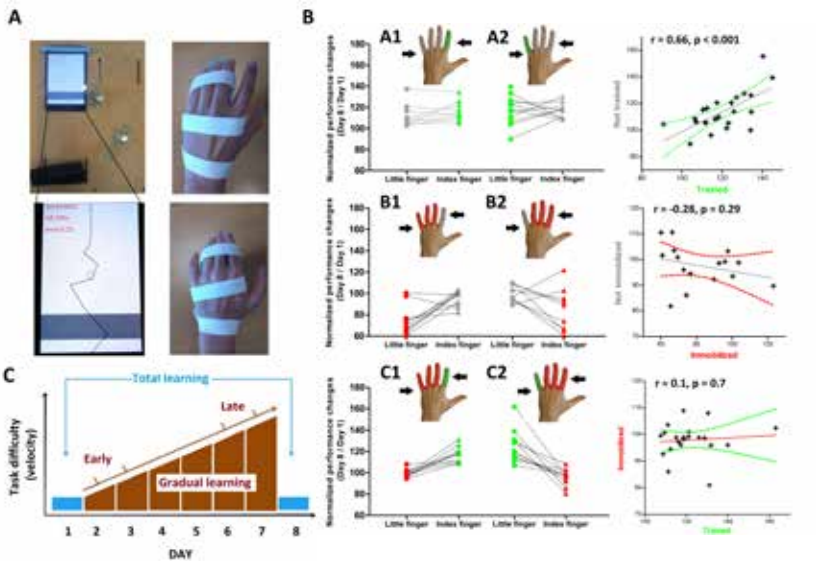
The Control of Movement (CoM) research group uses a "triple-M" approach to decipher the causal neuro-dynamics in sensorimotor brain networks by combining multimodal brain MAPPING with computational MODELLING and non-invasive MODULATION of sensorimotor networks. In 2017-2018, we made several important discoveries:

Volitional and skilled control of actions

Using EEG, we identified cortical theta oscillations as a important neural signature during the updating of action plans based on environmental cues (Pelligrino, 2018). Combining smartphone technology with neuronavigated TMS-based mapping, we uncovered the mechanisms that underpin representational plasticity in the primary motor hand area (M1-HAND). We found converging evidence for a synergistic rather than competing effect of training and immobilization on motor representations in human M1-HAND (Raffin & Siebner 2017). In another study, medical students trained bimanual endoscopic surgical skills for a week (Karabanov et al, 2018). Measurements of task-related activity with fMRI revealed bilateral activity increases in the frontoparietal grasping network, pointing to a critical role of the grasping network in acquiring novel tool-based bimanual skills.

Integration of sensation into action

Sensory inputs can effectively modify the motor output from M1-HAND to flexibly adjust our movements to an everchanging environment. To unravel the basic cortical mechanims, we mapped fast inhibitory and facilitatory effects of sensory inputs on motor cortex excitability with neuronavigated TMS. We showed for the first time that rapid sensorimotor integration in human M1-HAND is organized according to a center-inhibition and surround-facilitation principle (Dubbioso, 2017) . We also demonstrated that fronto-parietal communication is disturbed during sensorimotor conflict (Karabanov, 2017).



A Smartphone-based finger training and assesment of visuomotor skill.
B Individual changes in tracking accuracy from days 1 to 8. The scatter graphs plot performance changes for the two fingers of the same hand separately for each group.

GROUP MEMBERS

- **Prof. Hartwig Siebner**
- Senior researcher Anke Karabanov
- Senior researcher Jens Hjortkjær
- Postdoc Leo Tomasevic
- Postdoc David Meder
- Postdoc Kasper W. Andersen
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- PhD stud. Janine Kesselheim
- PhD stud. Sofie Nilsson
- PhD stud. Allan Lohse
- PhD stud Morten Gørtz Jønsson
- PhD stud. Line Johnsen
- PhD stud. Steffen Angstmann
- PhD stud. Mads A. Just Madsen
- PhD stud. Chloe Chung
- Research asst. Angeliki Charalampaki

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- Prof. Olivier David
- Assoc. Prof. Mark Schram Christensen
- Prof. Jens Bo Nielsen
- Prof. Torsten Dau

HOMEPAGE

www.drcmr.dk/control-of-movement

PUBLICATIONS

10, 25, 66, 87, 121

LIFESPAN IMAGING

Mapping of brain and behavioural changes across the lifespan

Lifespan Imaging centres around understanding the development of brain structure, function and chemistry throughout the lifespan. We are interested in both normal and pathological development, and to understand 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 repeated measurements of the same individuals. We also perform various intervention studies testing effects on brain health from e.g. physical exercise or cognitive training. 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.

Our passion

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

In 2018, Prof. Carl Johan Boraxbekk took over the coordination role from Senior researcher William Baaré.

Healthy Ageing

Brain Maturation

HEALTHY AGEING

The vision for the Healthy Ageing group is to identify and to optimize sustainable interventional strategies for improved or maintained brain health throughout the lifespan. The mission is to conduct interdisciplinary population-based neuroscience research that provides unique insights into the neuro-cognitive mechanisms of brain and cognitive aging. We are particularly interested in novel interventions for neuroenhancement.

Some of our key results the past years have been related to the influence of physical exercise, and how this may shape brain aeging. For example, we have shown how a lifespan of physical acitivty may improve brain-behavior relationships using a powerful multi-modal analysis of brain parameters. We have also been able to show that improving physical fitness when you are over the age of 65 may improve cognitive performance, increase the size of hippocampus volume, and increase functional connectivity from the medial temporal lobe to other parts of the brain. It should, however, be noted that we have also observed a rather large individual difference in the response from physical exercise. These findings question the "one-size-fits-all" approach that is often used, and more individually tailored interventions are necessary in the future.

The coming years, we are looking forward to digging into the analysis of some of our key projects that completed data collection during 2018. In the LISA study (see page 18), we are exploring strength training and brain health; in the LifeMabs study (see page 19), we are examining how certain life course trajectories influence current brain health; and in the Lifespan study, we are comparing three different age groups (young, middle, old) with a particular focus on MR-spectroscopy at 7T. So, there is plenty of exciting data about to be analyzed, interpreted, and finally written up, in the years to come.

GROUP MEMBERS

- **Prof. Carl-Johan Boraxbekk**
- Assoc. Prof. Esben Thade Petersen
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- Postdoc Kasper Winther Andersen
- Postdoc Anouk Marsman
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- Stud. Christian Nøhr

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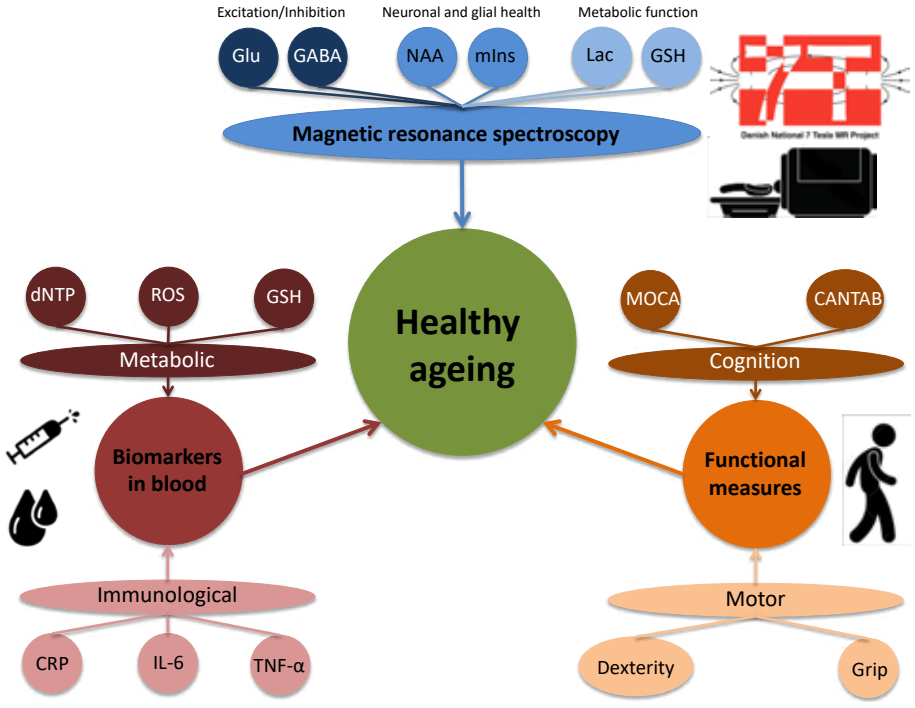
- Prof. Erik Lykke Mortensen
- Prof. Michael Kjær
- Assoc. Prof. Ellen Garde

HOMEPAGE

www.drcmr.dk/healthy-ageing

PUBLICATIONS

4, 12, 15, 18, 20, 23, 24, 42, 47, 49, 55, 57, 69, 71, 74, 75, 81, 82, 102, 104, 111, 117, 123, 124



General overview of the Lifespan project.

BRAIN MATURATION

The brain is shaped by a continuous interplay of genetic, physical, bodily, cognitive, social, cultural, and environmental factors that emerge on different timescales and drive developmental cascades across the lifespan. Thus, to understand and predict mental and cognitive (i.e. brain) health and illness, resilience and potential, we need to understand how brains are shaped throughout life. The Brain Maturation group studies brain and behavioral development during childhood and adolescence in health and disease, and the impact of genetic, biological and environmental factors. We address critical questions regarding the factors that place young people at risk of e.g. developing cognitive or emotional problems. Brain structure and function are assessed using multimodal magnetic resonance imaging (MRI) techniques. A key project is the HUBU ("Hjernens Udvikling hos Børn og Unge": Brain maturation in children and adolescents) project. HUBU is an ongoing longitudinal project, which started in Spring 2007, and included 95 children aged 7-13 years at baseline. The first 10 assessments were conducted with 6-month intervals, the 11th assessment one year later (2013), and the 12th assessment three years later (finalized July 2016). Since January 2017, the HUBU project has been part of the Horizon 2020 project Lifebrain, in which we are partners. Lifebrain integrates data of several existing large prospective brain imaging cohorts ranging in age from 4 to 90 years, incorporating more than 5,000 individual participants and 27,000 examinations in total. Lifebrain aims to build a solid knowledge foundation for understanding how brain, cognitive and mental health can be optimized throughout the lifespan. As part of the data enrichment for Lifebrain, we are planning a 13th assessment of HUBU participant, which should be finalized primo 2019.

GROUP MEMBERS

- **Senior researcher William F.C. Baaré**
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- Postdoc Louise Baruël Johansen
- PhD stud. Jonathan Holm-Skjold
- Research Medical Laboratory
- Technologist Sussi Larsen
- Datamanager Olga Rigina
- Stud. Natascha Larsen
- Stud. Mads Stehr
- Stud. Thilde Elena Kofoed Sørensen
- Stud. Amalie S. Ekstrand
- Stud. Zahra Salim Abd Al-Hassan

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- Prof. Terry Jernigan
- Assoc. Prof. Wesley Thompson
- Postdoc Marybel Robledo Gonzalez
- Prof. Sven Kreiborg
- Prof. Jesper Mogensen
- Prof. Katrine Pagsberg
- Assoc. Prof. Katrine Strandberg-Larsen
- Prof. Lars Bo Andersen
- Prof. Gitte Moos Knudsen
- Assoc. Prof. Alexander Leemans
- Prof. Erik Lykke Mortensen
- Assoc. Prof. Morten Mørup
- Prof. Kristine Walhoved
- EU Lifebrain partners

HOMEPAGE

www.drcmr.dk/brain-maturation

PUBLICATIONS

63, 88, 101, 124

CLINICAL PRECISION IMAGING

Paving the way for MR-based precision medicine

The field of Magnetic Resonance Imaging (MRI) continues to advance, expanding the possibilities to study how brain disorders affect the brain´s structure, function, and metabolism. We exploit the enormous biomedical potential of MRI to establish MR-based Precision Medicine as a powerful interface between diagnostic radiology and the clinical neurosciences. We will boost the role of MRI as a clinical tool that can help neurologists, neurosurgeons, and psychiatrists to tailor their therapy to the individual needs of their patients.

Our long-term vision is to realize the full potential of MRI in optimizing clinical decision-making through MR-based finger-printing. Our mission is to develop and validate novel MRI-based technologies which can reliably capture risk or resilience and visualize disease-related structural, functional and metabolic changes based on individual brain scans. MR-based imaging technologies and analytical tools are optimized to reliably identify clinically relevant MR-based "read-outs". It is our aim to further optimize the value of MR-based precision medicine by integrating longitudinal electronic health data (E-health) and genomic and biochemical data ("Omics"). Additionally, we will exploit MRI-based techniques to individualize the use of non-invasive transcranial brain stimulation (NTBS) to maximize therapeutic efficiency.

Our research will yield novel MR protocols that pick up disease-causing (pathogenesis) or disability-causing (pathophysiology) processes at high sensitivity and specificity. It is our aim to establish predictive MR-based neuroimaging markers ("read-outs") to assist clinical decision-making and personalized medicine. Another aim is to identify pre-symptomatic MRI-based neuroimaging markers of disease formation in large population cohorts bearing increased risk of a neurologic (e.g. Parkinson´s disease) or psychiatric (e.g. schizophrenia) disorder. We are equally interested in neuroimaging markers of "resilience" – rendering individuals resistant to brain disorders. Finally, we wish to establish novel MRI-based neuroimaging markers for the presence or magnitude of common disabling symptoms; markers that can be used to test and monitor the efficiency of symptomatic treatments at the individual level.

In 2018, after Prof. Hartwig Siebner received a 5-year clinical professorship with special focus on Precision Medicine, Kasper Winther Andersen took over the role as new coordinator for the Clinical Precision Imaging research area.

Movement Disorders

Neuroimaging in Multiple Sclerosis

Developmental Psychiatry

Traumatic Brain Injury

MOVEMENT DISORDERS (NIMODIS)

The Neuroimaging of Movement Disorders (NiMoDis) group focuses on applying non-invasive brain stimulation and magnetic resonance imaging in movement disorders. The primary focus of the NiMoDis group is Parkinson's disease with two major ongoing projects:

Unravelling the alteration of brain structure and function in Parkinson's disease with ultra-high field MRI (7TPD).

Parkinson's disease (PD) causes a loss of neurons in brainstem neuromodulatory nuclei such as the dopaminergic substantia nigra (SN) and the noradrenergic locus coeruleus (LC). In recent years it has become possible to capture these changes in vivo with MRI. Imaging these small structures with ultra-high field MRI, the NiMoDis group is currently investigating alterations of brainstem structure and function in PD. The aim is to identify the structural changes in SN and LC that most accurately identify PD, and explore how patterns of structural and functional alterations in SN and LC reflect clinical disease phenotypes.

Modulating and mapping dyskinesia in Parkinson disease

Parkinson's disease causes a loss of dopaminergic neurons. Levodopa is used to replace lost dopamine. Levodopa works well, but most patients eventually develop involuntary movements known as dyskinesia. Our group has previously shown that a single dosage of levodopa elicited abnormal activation of a cortical motor area known as the pre-supplementary motor area (preSMA) in dyskinetic PD patients. Building on this knowledge, we are now pursuing an interventional study in which we target the preSMA with repetitive transcranial magnetic stimulation (rTMS). Our aim is to prevent levodopa from eliciting abnormal activity in preSMA and thus prevent the appearance of dyskinesia.

GROUP MEMBERS

- **Professor Hartwig Siebner**
- Postdoc David Meder
- PhD stud. Allan Lohse
- PhD stud. Christopher Fugl Madelung

EXTERNAL COLLABORATORS

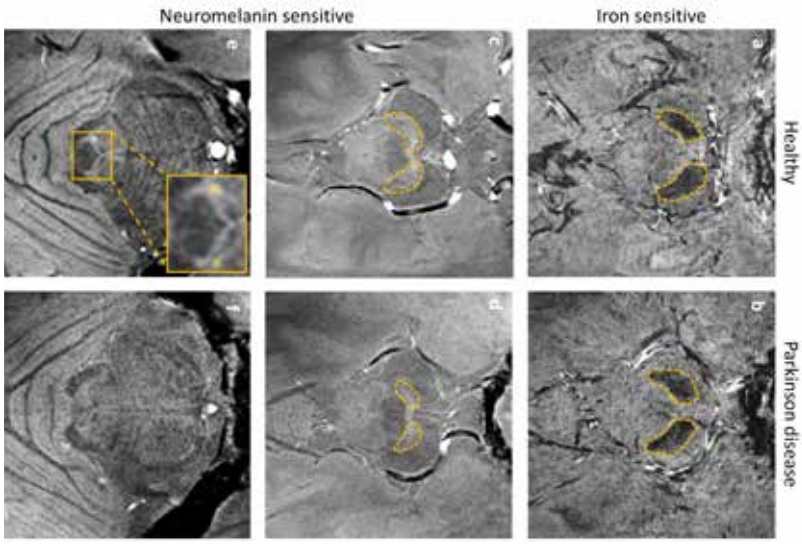
- Assoc. Prof. Annemette Løkkegaard
- Assis. Prof. Antoine Lutti

HOMEPAGE

www.drcmr.dk/movement-disorders

PUBLICATIONS

28, 59



Structural MRI of brainstem neurodegeneration in PD. Iron sensitive images (a & b) show nigral iron build-up associated with PD while neuromelanin sensitive images demonstrate neuronal loss in the substantia nigra (c & d) and locus coeruleus (e & f).

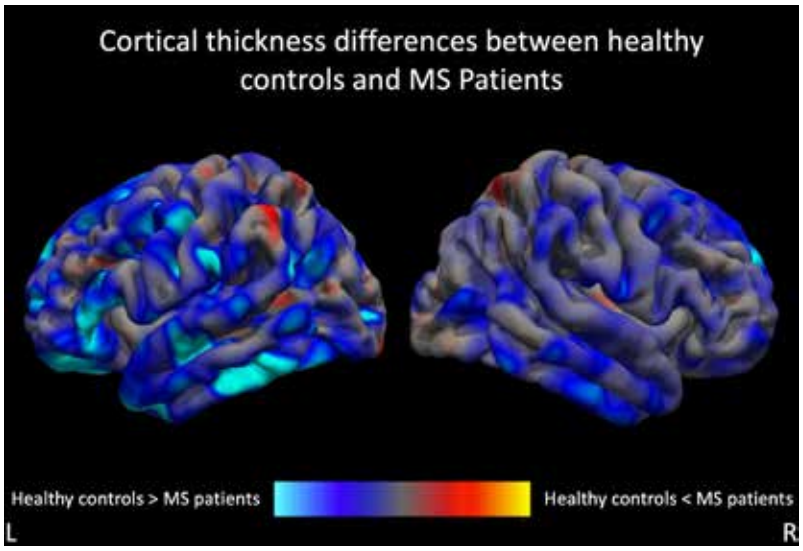
NEUROIMAGING IN MULTIPLE SCLEROSIS

Multiple Sclerosis (MS) is an autoimmune, demyelinating and neurodegenerative disease that diffusively attacks the central nervous system. White matter (WM) lesions are a hallmark of MS and are readily detectable on clinical magnetic resonance imaging (MRI), which is also the most sensitive tool for diagnosing and monitoring disease progression. However, WM lesions in themselves explain only a fraction of the diversity of clinical outcomes in MS.

The aim of the Neuroimaging in Multiple Sclerosis (NiMS) group is to look beyond WM lesions and uncover novel pathophysiological mechanisms by pushing the frontiers of MRI to capture MS-related tissue damage. The group uses a wide range of MR-based techniques such as functional MRI, magnetic resonance spectroscopy (MRS) and diffusion weighted imaging (DWI), to try to resolve what has been termed the clinico-radiological paradox in MS.

In a recent project, we delineated the neural correlates of fatigue using fMRI and structural MRI. We found that the cerebellum and premotor system are highly involved in the experience of fatigue and that cortical thickness also plays a role in this. Another project investigates novel DWI sequences to uncover the microstructural changes in MS.

The current focus of the group is to exploit the potential of MRI at ultra-high field strength (7T). We are currently conducting the first clinical 7T MR study in Denmark, combining MRS with DWI to investigate how MS affects the microstructure of major WM tracts in the brain. In another key project, we use the improved structural resolution of 7T MRI to characterize the impact of single neocortical lesions on hand motor and sensory function, which is a major issue in MS. Our group benefits from a longstanding collaboration with the Danish Multiple Sclerosis Centre and has received generous support from the Danish Multiple Sclerosis Society.



Multiple Sclerosis pathology goes beyond white matter lesions. Standardized brain volumes of mean cortical thickness. The blue colors indicate areas of reduced cortical thickness in a group af RRMS patients compared to healthy controls.

GROUP MEMBERS

- **Professor Hartwig Siebner**
- Assoc. Prof. Tim B. Dyrby
- Senior researcher Anke Karabanov
- Senior researcher Henrik Lundell
- Postdoc Kasper W. Andersen
- PhD stud.Christian Bauer
- PhD stud. Mads AJ. Madsen
- PhD stud. Stefano Cerri
- Stud. Marta FM. Marques
- Research radiographer Hanne Schmidt
- Research radiographer Sascha Gude
- Research medical laboratory technologist Sussi Larsen

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- Prof. Finn T. Sellebjerg
- Prof. Christian Dettmers
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- Assoc. Prof. Morten Mørup
- Assoc. Prof. Itamar Ronen
- Consultant Camilla G. Madsen
- Consultant Anne-Mette Leffers

HOMEPAGE

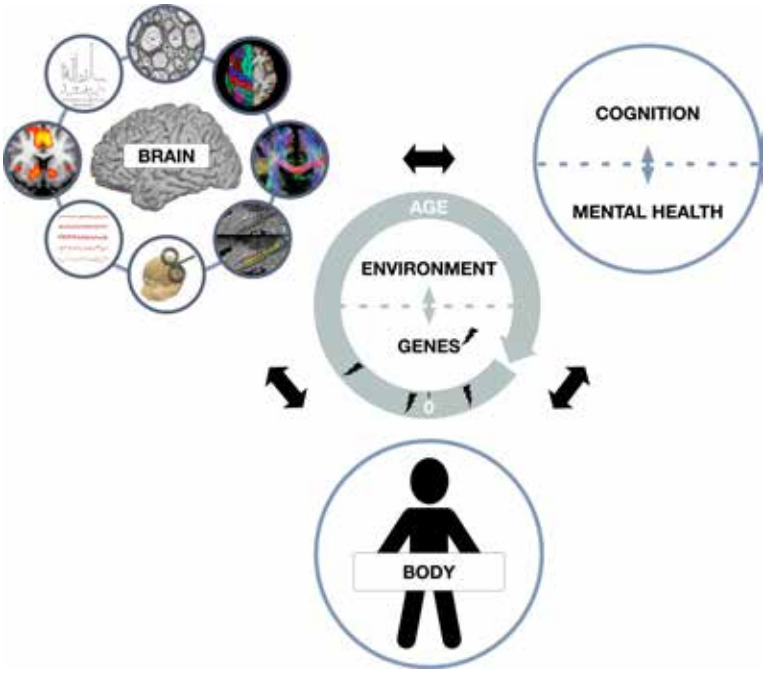
www.drcmr.dk/neuroimaging-in-multiple-sclerosis

PUBLICATIONS

31, 54, 65 ,120, 139

DEVELOPMENTAL PSYCHIATRY

Psychiatric disorders such as major depression, anxiety, schizophrenia and bipolar disorders are globally among the leading causes of years lived with disability. Many psychiatric disorders have their onset in chilhood, adolescence or early adulthood. Neuroscientific research, driven by the advances in in vivo brain imaging methods, established that psychiatric disorders are disorders of the brain. Nevertheless, diagnosis is still largely based on clinical assessment, and diagnostic categories are highly heterogeneous with respect to symptomatology and disease progression. Furthermore, available treatments are often generic and not tailored to the individual. Our vision is to improve the prediction and characterization of psychiatric disorders across the lifespan and contribute to developing new prevention and personlized treatment strategies and identifying new treatment targets. Our neuroscientific research is highly interdiciplinary. In close collaboration with our clinical partners, we employ state of the art multimodal brain imaging and electrophysiological techniques to elucidate, characterize and monitor the neurobiological and neurocognitve signatures of risk and disease in different at-risk and neuropsychiatric populations. We have a long history of doing research in the field of neuropsychiatry. Two recent key projects are the Danish High Risk and Resilience Study – VIA 11 (page 22), a national longitudinal study of 522 eleven-year old children born to parents with or without a diagnosis of either schizophrenia or bipolar disorder, and the TECTO study (page 28), that combines a randomized clinical trial and longitudinal case-control design in pediatric patients with obsessive-compulsive disorder.



Multimodal brain imaging and electrophysiological techniques characterize and monitor neurobiological and neurocognitve underpinnings of risk, resilience and mental disease across the lifespan. Bodily functions and fitness are assessed. Lightning bolts: genetic predispositions, prenatal events and postnatal stressors are thought to increase individuals' vulnerability to stressors that often impact during maturation.

GROUP MEMBERS

- **Senior researcher William F.C. Baaré**
- Postdoc Ayna Nejad
- Senior researcher Kathrine Skak Madsen
- Prof. Hartwig Siebner
- PhD stud. Line Korsgaard Johnsen
- PhD stud. Anna V. L. van Themaat
- PhD stud. Valdemar Uhre
- PhD stud. & Radiographer Christian Bauer
- PhD stud. Sigurd W. Uldall
- PhD stud. Katrine Maigaard
- PhD stud. Tine Pedersen
- Postdoc Melissa Larsen
- Postdoc Louise Barüel Johansen
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- Prof. Kerstin Plessen
- Prof. Thomas Werge
- Prof. Lars Kessing
- Prof. Kamilla Miskowiak
- Assoc. Prof. Maj Vinberg
- Prof. Gitte Moos Knudsen

HOMEPAGE

www.drcmr.dk/DevelopmentalPsychiatry

PUBLICATIONS

5, 9, 13, 21, 38, 39, 40, 42, 45, 72, 76, 88, 97, 99, 100, 103, 105, 109, 115

TRAUMATIC BRAIN INJURY

How can brain mapping techniques capture the structural and functional sequelae of severe traumatic brain injury (TBI)? How can multimodal brain imaging be used to estimate the chances to regain consciousness? The TBI group strives to answer these pressing questions by combining multiple brain mapping modalities to prospectively assess the full spectrum of structural and functional changes that occur after TBI. One line of research examines the relation between TBI severity and the spatial distribution of microbleedings and microstructural changes in the subacute stage of TBI. The other line of research adopts a prospective study design to disentangle the brain structural and functional mechanisms that underlie the recovery of consciousness after severe TBI. Our central hypothesis is that the long-range cortico-cortical and thalamo-cortical connectivities determine the outcome regarding the recovery of consciousness. We employ a wide range of brain mapping methods to identify predictive markers of recovery from a TBI-derived disorder of consciousness. We use EEG to record the evoked cortical response to single-pulse Transcranial Magnetic Stimulation (TMS) which is thought to reflect whole-brain effective connectivity. We recently published a metodological validation study in healthy individuals which revealed that peripheral co-activation makes a substantial contribution to the evoked TMS response (Conde et al., 2018). We currently test whether whole-brain effective connectivity can also be revealed by peripherally evoked cortical activity.

The currently running projects in the TBI group are funded by three independent Danish funding agencies, namely the Independent Research Fund Denmark | Medical Sciences, Lundbeck Foundation, and the research fund of the Capital Region of Denmark.

GROUP MEMBERS

- **Prof. Hartwig Siebner**
- Postdoc Virginia Conde
- Postdoc Kasper W. Andersen
- Assoc. Prof. Tim Dyrby
- Assoc. Prof. Kristoffer Madsen
- PhD stud. Sara Hesby Andreasen

EXTERNAL COLLABORATORS

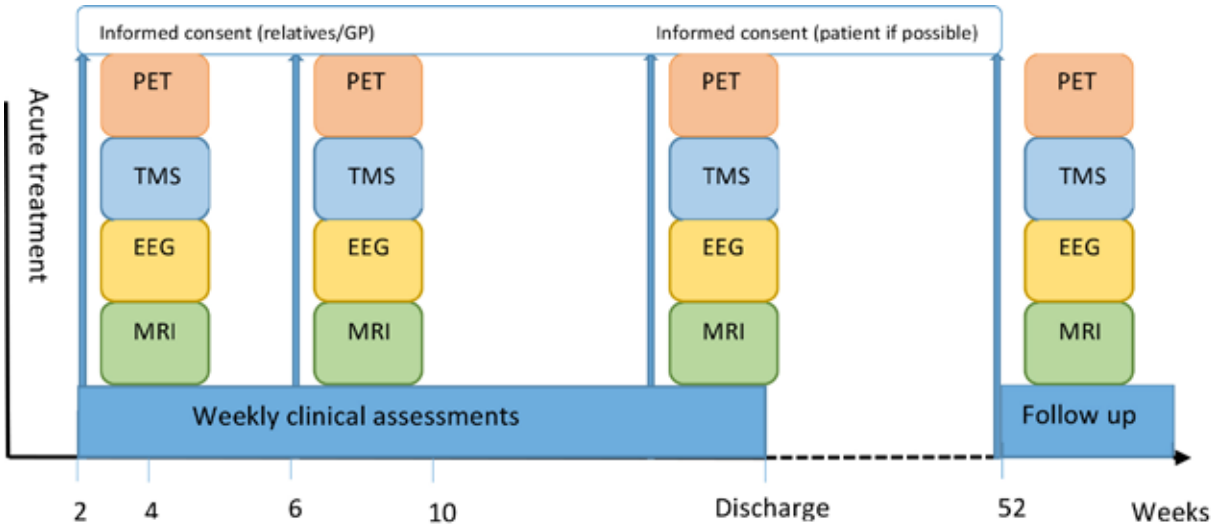
- Research leader Ingrid Poulsen
- MD Lars Peter Kammersgaard
- Postdoc Karine Madsen
- MD Christian Pilebæk Hansen
- Nurse Mia M Wolffbrandt
- Senior researcher Til Ole Bergmann
- Prof. Jesper Mogensen
- Prof. Lars Kai Hansen

HOMEPAGE

www.drcmr.dk/tbi

PUBLICATIONS

33, 50



The ABC in TBI workflow from patient inclusion to 1 year follow up.

INFRASTRUCTURE

INFRASTRUCTURE

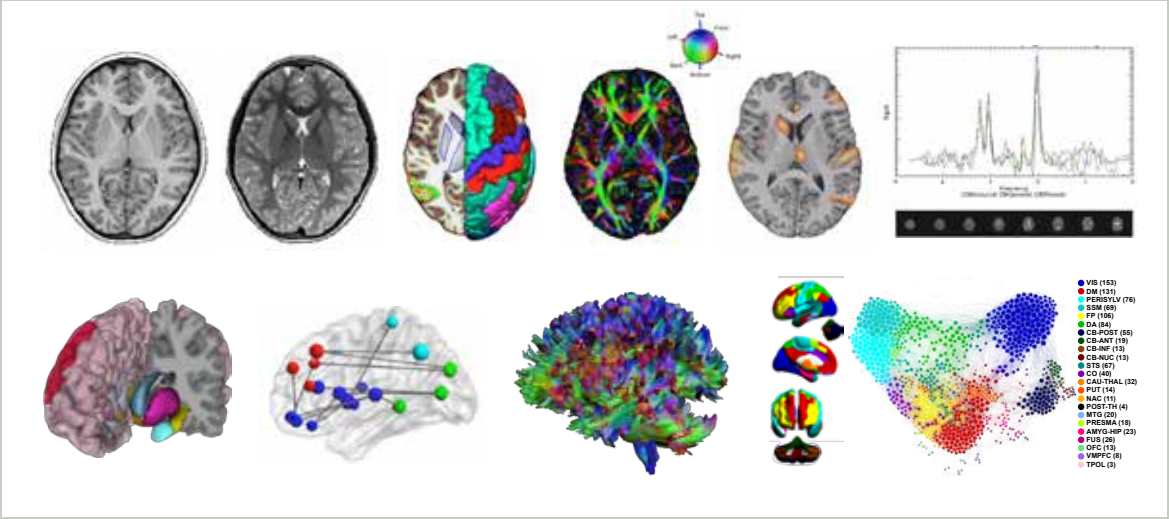
SCANNERS

1 x 7.0 tesla
1 x 7.0 tesla preclinical
3 x 3.0 tesla
2 x 1.5 tesla
1 x MRI simulator

LABS

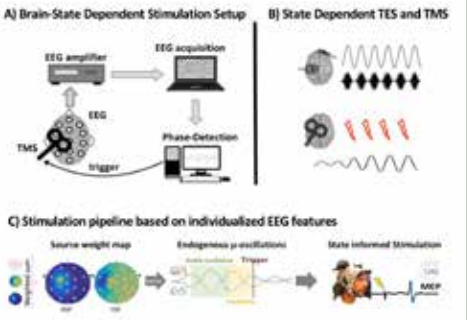
2 x Non-invasive brain stimulation
1 x EEG
2 x Non-invasive brain stimulation & EEG
1 x Hardware

STRUCTURAL, FUNCTIONAL AND NEUROCHEMICAL MRI

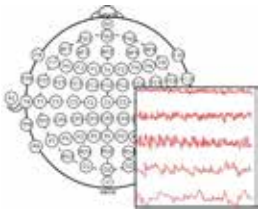


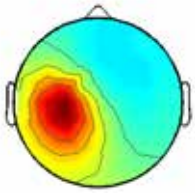
NON-INVASIVE PRECISION BRAIN STIMULATION

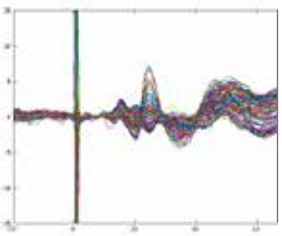
Field estimation for transcranial magnetic and electric stimulation



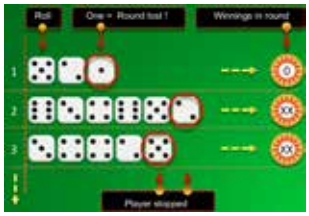
ELECTROENCEPHALOGRAPHY (EEG)







BEHAVIOURAL ASSESSMENTS



METHOD GROUPS

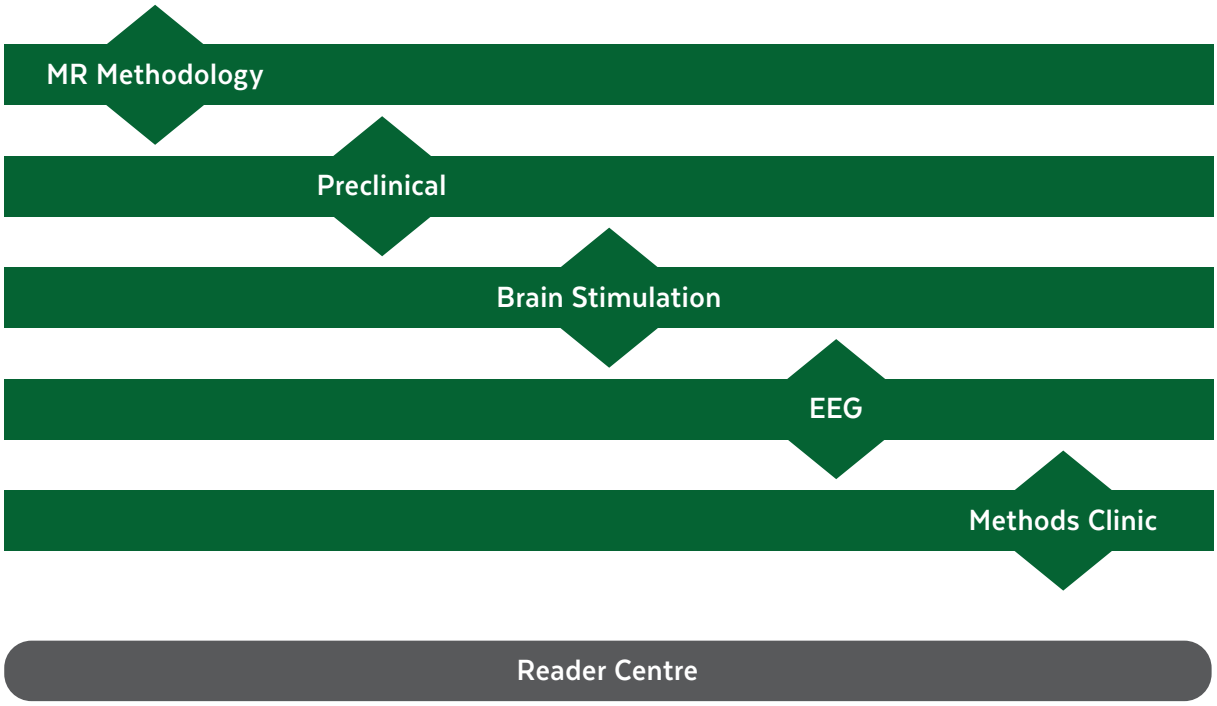
Mapping of brain and behavioural changes throughout life

The central aim of our research is to understand how people develop across the lifespan. How do biological and socio-environmental factors drive developmental cascades in our brain and body? How do these cascades impact on our well-being and how do they shape our behaviour?

We tackle these questions using a multi-dimensional prospective approach that combines state-of-the-art multimodal imaging techniques with advanced imaging and data analysis methods and perform elaborative assessments of biological, physical, environmental and behavioural variables.

MR Methodology

Preclinical



Brain Stimulation

EEG

Methods Clinic

Reader Centre

MR METHODOLOGY

The MR methodology group supports the research activities that involve magnetic resonance (MR) at the 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 DRCMR has 7 MR scanners of which four are used for both research and clinical purposes. Clinic: two 3T Siemens Prisma and Verio and two 1.5T Siemens Espree and Avanto, and research two Philips Achieva systems (3T and 7T). 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 data quality across research projects at DRCMR, and we also try to maximize the potential of the different systems used across the projects. 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 the DRCMR.

GROUP MEMBERS

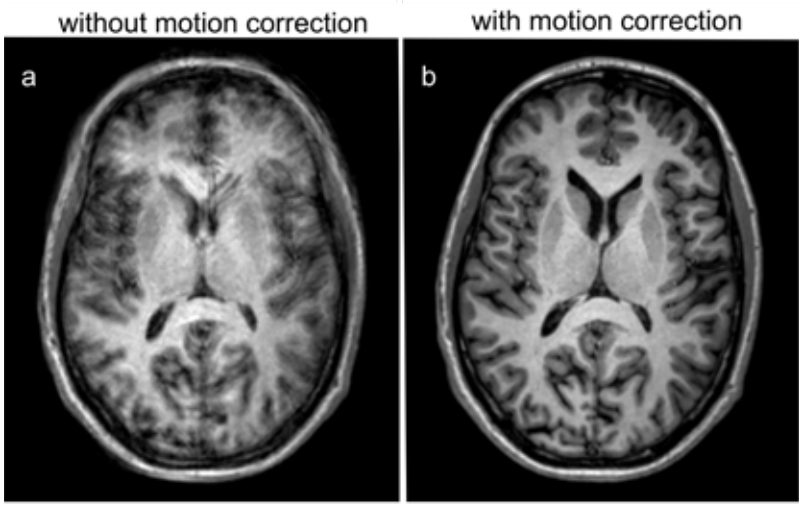
- **Postdoc Vincent Boer**
- **Senior researcher Henrik Lundell**
- Assoc. Prof. Lars G. Hanson
- Physicist Lasse Rahbek Søndergaard, PhD
- Assoc. Prof. Tim Dyrby
- Assoc. Prof. Axel Thielscher
- Assoc. Prof. Esben Thade Petersen
- Postdoc Kasper Winther Andersen
- Postdoc Cihan Göksu
- Assoc. Prof. Kristoffer Hougaard Madsen

HOMEPAGE

www.drcmr.dk/mr-methods

PUBLICATIONS

98, 107



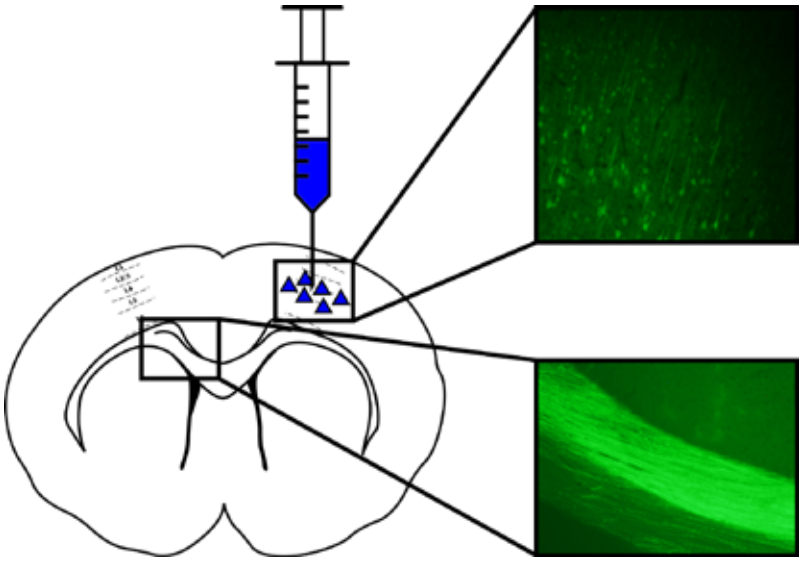
One of our new developments is motion-robust imaging. Subjects movement can lead to severe loss of image quality (a). With this new approach to motion correction, we continuously measure the position of the head and follow the movement to restore high quality images even with severe motion (b).

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 to improve the treatment and diagnosis of brain disorders. Our research spans multi-modal microstructural, functional and metabolic imaging in combination with brain stimulation and other interventions with potential therapeutic relevance.

The preclinical research facilities were refurbished in 2016 with a new 7T Bruker Biospec MRI scanner system and fully equipped laboratory for electrophysiology in rodents. All approvals in terms of animal facilities and a virus lab (GMO class 2) have been obtained to realize optogenetic brain stimulation. Naturally, it takes time to get such a new and advanced experimental setup, combining MRI and electrophysiology, to work robustly. Christian Skoven has been a driving force establishing the electrophysiology setup which combines neuronal LFP recordings and optogenetic brain stimulation. Optogenetics is introduced by injection of a virus that expresses a light-sensitive protein on the cell membrane allowing activation when the neuron is exposed to laser light at a specific wavelength (see figure).

High-quality ex vivo MRI of post mortem tissue samples for microstructure imaging (diffusion-weighted and quantitative MRI; relaxation and myelin mapping) and in vivo functional MRI have been established. fMRI in animals is different from fMRI in humans as anaesthesia severely impacts the BOLD signal. Yi He has established online functional MRI which allows to continuously inspect how anaesthesia impacts the BOLD signal. Freja Østergaard has collected the first fMRI data as part of her "NextGen" ITN EU supported PhD project on how alpha-synuclein inserted into basal ganglia as a model of Parkinson's impacts the visual system.



Fluorescence labelling histology has been used to verify if a virus injected into cortex has transported a light-sensitive protein to cell membranes. The green color show that the protein is well expressed in the cell membrane and along axons.

GROUP MEMBERS

- **Assoc. Prof. Tim B. Dyrby**
- Senior researcher Henrik Lundell
- Postdoc Yi He
- Postdoc James Breen-Norris
- Research medical laboratory technologist Sascha Gude
- PhD stud. Christian Skoven
- PhD stud. Mariam Andersson
- PhD stud. Cristina Pasquinelli
- PhD stud. Freja Østergaard

HOMEPAGE

www.drcmr.dk/preclinical-research

PUBLICATIONS

2, 8, 22, 68, 79, 98, 107, 115

BRAIN STIMULATION

Transcranial Brain Stimulation (TBS) is a versatile neuroscientific tool and many research groups at DRCMR use TBS to influence brain activity and to evaluate electrophysiological markers in health and disease (e.g. Motor Control, Movement Disorders, Multiple Sclerosis, Neurophysiology, Neurophysics, and Traumatic Brain Injury).
The TBS Methods Group is focused on facilitating, supporting and advancing all forms of transcranial brain stimulation research at DRCMR. We work on improving state-of-the-art stimulation protocols by taking interactions with individual anatomy, activation history and attention levels into account. We develop in-house tools for easier and faster detection of brain stimulation (Motor Evoked Potentials/ Motor Thresholds) and assist with the establishment of novel stimulation protocols (e.g. Closed-loop/ Brain-state dependent stimulation). In 2017-2018 we have also expanded our focus to Transcranial Electric Stimulation with stimulation designs which give us the possibility of controling better for the effects of periopheral stimulation.
The group also has a strong educational focus: We provide teaching in brain stimulation techniques both internally, as local science out-reach events, with international graduate-level workshops, and in 2017-2018 more than 60 participants from across Europe, America and Asia have participated in our workshops. The TBS methods group meets every second Monday and welcomes all researchers at DRCMR who wish to use TBS in their research.

GROUP MEMBERS

- **Senior researcher Anke Karabanov**
- Phd stud. Janine Kesselheim
- Phd stud. Mads A.J. Madsen
- Postdoc Syoichi Tashiro
- Phd stud. Allan Lohse
- Phd stud. Lærke Krohne
- Research asst. Marie-Luise Lui
- Research asst. Marjolein Piek
- Stud. Felix Schmidt
- Stud. Martha Marques

HOMEPAGE

www.drcmr.dk/tms-group

PUBLICATIONS

10, 25

Placing the TMS-coil on the stimulation location using the TMS-Robot.

ELECTROENCEPHALOGRAPHY

The main focus of the group is to support electroencephalography (EEG) related studies at DRCMR by applying state-of-the-art methodologies and develop new methods and procedures.

EEG can be combined with brain stimulation techniques providing us with important information to understand the effects of the specific brain stimulation method. In our case, we have mainly focused on EEG in combination with transcranial magnetic stimulation (TMS). This has been pursued by following three directions.

1) We have described the effects of the pulse instrumental artefact provoked by TMS when this is delivered synchronously to EEG acquisition (see figure). A time constraint between EEG sampling and TMS delivery can effectively reduce the artefact variability in EEG data. This is a first step in having cleaner acquisitions in the first milliseconds after stimulation.

2) We have studied the unspecific and undesired cortical responses to TMS by analyzing the effects of the auditory response to TMS click and somatosensory response to the skin sensation. These sensory responses are overlapped to direct transcranial responses and their proper definition will allow us to disentangle desired and undesired effects of stimulation.

3) We have developed procedures for brain informed stimulation, which is a new emerging method to stimulate the brain in specific brain states (see figure). This approach is very interesting to discover brain features or to develop new stimulation protocols for therapeutic purposes.

GROUP MEMBERS

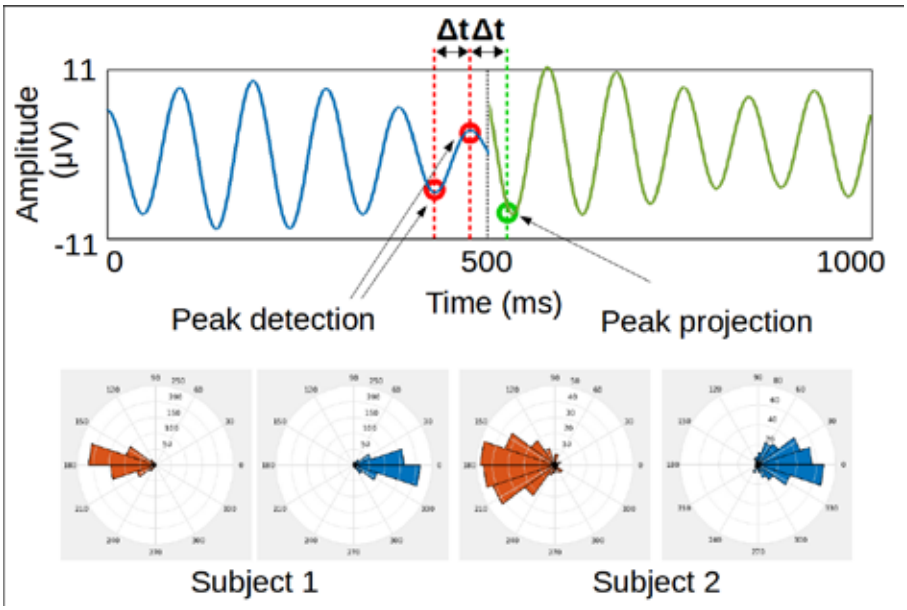
- **Postdoc Leo Tomasevic**
- Postdoc Syoichi Tashiro
- Postdoc Virginia Conde Ruiz
- Postdoc Mitsuaki Takemi
- Postdoc Violaine Michel Lange
- PhD stud. Janine Kesselheim
- PhD stud. Mads A.J. Madsen
- PhD stud. Anna Hester V. L. v.Themaat
- PhD stud. Melissa Larsen
- Stud. Felix Schmidt
- Stud. Oliver Naaby
- Research asst. Irina Akopian
- Research asst. Angeliki Charalampaki
- Research asst. Farzaneh Akhavan
- Stud. Borhan Javanmiri
- Research asst. Carolina Czichos

HOMEPAGE

www.drcmr.dk/eeg

PUBLICATIONS

48, 62, 113



The algorithm for phase detection from EEG data in real time. (Up) The future phase is predicted from the last peaks of the filtered signal. (Down) The example of the reliability of the algorithm from two subjects.

METHODS CLINIC

We are an informal group that operates a weekly clinic open to all members of DRCMR, and their collaborators. We aim to answer audience questions pertaining to statistical analysis and computational modelling of data. We can take questions from any domain (behavioral, neural, physical etc.), and any data modality (behavior, cognitive, MRI, fMRI etc.). We can help with any step in the scientific chain, from conception, experimental design, analysis, and interpretation, also including help with the review process. The meetings are chaired and organized by Senior researchers Ollie Hulme, Kristoffer Madsen, and Jens Hjortkjær. Attendance is voluntary but recommended for all researchers as a function of their needs.

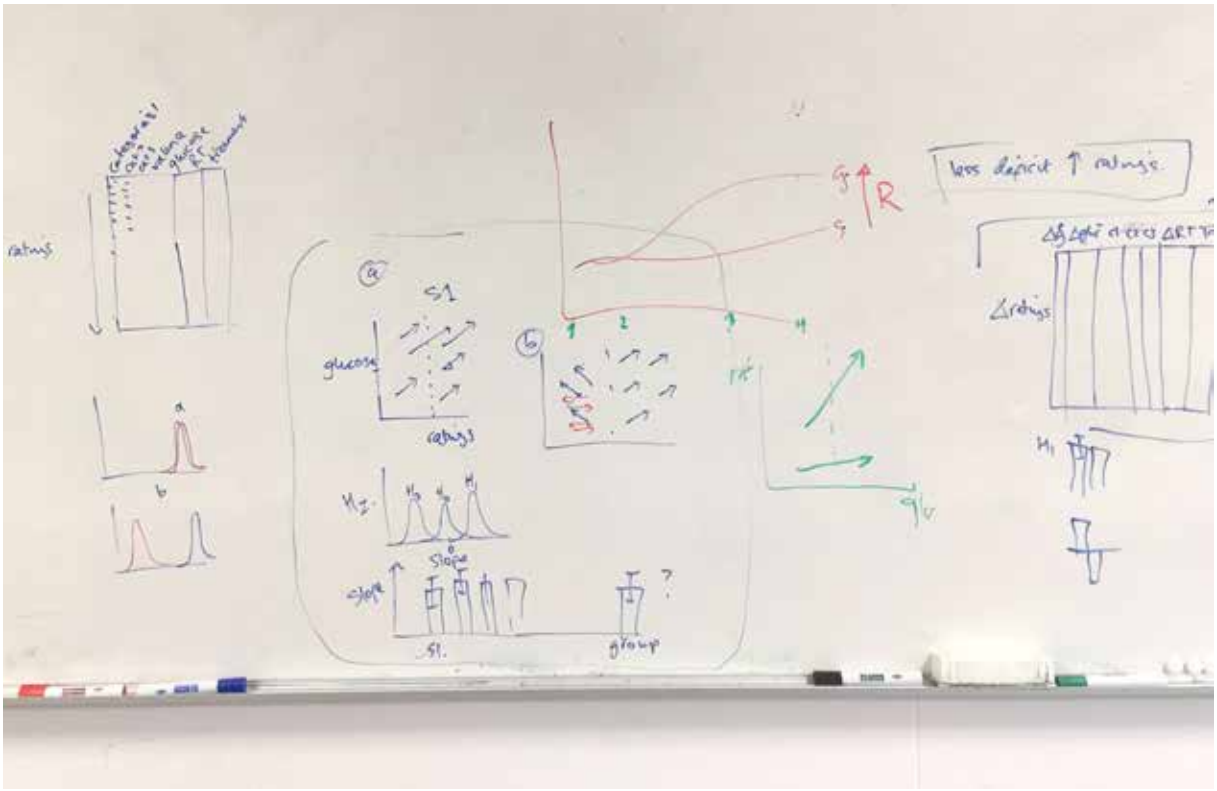
ORGANIZED BY

- Senior researcher Oliver Hulme
- Assoc. Prof. Kristoffer H. Madsen
- Senior researcher Jens Hjortkjær

Clinic meetings are open to all members of DRCMR and their collaborators

HOMEPAGE

www.drcmr.dk/methods-clinic



Perhaps unsuprisingly, we use whiteboards to sketch out our problems and ideas on.

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. The image analysis technology developed by the DRCMR research groups is continuously integrated into a workflow system for rapid configuration to accommodate specific requirements. Thus, the Reader Centre offers analysis of advanced MR measures such as diffusion tensor imaging, magnetization transfer imaging, resting-state fMRI as well as 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 and leg muscles.

The Reader Centre supports several research groups at DRCMR, e.g. the Healthy Ageing and the Neuroimaging in Multiple Sclerosis groups, but is also a partner in several investigator-driven clinical studies with the Danish Multiple Sclerosis Center.

GROUP MEMBERS

- **Manager Karam Sidaros**
- Postdoc Nina Højland Reislev
- Senior researcher Henrik Lundell
- Assoc. Prof. Ellen Garde
- Research radiographer Hanne Schmidt
- Research medical laboratory technologist Sascha Gude
- Research medical laboratory technologist Sussi Larsen

EXTERNAL COLLABORATORS

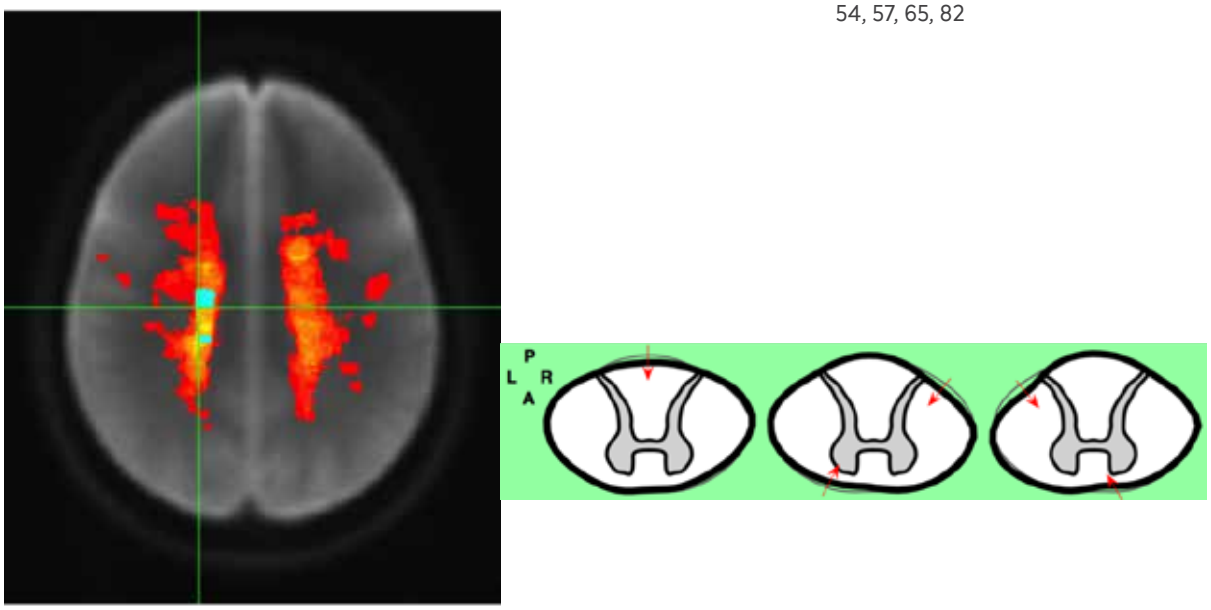
- Danish Multiple Sclerosis Center, Rigshospitalet
- Center for Healthy Ageing, University of Copenhagen
- Department of Clinical Medicine, Bispebjerg Hospital

HOMEPAGE

www.drcmr.dk/reader-centre

PUBLICATIONS

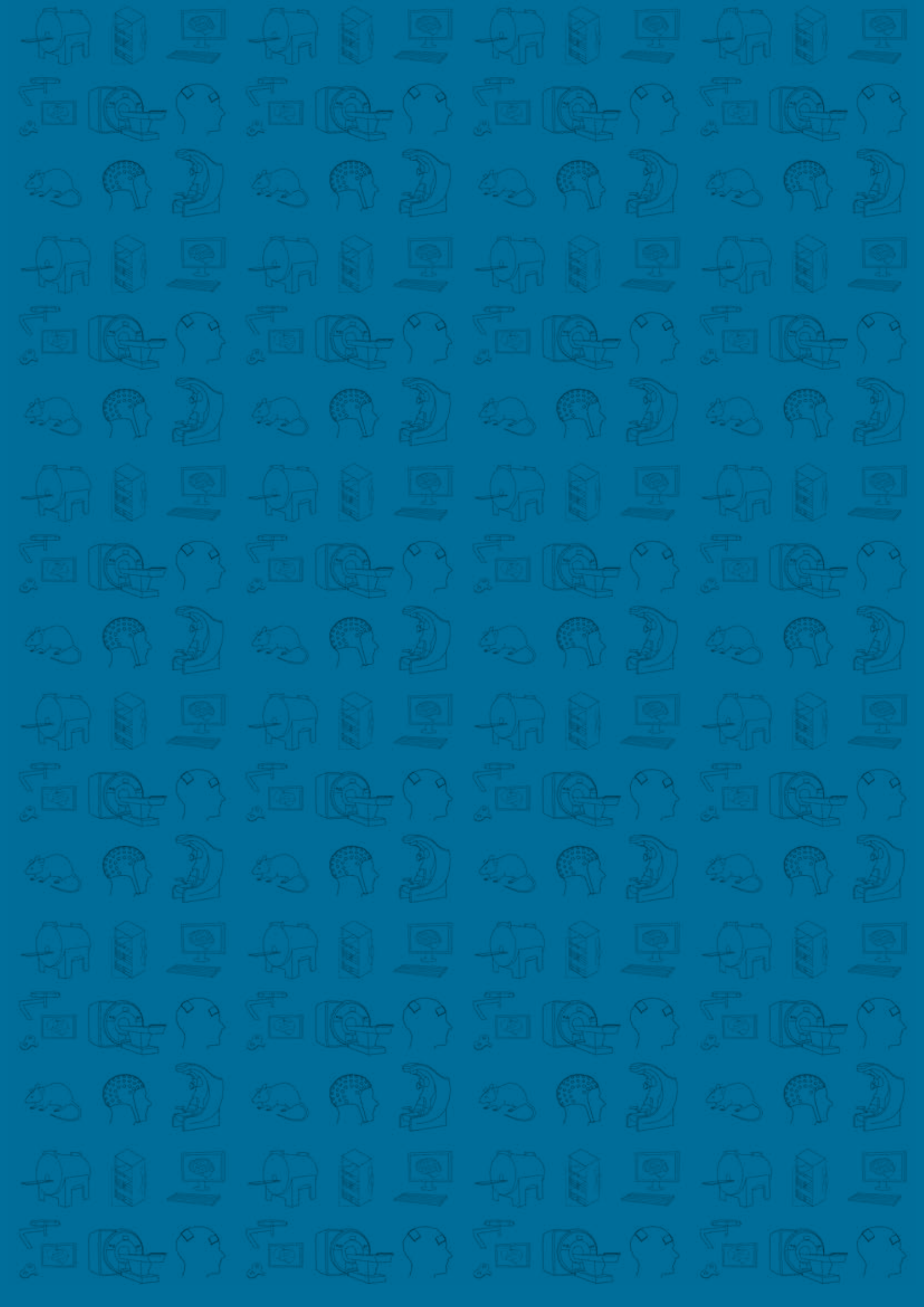
54, 57, 65, 82



Example of structural data analyses. Left: frequency of lesions (red to yellow colors) in a group of patients with MS and one participant's lesions marked out (blue). Right: typical patterns of atrophy in the spinal cord in the same group.

ACTIVITIES

2017-2018 have been two dynamic years with many engaging activities and events at DRCMR. Our researchers have been extremely active, and their research results have attracted attention from Danish media, led to new collaborations and resulted in interesting events.



1ST DANISH NATIONAL 7 TESLA MR PROJECT SYMPOSIUM

The 1st Danish National 7 Tesla MR Project symposium was held on the 16th of April 2018 and it was a great success. Approx. 90 guests from across Denmark and Sweden attended the symposium for which we managed to attract world-recognized speakers. The symposium was the first within the Danish National 7 Tesla Project aiming at highlighting the possibilities and show-case the work done on the system.

The aim of the Danish National 7 Tesla Project is to provide a state-of-the-art facility for cutting edge imaging research open to all researchers in Denmark. The installed 7 tesla ultra-high field human MR scanner is equipped with the latest hardware and it will keep Denmark in a leading position within imaging research. This setup fosters close collaborations across research institutions and hospitals, both nationally and internationally, and the good synergy will therefore ensure fast progress, not only within imaging sciences but also in basic science and clinical research. http://www.drcmr.dk/resources/national-7t.

SPEAKERS AT THE 1ST DANISH NATIONAL 7 TESLA MR PROJECT SYMPOSIUM

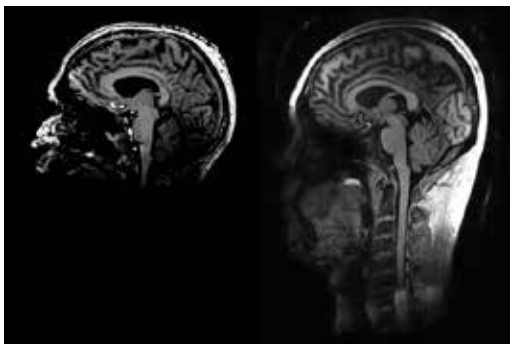
- **Hartwig Siebner**, Prof., Head of Danish Research Centre for Magnetic Resonance
- **Peter Luijten**, Prof., Director, Imaging Division, University Medical Center Utrecht
- **Emrah Düzel**, Prof., Director, Institute of Cognitive Neurology and Dementia Research, University Hospital Magdeburg
- **Karin Markenroth Bloch**, Site coordinator, Swedish 7T facility, Lund
- **Klaas Prüssmann**, Prof., Institute for Biomedical Engineering, ETH and University of Zurich
- **Henrik Lundell**, Danish Research Centre for Magnetic Resonance, Hvidovre Hospital
- **Vincent Boer**, Danish Research Centre for Magnetic Resonance, Hvidovre Hospital
- **Kyungmin Nam**, Danish Research Centre for Magnetic Resonance, Korea Basic Science Institute, South Korea
- **Giske Opheim**, Neurobiology Research Unit, Rigshospitalet, Copenhagen
- **Peter Bandettini**, Director, Functional Magnetic Resonance Imaging Core Facility, NIH, Bethesda, USA
- **Anouk Marsman**, Danish Research Centre for Magnetic Resonance, Hvidovre Hospital
- **Samaira Younis** and **Casper Christensen**, Human Migraine Research Unit, Rigshospitalet, Glostrup
- **Anna Lind Hansen**, Danish Research Centre for Magnetic Resonance, Hvidovre Hospital

ADVANCEMENTS AT THE NATIONAL 7T FACILITY

The only ultra-high field MR scanner in Denmark is placed at DRCMR. It is a national facility available for all researchers in Denmark. The aim of the Danish National 7 Tesla Project is to provide a state-of-the-art facility for cutting-edge imaging research in Denmark. The 7 tesla whole-body human MR scanner is equipped with the latest hardware. The setup fosters close collaborations across research institutions, both nationally and internationally, and the good synergy will hopefully ensure a fast progress, not only within imaging sciences but also in basic science and clinical research. The scanner has been officially in use since 2016, and the number of DRCMR studies conducted at the 7T facility is steadily growing. The following studies are currently the main projects DRCMR based researchers are running at the 7T facility.

IMPROVED COVERAGE FOR FUNCTIONAL, METABOLIC AND ANATOMICAL IMAGING WITH 7 TESLA MRI

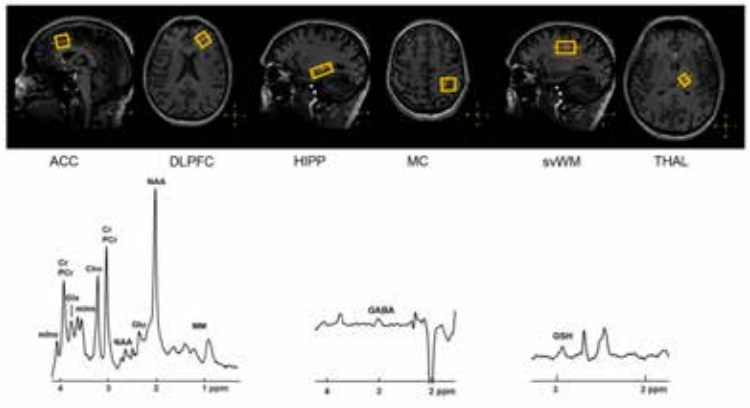
The objective of this project is to improve the coil configuration of the 7 tesla MR system to unfold the foreseen advantages of ultra-high field MRI. For example, Arterial Spin Labeling (ASL) is a technique that so far has eluded the full potential of ultra-high field MRI. In this technique arterial blood in the neck is magnetically labeled and generates a measurable image contrast in the brain that can be used to measure perfusion. Unfortunately, with the current coil configuration, labeling cannot be performed in the neck area because low radiofrequency (RF) fields and the dark shading in the brain corrupts the image quality severely. Using an improved 8-channel transmit coil configuration we can now generate stronger RF fields in the neck region which we intend to utilize to improve ASL at 7 tesla. In this project we will continue to enable labeling in the neck and push the quality, coverage and resolution of ultra-high field MRI.



Using an improved 8-channel transmit coil configuration (right) it is now possible to generate stronger RF fields in the neck region.

BRAIN METABOLITE CHANGES ACROSS THE LIFESPAN

Magnetic resonance spectroscopy (MRS) is a non-invasive MR technique that can be used to study the molecular composition of tissues in vivo and to identify metabolites that are involved in physiological or pathological processes. The magnetic field strength of 7T allows us to assess not only neuronal, glial, metabolic and membrane turnover markers (resp. NAA, inositol, (phospho)creatine and cholinergic compounds), but more importantly, it allows us to separate the glutamate and glutamine signals and assess GABA, glutathione and lactate in a more robust and time-efficient manner than at lower clinical field strengths. In this study, 1H-MRS is acquired in six different brain regions in young, middle-aged and elderly participants. Apart from MR, blood samples are collected, and participants undergo cognitive testing in order to investigate associations between brain and peripheral aging, and between brain chemistry and cognition.



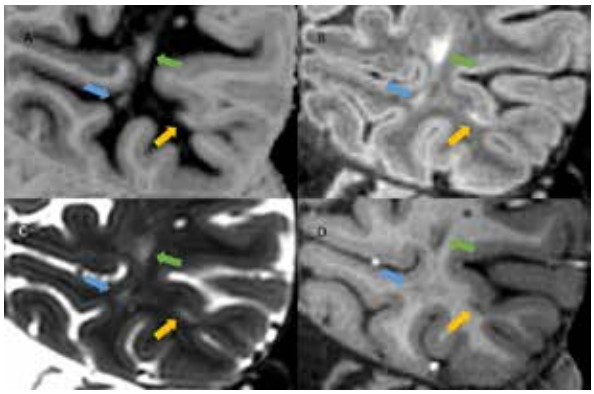
MRS voxel placement and example spectra for conventional MRS, GABA-edited MRS and GSH-edited MRS.

CORTICAL LESIONS IN PRIMARY SENSORIMOTOR HAND AREA AND THEIR IMPACT ON DEXTERITY IN MULTIPLE SCLEROSIS: A 7T MRI STUDY

Multiple sclerosis (MS) significantly affects cortical grey matter and the degree of cortical grey matter pathology is associated with cognitive and physical disability. Yet the specific impact of single cortical lesions is unknown, since cortical lesions are hard to detect on conventional MRI at 3T. Ultra-high field 7T MRI has a higher diagnostic sensitivity and more than doubles the detection of cortical lesions.

Exploiting the increased sensitivity of 7T MRI to detect cortical lesions, we will assess the number, size and regional distribution of cortical lesions in the sensorimotor area and relate regional lesion load in to MRI-based, electrophysiological, and clinical correlates of hand function.

This study will improve our understanding of the relevance of cortical lesions to MS-related disability. Furthermore, the project will advance the possibilities of MRI to capture cortical involvement in Danish MS patients with clear clinical implications in terms of future monitoring of disease progression or capturing the individual response to therapy.



A leukocortical (yellow arrow), juxtacortical (blue arrow) and white matter (green arrow) lesion identified on four different MRI sequences at 7T:
a) MP2RAGE (bright CSF, grey GM, black WM and hyperintense lesions)
b) MP-FLAIR (Black CSF, bright GM, grey WM, hyperintense lesions)
c) T2w (white CSF, bright GM, dark WM, hyperintense lesions)
d) MPRAGE (dark CSF, grey GM, bright WM, hypointense lesions).

Part 1: Identification of cortical lesions with ultra-high field MRI

Clinical assessment
EDSS
Depression
Fatigue

7T structural MRI
- MPRAGE
- MP2RAGE
- FLAIR
- T2w
- T2*

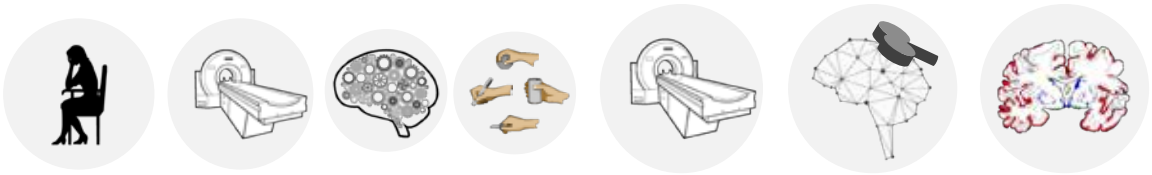
Cognitive and behavioural testing
- PASAT
- SDMT
- GODT
- 9-HPT
- JTHFT

Part 2: Neurophysiological consequences of cortical lesions in SM1-HAND

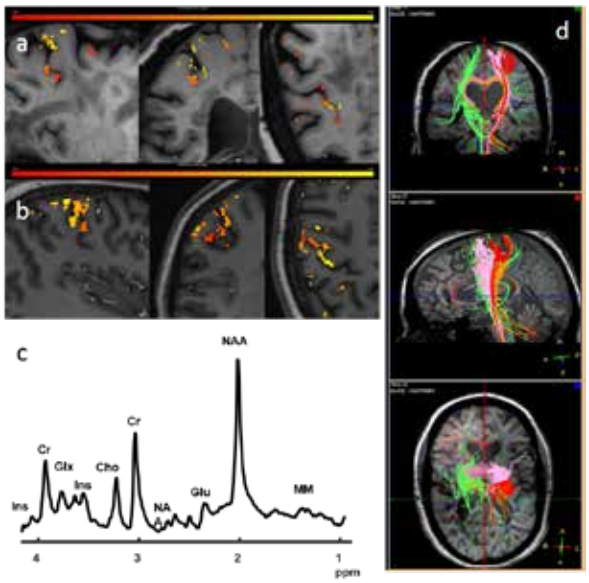
7T functional and structural MRI
- MP2RAGE
- DWI
- H^1-MRS
- fMRI

TMS & EEG
- M1 mapping of sensory-motor integration
- SICI
- ICF
- iSP
- Corticospinal conduction

Lesion detection
- WM lesion load
- GM lesion load
- Cortical atrophy
- CL lesions in SM1-HAND



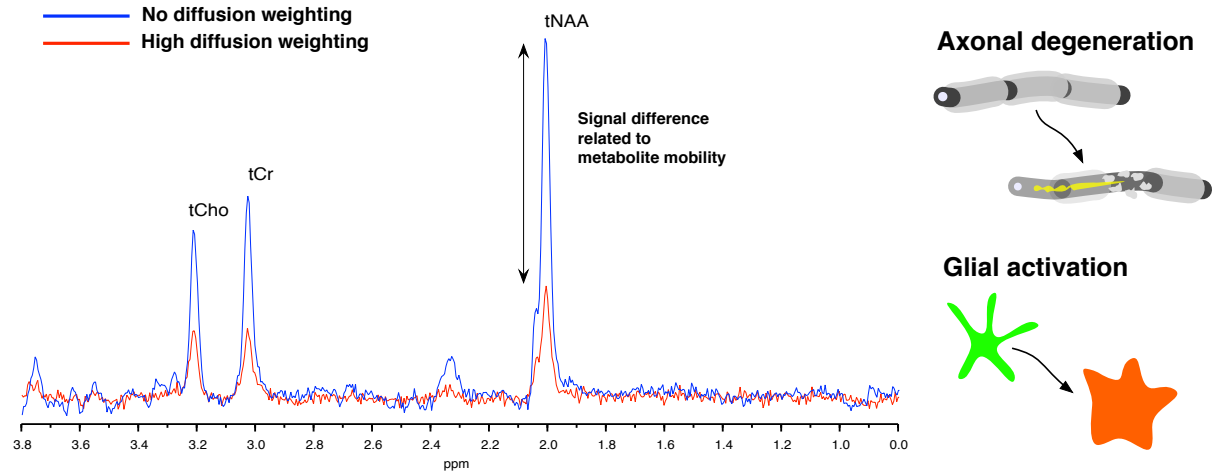
A general overview of the experimental protocol for the two parts of the study.



Preliminary results. a & b) BOLD fMRI response following a unimanual sensorimotor task (vibration and 1Hz finger tapping) from an MS patient (PT) (a) and a healthy control (HC) participant (b). Notice the larger degree of activation in the HC.
c) MRS spectrum from a 2x2x2 voxel over the primary sensory motor cortex in a PT.
d) tractography of the corticospinal tract of a PT using diffusion MRI and diffusion tensor imaging.

ULTRA-HIGH FIELD MRI CHARACTERIZATION OF BRAIN NETWORK MICROSTRUCTURE AND CONNECTIVITY IN INDIVIDUALS WITH MULTIPLE SCLEROSIS

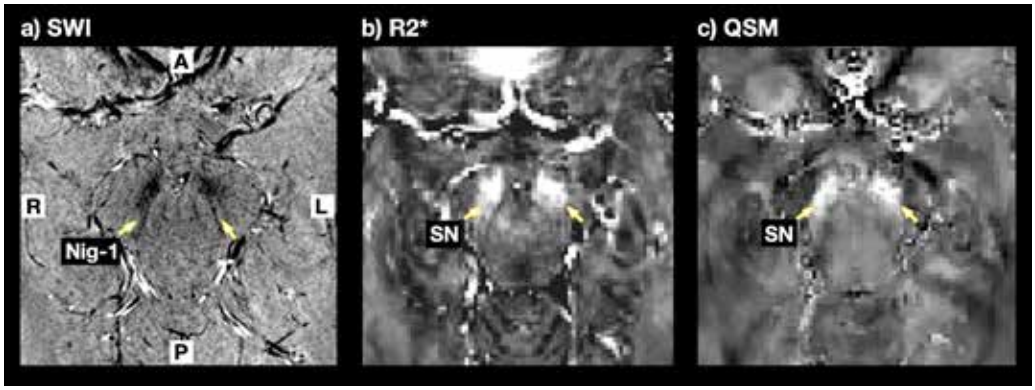
Diffusion weighted spectroscopy (DWS) is a hybrid between magnetic resonance spectroscopy (MRS) and diffusion weighted imaging (DWI). Traditional DWI is a sensitive probe to tissue microstructure but is very unspecific as water resides in all intra- and extracellular spaces. DWS provides measurements of metabolite mobility, which can provide biomarkers related to the intracellular space of specific cell types. In brain tissue DWS can for instance separate structural changes related to glial and neuronal cells reflecting different pathological mechanisms. The main initial application is differentiation of demyelination and neuroinflammation in multiple sclerosis. Future perspectives are to achieve a new level of specificity in microstructural imaging in general for precise characterization of cell specific morphology in pathologies. This research will be developed further in the C-MORPH project funded by a starting grant from the European Research Council.



The diffusion weighted spectrum enables the measurement of mobility of individual metabolites that, unlike water, are more specific to certain cell types. For instance, N-acetyl aspartate (tNAA) is intraneuronal and choline compounds (tCho) are mainly in supporting glial cells. This unique information relates to morphology of the respective cell types and are potential markers for individual pathological mechanisms.

7T QUANTITATIVE MRI IN PARKINSON'S DISEASE

Parkinson's disease is characterized by degeneration of neurons and accelerated iron accumulation in the dopaminergic neurons of substantia nigra pars compacta (SNc). Quantitative susceptibility mapping (QSM) and maps of effective transverse relaxation rates (R2*) are promising biomarkers for SNc iron load. However, long acquisition times limit the clinical applicability of quantitative MRI in PD. Using inner-volume imaging of the midbrain and basal ganglia, the 7T group has developed a protocol for acquiring high-resolution quantitative maps of SNc iron load in under 10 minutes.



Iron sensitive imaging of the substantia nigra (SN) in the axial plane. a) Susceptibility weighted image (SWI), 0.4mm isotropic resolution; b) Quantitative map of the effective transverse relaxation rate (R2*); and c) Quantitative susceptibility map (QSM), 1mm isotropic resolution. Nig-1 denotes the dorsolateral nigral hyperintensity corresponding to nigrosome-1.

RESEARCH RETREAT – A DAY DEDICATED TO OUR NEW RESEARCH AREAS

In 2016 we focused on developing our research strategy as well as organization and ended up identifying five research areas which now constitute our main lines of research. The five research areas were the core of our research day at the Elsass Foundation in October 2017.

All researchers affiliated to DRCMR were invited. The program was a combination of plenum sessions with presentations and general discussions and two break-out sessions organized as workshops. The workshops were led by the five research areas coordinators together with the leadership and the objective was to discuss and further develop research and collaboration within the five research areas.

The day was also a social event where students, researchers and administrative personnel had a chance to meet and talk outside the office. We had a nice lunch and ended the day with a glass of wine enjoying the beautiful surroundings the Elsass Centre offers – and waiting for the rain to pass.

WORKSHOP 1

Who are we?
What is our vision?
Which grand challenges will we address?
How far are we?

WORKSHOP 2

Which specific outcome/milestones are we aiming at?
What do we need to do to obtain these outcomes?
How do we measure that we are on the right track in reaching our targets?
What is our time frame? Where are we in 5 years?
Interactions between the areas

DRCMR researchers and staff after a nice but rainy day at the Elsass Foundation.

RESEARCH DAY AT HVIDOVRE HOSPITAL 2018

The yearly Research day on 13 April 2018 at Hvidovre Hospital was a special day for DRCMR and our young talented PhD stud. Allan Lohse. Allan's abstract on "Presupplementary Motor Area Controls Risk Taking Behavior Exclusively in Novel Situations" was 1 of 5 chosen for the yearly pitching competition out of a total of 84 abstracts accepted for the Research Day. Allan's pitch was nicely delivered in a comprehensive language with beautiful slides – and he actually ended up winning the pitching competition, congratulations Allan.

PhD stud. Allan Lohse pitching at AHH Research Day 2018.

DRCMR POSTERS AT THE ANNUAL RESEARCH DAY AT HVIDOVRE HOSPITAL 2018:

Allan Lohse
Presupplementary Motor Area Controls Risk Taking Behavior Exclusively in Novel Situations

Amalie Sofie Ekstrand
Maturation of major white matter tracts during childhood and adolescence A longitudinal study with up to 11time points

Anna Hester Ver Loren van Themaat
Electrophysiological correlates for error monitoring in 11-year-old children at familial risk for developing schizophrenia or bipolar disorder during the Eriksen-Flanker task

Anna Lind
Reproducible in vivo assessment of GABA and GSH using MR spectroscopy

Christian Bauer
Asymmetries in structural connectivity correlates with fatigue in multiple sclerosis

Christian Skoven
Uncovering neurobiological mechanisms of non-invasive transcranial brain stimulation

Christopher Fugl Madelung
Unravelling the alteration of brain structure and function in Parkinson's Disease with ultra-high field MRI (7TPD)

Cihan Göksu
Human In-vivo Brain Magnetic Resonance Current Density Imaging (MRCDI)

Cristina Pasquinelli
TFUS experimental design The impact of transducer modelling in simulations

Freja Gam Østergaard
Development of visual assay for detection of -synuclein in a rat model of Parkinson's disease

Guilherme Bicalho Saturnino
Optimizing Electric Fields for Transcranial Electrical Stimulation

Henrik Lundell
Characterization of axonal microstructure and transmission in MS Combining 7T MRI diffusion weighted spectroscopy and electrophysiology

Janine Kesselheim
Can oscillatory transcranial brain stimulation of human sensorimotor cortex (TACS) at beta frequency modify sensorimotor inhibition?

Jonathan Holm-Skjold
Development of emotional processing is linked to maturational changes in leftright cingulum asymmetry during adolescence

Kasper Winther Andersen
Multi-dimensional microstructural imaging offers novel in-vivo insights into brain pathology and application to multiple sclerosis

Line K. Johnsen
Neuroimaging correlates of cognitive control in children at high risk for schizophrenia or bipolar disorder

Louise Baruël Johansen
Reduced orbitofrontal functional network centrality characterizes high neuroticism across childhood and adolescence

Lærke Gebser Krohne
Does corticospinal excitability depend on the oscillatory phase of the pericentral μ-rhythm

Mads Alexander Just Madsen
What is the impact of a cortical lesion? – A 7T MRI study in multiple sclerosis patients

Magnus Koudahl
Phenotyping Losers
Parietal Traits as Predictors of Risk Preferences for Consequential Losses

Malte Laustsen
Slice-wise motion tracking during simultaneous EEG-fMRI

Mariam Andersson
Using X-ray Imaging to Visualize the 3D Architecture of White Matter

Nayome Rey Calvo
Assessment of white matter hyperintensity volume in large-scale MR population-based studies

Nina Højland Reislev
DRCMR Reader Centre – From study design to quality-assured results

Sara Andreasen
Alterations in the Brain´s Connectome during recovery from severe Traumatic Brain Injury (TBI)

Syoichi Tashiro
Focal Transcranial Alternating Current Stimulation of the primary motor cortex Impact of stimulation pattern

GLOBAL EXCELLENCE 2017-2020

In 2014, the DRCMR was announced one of the winners of the Global Excellence Award of Region Hovedstaden (The Capital Region of Denmark), and in 2017, the Regional Council decided once again to award the DRCMR the prize.
With the re-announcement, the status of the department as the winner of Global Excellence was prolonged to the year 2020. In addition, a DKK 250,000 grant was given to DRCMR. The grant is to be used to attract international researchers and practitioners as well as to conduct international symposia, workshops and similar.
The Global Excellence prize is a prize awarded by the Capital Region of Denmark to outstanding research environments at hospitals and universities in the Capital Region, whose efforts are considered world-class when it comes to research, development and deployment of new knowledge about technologies and new kinds of treatments in the Danish healthcare system.

The re-announcement was a great honor for the DRCMR. Head of Research at DRCMR, Professor Hartwig Siebner said:

"At DRCMR we work hard to ensure that our research is of the highest quality, and we constantly generate new knowledge which can ensure better diagnostics and treatment for patients in the Capital Region and in the rest of Denmark".

and

"The Global Excellence Award is a mark of quality of which we are very proud."

The Review Committee based their evaluation of the applications on a number of professional criteria as well as the original applications. In their review of the DRCMR re-announcement, the following was stated:

"The Review Committee's reason for nominating DRCMR for the re-announcement is based upon how you in extent and quality represent a very high level of research and development, education, study and treatment, innovation and communication.

The winner of GE has, as required, developed positively since they have been awarded with the prize, and they have actively made use of their Global Excellence status, which contributes to the development of their international level and collaborations."

GLOBAL EXCELLENCE AT THE DRCMR

The Global Excellence prize has given us the unique chance to invite the best and most relevant speakers from all over the world. With the aid of the Global Excellence programme, we received the world's leading international researchers that inspired us to ensure innovative research ideas, to conduct high quality research, and to generate new international collaborations. The Global Excellence prize has played an important and contributing role in performing research on a first-rate level which has strengthened our international profile. The outcomes have led to the development and implementation of treatment methods and products for the benefit of patients.

GLOBAL EXCELLENCE SEMINAR PROGRAM 2017-2018

Date	Speaker	Affiliation	Title of talk
15-09-2017	Guido Makransky	Assoc. Prof.r of Psychology, University of Copenhagen, Denmark	The Role of Virtual Reality in Education and Training
17-11-2017	Katrine Strandberg-Larsen	Assoc. Prof. at the Department of Public Health, University of Copenhagen, Denmark	Epidemiological studies of prenatal origin of cerebral palsy
05-01-2018	Mattias Rickhag	Assis. prof. of Neuropharmacology at Molecular Neuropharmacology Laboratory, University of Copenhagen, Denmark	Spatially-Selective Striatal Projection Neurons Govern Distinct Motor Behavior Paradigms
08-01-2018	Mark Does	Prof. of Biomedical Engineering, Electrical Engineering, Radiology and Radiological Sciences, at Vanderbilt University, Nashville, USA	Quantitative MRI: Methods and Experimental Studies
19-01-2018	Wolfram Schultz	Prof. of Neuroscience at the Department of Physiology, Development and Neuroscience at the University of Cambridge, UK	Neural signalling of reward and reward-based decisions
26-01-2018	Hyunjoo Jenny Lee	Assis. Prof. at the Korea Advanced Institute of Science and Technology, Daejeon, South Korea.	Biomedical microsystems for neuro interface
05-02-2018	Raymond Chan	Prof. of Neuropsychology and Applied Cognitive Neuroscience at the Chinese Academy of Sciences, Beijing, China	Hedonic processing impairments in clinical and subclinical samples: convergent evidence from findings of self-reported, behavioral and imaging paradigms
23-02-2018	Søren Brunak	Prof. of Bioinformatics at Technical University of Denmark and Copenhagen University Hospital, Denmark	Big biomedical data analysis in support of precision medicine
16-03-2018	Thomas Rainer Heimburg	Prof. of Biophysics at the Niels Bohr Institute, University of Copenhagen, Denmark	Sound propagation in nerves and the action of anesthetics
22-03-2018	Ingolf Sack	Prof. of Experimental Radiology and Elastography at the University Medicine of Berlin, Germany	Elastography by time harmonic shear waves in MRI and ultrasound
06-04-2018	Per Borghammer	Prof. of Nuclear Medicine & Neuroscience, Aarhus University Hospital, Denmark	Parkinson's Disease, does it start in the gut?
13-04-2018	Ray Dolan	Prof. of Neuropsychiatry at the Institute of Neurology, and Director of the Wellcome Centre for Human Neuroimaging, University College London, UK	Building cognitive models of the world
18-05-2018	Christos Pantelis	Prof. of Neuropsychiatry at the University of Melbourne, Australia and Scientific Director of the Melbourne Neuropsychiatry Centre, Australia	Mapping brain changes in psychosis and schizophrenia
31-05-2018	Kirstine Nyvold Bojsen-Møller	Research Fellow at Department of Endocrinology, Copenhagen University Hospital Hvidovre, Denmark	Metabolic effects of bariatric research
15-06-2018	Aviv Mezer	Assis. Prof. at the Edmond & Lily Safra Center for Brain Sciences, at the Hebrew University of Jerusalem, Israel	How human white-matter studies can be improved beyond diffusion imaging: The quantitative MRI perspective
25-06-2018	Adam Aron	Prof. of Psychology at University of California San Diego, USA	From Stopping Action to Stopping Thoughts
29-06-2018	Susan Francis	Assoc. Prof. of Physics at the University of Nottingham, UK	MRI measures associated with cirrhosis and portal hypertension
19-09-2018	Terry Jernigan	Prof. of Cognitive Science, Psychiatry, and Radiology at the University of California San Diego, USA	Developmental Population Neuroscience: The Adolescent Brain and Cognitive Development (ABCD) Study
27-09-2018	Sara Hollingsworth Lisanby	Prof. of Clinical Psychiatry at Columbia University, USA, and chair of the Department of Psychiatry and Behavioral Sciences at Duke University Medical Centre, USA	Non-invaisve brain stimulation of depression - reducing side effects and increasing efficacy through individualized treatment
28-09-2018	Markus Schirmer	Research Fellow at the J. Philip Kistler Stroke Research Center, Massachusetts General Hospital, USA	Studying stroke outcome by utilizing clinical data segmentation
09-11-2018	Lars Nyberg	Prof. of Neuroscience (Radiation Sciences & Integrative Medical Biology) at Umeå University, Sweden	Brain aging and brain maintenance
23-11-2018	Elinor Tzvi-Minker	Senior Researcher at the Department of Neurology, University of Leipzig, Germany	The beneficial effects of tDCS on the motor learning network

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 treatment of patients – or to promote health and wellbeing and thus avoid that we become patients. We have strengthened our translational research by reinforcing the collaborative ties with the clinical research groups at our own hospital, Hvidovre Hospital, but also with other hospitals in the Capital Region of Denmark, especially Bispebjerg and Frederiksberg Hospital. Strong collaborative ties exist with Copenhagen University Hospital Bispebjerg and Frederiksberg 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 between Prof. CJ Boraxbekk (DRCMR) and Prof. Michael Kjær´s group at the Dept. for Orthopaedic Surgery. But many other collaborations have also been established with research groups at Herlev and Gentofte Hospital and Rigshospitalet. We are currently in the process of starting new projects with Hillerød Hospital as well.

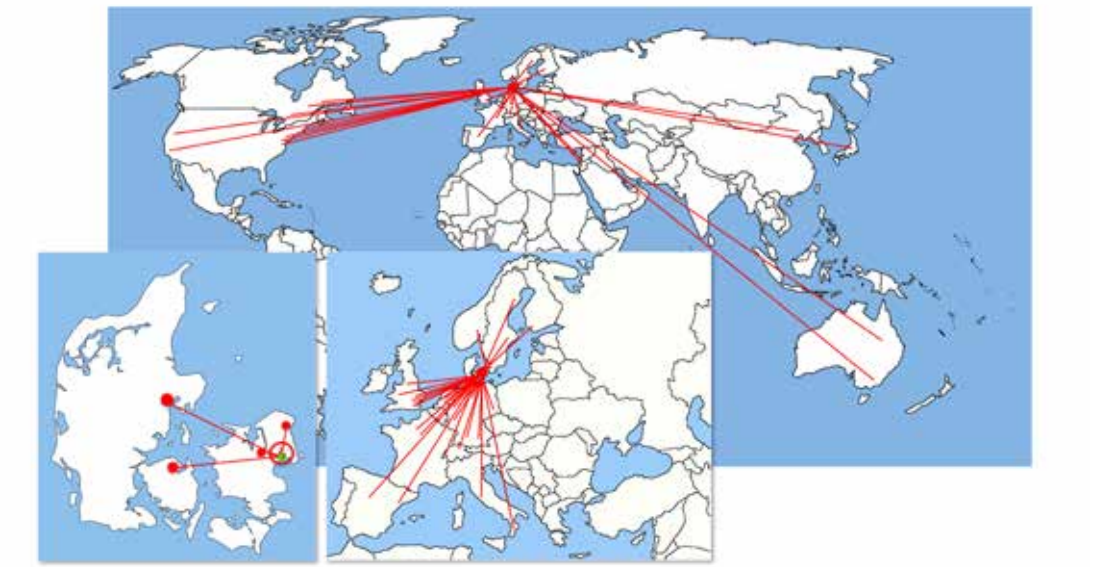
The Capital Region of Denmark has also emphasized the need for better integration of research activities among universities and hospitals in the region. The Greater Copenhagen Health Science Partners have funded several Clinical Academic Groups which bring together researchers and clinicians in strong clinical research groups with a shared vision. We appreciate the initiative and so far, DRCMR takes part in the Academic Alliance on Physical activity and sport in clinical medicine (imPAct) led by Professors Michael Kjær and Flemming Dela.

NEW COLLABORATIONS WITH BRAIN PRIZE WINNERS

In 2017, Prof. Ray Dolan and Prof. Wolfram Schultz received the Brain Prize for their analysis of how the brain recognizes and processes reward through dopamine signaling. Both winners have since visited the DRCMR to give a Global Excellence talk. The talks developed into extremely interesting discussions and kickstarted new collaborations. Ray Dolan will come to DRCMR as a visiting Professor on a Lundbeck grant in fall 2019. We are looking forward to the visit.

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 center in Lund, but also within two European brain imaging networks "EUFIND" and "ASAP SYNTAU" on brain imaging of neurodegenerative brain diseases, causing dementia or atypical forms of parkinsonism. Both projects were funded by the EU Joint Project on Neurodegenerative Disease Research (JPND). We were able to



strengthen synergistic research within Europe thanks to multilateral collaborations in especially H2020 funded projects as LifeBrain, STIPED, TRABIT and bilateral collaborations with research groups in Germany, The Netherlands, Switzerland, United Kingdom, Italy, Sweden, Norway, and France. We are particularly proud about the considerable increase in transcontinental collaborations with China, Japan, Korea, Australia, and the USA in recent years. Running synergistic projects together, exchanging students, researchers, knowledge, and ideas help us to maintain a vibrant research environment

UNIVERSITIES IN THE CAPITAL REGION OF DENMARK

We 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 at University College Copenhagen. Our closest regional university collaborations are with the Technical University of Denmark, where we have had strong collaborations with the Department of Applied Mathematics and Computer Science, and the Department of Electrical Engineering for more than a decade. Recently we have also started started collaborations with the Department of Physics. 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.

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. Currently, we have five shared Associate professorships with DTU, one shared senior assoc. lecturer with University College Copenhagen and one professor shared with University of Umeå, Sweden. In addition, Tim Dyrby is currently also associated to École Polytechnique Fédérale de Lausanne (EPFL), Switzerland as visiting Professor. And finally, Prof. Hartwig Siebner is professor at University of Copenhagen and affiliated to Bispebjerg and Frederiksberg Hospitals.

TIM DYRBY

Assoc. 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

AXEL THIELSCHER

Assoc. prof. in magnetic fields and stimulation

Technical University of Denmark, Department of Electrical Engineering (DTU-Electro), Center for Magnetic Resonance (as of January 2019, Department of Health Technology)

LARS G. HANSON

Assoc. prof. in magnetic resonance imaging

Technical University of Denmark, Department of Electrical Engineering (DTU-Electro), Center for Magnetic Resonance (as of January 2019, Department of Health Technology)

ESBEN THADE PETERSEN

Assoc. prof. in ultra-high field MRI

Technical University of Denmark, Department of Electrical Engineering (DTU-Electro), Center for Magnetic Resonance (as of January 2019, Department of Health Technology)

KATHRINE SKAK MADSEN

Senior assoc. lecturer in neuroimaging

University College Copenhagen, Department of Technology

KRISTOFFER HAUGAARD 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

CARL-JOHAN BORAXBEKK

Prof. of cognitive neuroscience of aging

University of Umeå, Sweden

Faculty of Social Science, Center for Demographic and Aging Research (CEDAR) // Umeå Center for Functional Brain Imaging (UFBI)

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 IS ON THE NEWS!

The researchers at DRCMR and collaborators have not only been very productive during the last two years, they have also produced extremely interesting results. These results have triggered the interest of several Danish media and a number of articles describing the results of DRCMR researchers and collaborators have been published. Below you get a short insight on what has been of particular interest for the media in 2017-18.

HEARING IN A CROWDED ROOM

While people with normal hearing can easily distinguish and concentrate on listening to what a person is saying in a crowded room filled with noise, it is difficult for a person with a hearing aid, for whom all the sounds are equally amplified. However, researchers at DRCMR and DTU Electrical Engineering have now managed to decode the processes in the brain that enable us to differentiate sound and concentrate on a particular sound, such as what one person is saying in a crowded room.

Image: Adrian Hillman © 123RF.COM

"It's an exciting step in the development of a new type of cognitively controlled hearing aid that hopefully will help the user to hear more like someone with normal hearing. Other types of cognitive control might include amplifying the sound of the person the user is looking at—for example by registering the user's eye direction with EEG electrodes," says Jens Hjortkjær, who is a Senior researcher at DTU Electrical Engineering and Danish Research Centre for Magnetic Resonance at Hvidovre Hospital.

Based on articles in Berlingske (13 May 2018), DTU Elektro (14 May 2018), videnskab.dk (15 May 2018), KamikPosten (May 2018) and Jyllands-Posten (16 May 2018).

HOME GROUND ADVANTAGES

In April 2018, Postdoc David Meder from DRCMR, was heard on the radio talking about home ground advantages. Research has proven that before a soccer match, the home ground players have a higher level of testosterone and cortisol, compared to the guest players. "In animals, we have discovered how their testosterone level increases when they need to defend their territory. And it makes perfect sense that cortisol, which is a stress hormone, also increases." Our body is telling us that we need to put our life at risk to defend our territory, and the cortisol is getting the body ready to fight. However, a research project at the Technical University in Dortmund, Germany showed that the number of won soccer matches on home turf was far higher in the end of the 1980s compared to the season 2006/2007. However, David Meder believes that due to the increasing professionalism in soccer over the years, " sport psychologists are being used to e.g. work with the challenges of playing away" by for instance using tricks to make the body release dopamine and endorphins to enhance the motivation.

Postdoc David Meder. Photo: Communication AHH.

Based on interviews on the radio P1, P3, and P4 Nord on 24 April 2018.

PROFESSORSHIP IN PRECISION MEDICINE

In 2017, Neurologist Hartwig R. Siebner received a grant for a Clinical Professorship in Precision Medicine within the field: Disease-related MRI brain research & non-invasive transcranial brain stimulation. This grant is used for research to find the key to diagnosis and treatment with the help of advanced imaging of the brain – a key which exactly fits the individual patient. "Speaking about Precision Medicine, it is usually genetics and chromosomes which come into one's mind. However, fingerprinting of brain diseases with MRI plays a very fundamental role which is presently somehow underrated in the emerging field of Precision Medicine," Hartwig Siebner says. Precision Medicine is increasingly coming into focus within the field of brain imaging and especially magnetic resonance imaging (MRI) has great potential because many modalities can be integrated to characterize how the brain's structure, function, and metabolism is affected in a single patient. Thus, Hartwig Siebner was very pleased to hear that he was chosen for the professorship in Precision Medicine.

Image: Arak Rattanawijittakorn © 123RF.COM

Based on "Fingerprints in the brain" on the webpages of Hvidovre Hospital and DRCMR May 2018 and on.

YOUR INGENIOUS BODY

In the program "Din geniale krop" [Your ingenious body] many mysteries of the human body were explored. Focus was upon birth, teenage years, grown-up life, and ageing. Through the four episodes televised at DR, researchers shared their knowledge on the themes. The four researchers from DRCMR shared data found in their research about different milestones in life. Senior Researcher Kathrine Skak Madsen from DRCMR focused upon teenagers and their experiences with hormones, pimples, emotions, alcohol, etc.) while Kasper Winther Andersen and David Meder, both Postdocs from DRCMR, talked about adult life, and in particular the effects of love. Senior Researcher Ellen Garde contributed with research performed on aging and how staying physically and socially active, continuously challenging the brain, and using all senses, can keep the brain sharp as a knife.

Image: Kheng Ho Toh © 123RF.COM

Based on the DR Program "Din geniale krop", televised February and March 2018.

SMART CHOICES

"The brain helps you to make smart choices!" was one of the statements Postdoc David Meder from DRCMR made when interviewed by Lokalavisen Hvidovre Avis on 16 January 2018. He has taken part in a project doing research on what happens in the brain when the focus is upon decision-making. "When placed in a situation where you have to make a choice, the brain calculates a lot of probabilities simultaneously based upon both old and new experiences. So, depending on the situation, it makes sense to make a choice based upon a long-time frame of experiences or only the latest experiences. At the same time, the brain uses most of its resources calculating the best action options in your specific situation depending on how familiar or new the situation is," David Meder says. The team now intends to use the techniques from the research on patients suffering from Parkinson's Disease. "We are going to look at whether the same things happen in their brain when they make decisions. We hope to get an understanding of why they make inappropriate decisions. And when reaching an understanding of why this happens, one might be able to do something about it", David says.

Photo: Rungaroon Taweeapiradeemunkohg © 123RF.COM

Based on article in Lokalavisen Hvidovre Avis, 16 January 2018.

LONG LIVE THE BRAIN!

The Danish magazine "Demenskoordinatorer i Danmark" published a story about the work of Carl-Johan Boraxbekk, a Professor at DRCMR, and collaborators on how to keep the brain sharp and healthy during the aging process. Carl-Johan Boraxbekk and collaborators are carrying out research using older voluntary subjects, dividing them into two groups, letting one group go through physical exercises and memory training, while letting the other group do nothing, and then testing how they react in different situations under pressure. "We test the memory of our subjects before and after an intervention and scan their brain as well. By doing so, we can see how the different activities affect the structure, activity and chemistry of the brain, and how much these actions increase the functional reserves of the brain," he says. At DRCMR, we hope that this kind of research potentially could contribute to delaying diseases such as dementia.

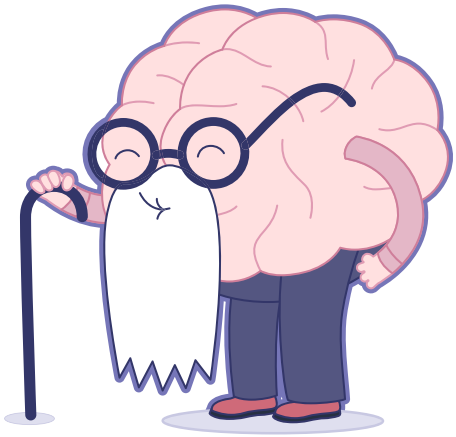


Image: Oxana Grivina © 123RF.COM

Based on "Længe leve hjernen" in the magazine Demenskoordinatorer i Danmark, May 2018.

HOW TO MAINTAIN A HEALTHY BRAIN

Senior researcher Ellen Garde told the Danes about heathy ageing and the three pillars for maintaining a healthy brain throughout life on Danish Radio April 2017. Physical activity, mental activity, and social activity were the three major things when keeping the brain network in shape. The way of keeping the entire network in shape is to keep our expectations of the brain intact. Ellen says: "We expect something of the brain which involves several areas, several functions. So, when I sit here and talk to you, I remember things, I have some memories, I have some knowledge which I pull out from somewhere in the brain, which I must combine with the fact that I have to say it in a way that is understandable. And I have to be able to literally say it, motorically. In addition, I also have to generate sentences and use words which I believe are relevant in this context. This means that I use different areas in my brain. And

if that wasn't enough, I am also sitting here on this chair and I am looking at you and I am registering where I am located, etc." So, by being physically active, mentally active, and socially active, the brain is being fit throughout life.

Based on interview with Senior researcher Ellen Garde, DR P1, 4 April 2017.

BETTER MR IMAGES TO BETTER UNDERSTAND THE BRAIN

Engineer and Senior Researcher Henrik Lundell from DRCMR was granted 1.5 million Euro from the European Research Council in Brussels in Autum 2018. The grant is to be used in a project aiming at developing more accurate MR images – something a number of Danish media found very interesting. Henrik Lundell's goal is to develop technical methods which can provide far more detailed maps of cell changes in the brain. Henrik Lundell explains: "MR scanning is a very sensitive but not very precise method. We can identify a lesion, but we are not as good at displaying individual disease processes. What we want now is to move the scanning methods to the next level where it is possible for us to differentiate changes in different inflammatory processes or degeneration of cells, which is e.g. found in patients with multiple sclerosis and Alzheimer". The goal is to make it possible to see the cells and changes while the scanning takes place, and then analyze the imaging more thoroughly.

Based on interviews with Senior researcher Henrik Lundell published in Politiken (11 September 2018), Lokalavisen Fredensborg (13 September 2018) and Kristeligt Dagblad (24 September 2018).

IS IT OKAY TO TELL A WHITE LIE?

Research has shown how people tell lies several times every day. Sometimes it is deliberate while at other times completely spontaneous in the social context. Postdoc Ayna Baladi Nejad explains what happens in the brain when we tell our close ones a white lie: "We use many resources in the brain when lying. It may be caused by the fact that we try to read the recipient's reaction and emotions by putting ourselves in that person's place. But if we excuse the lie by saying it is for another person's sake, we don't get as affected by it – and it makes it easier to tell a white lie". The processes that may be activated in the brain when people lie are very similar to those found when people feel empathy. So, for people with psychopathic features, it is easier to lie – they simply don't feel guilt.

Photo: Ion Chiosea © 123RF.COM

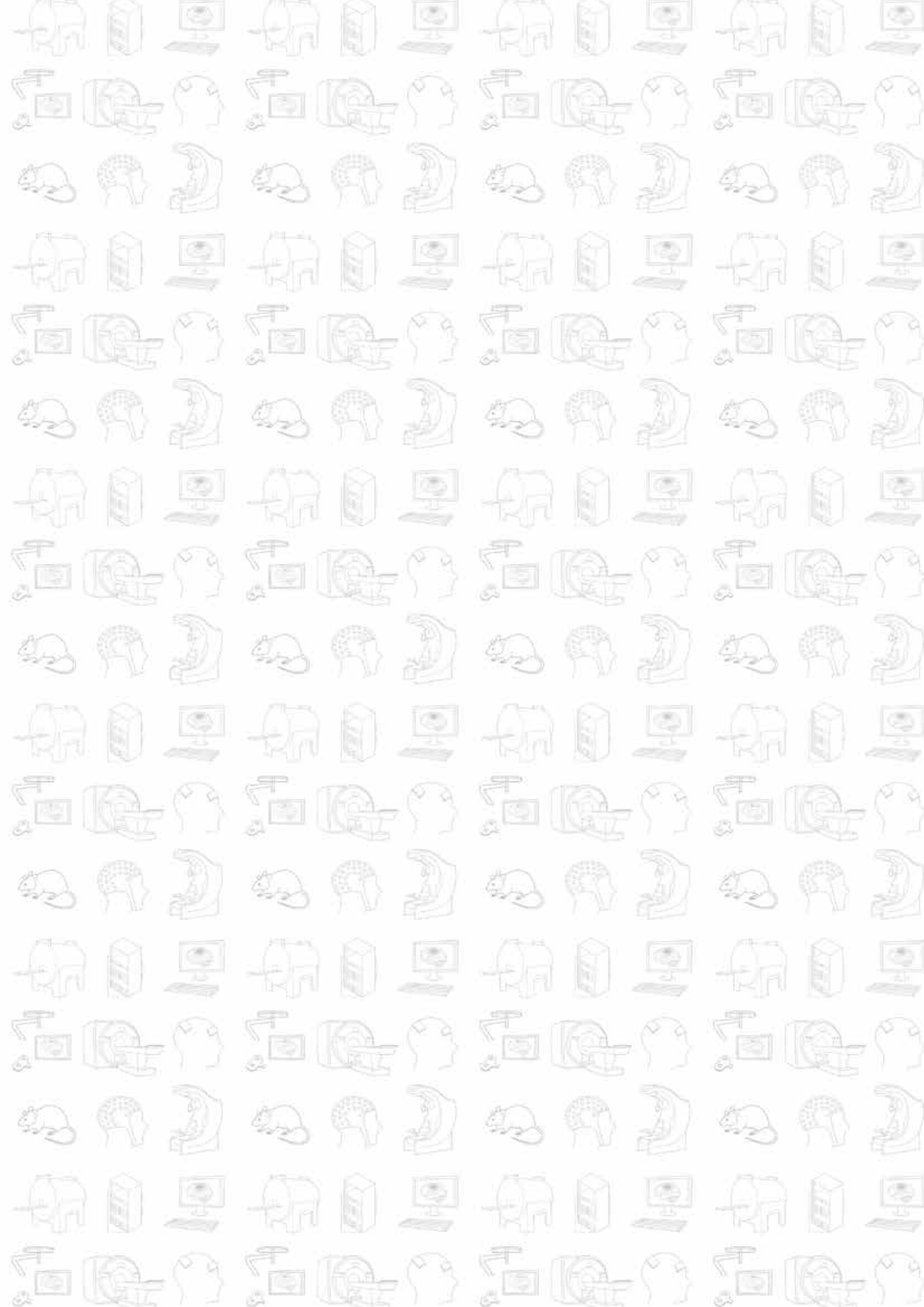
Based on an article from Kristeligt Dagblad, 2 November 2018.

THE EXPERIMENT

Today, most of us spend hours in front of screens, but what does the screen-time do to us? "The experiment" on DR2 stepped into the gray zone of a field, which we still need to explore further, to find out what the cell phone, the tablet and the laptop actually do to us. Postdoc David Meder and PhD stud. Line Korsgaard Johnsen from DRCMR joined the DR2 research group set up in order to investigate further. A brave young family volunteered, and an experiment was set up to study how screen-time affects humans. The experiment ran for a month and a half. During the first three weeks, all family members were to maximize their use of a screen to the utmost. During the last three weeks, the family was asked to turn off all the screens and do without laptops, tablets, TVs, and cell phones. "When the family's use of screens was at its highest, the brain network while resting was affected in a way which indicated that their ability to rest was worsened. They had a hard time calming down and letting the thoughts wander," David Meder stated.

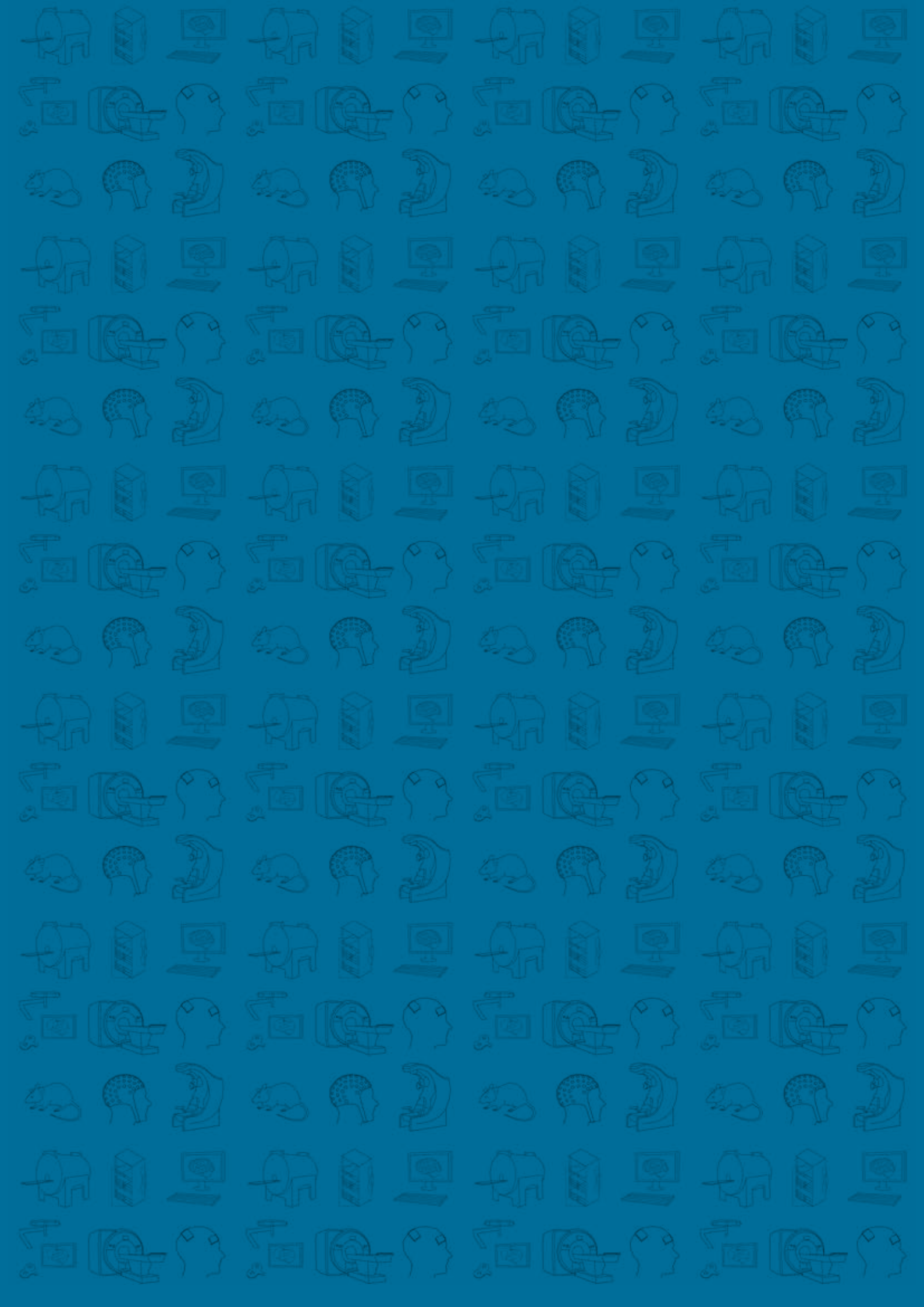
"The experiment" was shown on DR2, 20 and 27 August 2018.

David Meder and Line Korsgaard Johnsen scanning one of the participants from "The experiment".



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

We offer a yearly course called **Foundational Skills for Neuroimaging** in cooperation with the Graduate Programme in Neuroscience at the University of Copenhagen, Neurograd. The course teaches all students the basics of everything no matter what their previous training. During the course students learn the most foundational skills necessary to work with the methods and techniques that are commonly employed at DRCMR and in neuroimaging in general. The foundations course focuses on philosophy of science, foundational maths, statistics, and programming in Matlab.

The internal DRCMR course **Neuroimaging Basics** is taught as a peer2peer course where students teach each other with expert help. We cover every major technique used at DRCMR.

Neuroimaging Pragmatics is an informal series of lectures, organized by our student group, on pragmatic skills such as grant writing, giving talks, paper writing, ergonomics, and so on.

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.

Our yearly **MRI acquisition** course teaches the fundamental physics underlying the MR techniques employed at DRCMR.

Students at a DRCMR course.

The course introduces MRI starting from a level requiring little or no MR experience. Lectures cover MR understanding, acquisition methods and parameters.

On a rolling basis, we also have **stand-alone workshops** on relevant topics such as Brain stimulation techniques with **the annual TMS/NTBS workshop**, or workshops on Neuroanatomy, Basic Neuroscience, Data quality and much else.

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 arranged approximately once a year, in 2017 the Precision Brain Stimulation research area organized a course on **Human Brain Stimulation** and in 2018 the MR Physics and Analyses research area organized a course called **Anatomical and physiological fingerprinting of the human brain with multi-modal MRI.**

Image: Dejan Bozic © 123RF.COM

PHD COURSE 2018

ANATOMICAL AND PHYSIOLOGICAL FINGERPRINTING OF THE HUMAN BRAIN WITH MULTI-MODAL MRI

The PhD course on *Anatomical and physiological fingerprinting of the human brain with multi-modal MRI* took place between 26 February - 2 March 2018 at DRCMR. The aim of the course was to teach the students advanced MR imaging and in particular how different contrast mechanisms can reveal various information about the brain. The course was very hands-on oriented and inspired a lot of good reflections and discussions. The course was fully booked – with a total of 20 students attending the course and 14 local and international teachers.

The PhD course provided an overview of how Magnetic Resonance Imaging (MRI) can be used in neuroimaging. Four cutting edge MRI topics were introduced, addressing the increasing need for combining several MRI modalities. It covered how to improve the specificity for mapping anatomical features for precision medicine, and how to create a better link between brain structure and function, which is partly missing today. The four MRI topics covered were Neurovascular contrast imaging, Quantitative MRI, Diffusion MRI and Spectroscopy. The possibilities of using the Danish National Ultra-High Field human 7T scanner was integrated within the lectures. The course combined lectures and practical hands-on exercises for introducing the participants to the state-of-art experimental designs within each of the topics, their possibilities and challenges. Exercise presentations and discussions between participants were emphasized. International keynote speakers gave lectures at the course to inspire the discussions of multi-modal imaging within the four MRI topics.

The course was organized by Assoc. Prof. Tim Dyrby, Prof. Hartwig Siebner and the members of the MR Physics and Analyses research area and offered together with the Graduate Programme in Neuroscience at the University of Copenhagen, Neurograd.

TOPICS COVERED

Introduction to MRI: How does an MRI scanner work? Basic tissue contrast mechanisms, T1 and T2 relaxation useful for tissue characterization, Ultra-High Field MRI (7 tesla) and MR safety.

Functional MRI: Blood-oxygen-level dependent contrast imaging (BOLD) and Arterial Spin Labelling (ASL) for hemodynamic assessment of changes in CBF, CBV, OEF and CMRO2 during neural activation, potential and analysis.

Quantitative MR: T1/T2/T2* relaxations, magnetization transfer, susceptibility weighted imaging, analysis and tissue compartment modelling.

Diffusion MRI: Basic diffusion concepts, non-parametric (diffusion tensor and kurtosis imaging) and parametric tissue compartment models e.g. axon diameters, diffusion sequences, tractography, pre-processing pipeline.

Spectroscopy: Basic spectroscopy concepts, detectable metabolites and their significance, acquisition strategies (water suppression, single voxel, spectroscopic imaging), data processing/analysis, quantification, multinuclear spectroscopy.

"I have learnt so much about various areas of MRI, their application & the advantages of combining them."

- Anonymous course participant

"Very good! The course is on a very high theoretical MRI-level for us as veterinarian, so I have really learned a lot!"

- Anonymous course participant

From the PhD course on Anatomical and physiological fingerprinting of the human brain with multi-modal MRI.

PHD COURSE ON HUMAN BRAIN STIMULATION 2017

In March 2017 The "Precision Brain Stimulation" research area organized a PhD course on Human brain stimulation. The course provided a systematic and comprehensive overview of current brain stimulation techniques, highlighting their neuroscientific and therapeutic potential. The students were introduced to the various stimulation techniques (e.g. optogenetics, transcranial magnetic stimulation, transcranial current stimulation, deep-brain stimulation) and gained in-depth knowledge about the basic biophysical mechanisms and the most commonly used neuroscientific and therapeutic stimulation techniques. Theoretical lectures were complemented by practical sessions and demonstrations. The course consisted in introductory lectures in the morning (three to four lectures per day), followed by a student presentation of the lecture highlights and supervised practical exercises and demonstrations based on different brain stimulation techniques in the afternoon.

The course was organized by Senior researcher Anke Karabanov, Prof. Hartwig Siebner and the members of the Precision Brain Stimulation research area and offered together with the Graduate Programme in Neuroscience at the University of Copenhagen, Neurograd.

MRI ACQUISITION COURSE 2017 AND 2018

The popular annual course *Magnetic Resonance Imaging Basics* is offered yearly by Assoc. Prof. Lars G. Hanson. The course provides a basis for understanding MRI measurements, pitfalls and literature and is a good starting point for further studies. It covers introductory MRI acquisition in a series of 7 weekly interactive lectures. These include MR basics, acquisition methods and parameters with a focus on understanding.

The course is meant as an introduction course and starts at a level requiring little or no MR experience, and a technical background is not required. The target audience is employees and students at the MR department, but the course is open for external participants as well.
The course is well attended and extremely popular among DRCMR students.

"To my mind, the course was a very broad and comprehensive overview of the principles behind MR and really helped deepening the understanding of this fascinating method"

- Stud. Felix Schmidt

"Teaching a mixed group of students (radiographers, MDs, psychologist, physicists) forces me to focus on the understanding of MRI rather than formalism that is well covered in books anyway. Also, making common sense of MRI happens to be my favorite topic. Interestingly, the students seem equally challenged and interested independent of background. Learning MRI is all about curiosity and perseverance".

- Teacher, Assoc. Prof. Lars G. Hanson

NTBS WINTER SCHOOL
NON-INVASIVE TRANSCRANIAL BRAIN STIMULATION

The NTBS Winter School in Copenhagen is an intensive four-day workshop providing participants with in-depth knowledge of the most common noninvasive transcranial brain stimulation techniques (TMS/TDCS/TACS). The winter school has been arranged by DRCMR researchers once a year for the past 5 years and continues to attract researchers, students and practitioners from all over the world.

The workshop is tailored to researchers and clinicians who wish to gain extensive insight into the basics and state-of-the art application of noninvasive brain stimulation. The workshop covers basic physical and physiological principles, electric field modeling, and a wide range of cognitive and clinical applications. A special focus is put on multimodal combinations of NTBS with other neuroimaging techniques (EEG, fMRI). All teaching modules are accompanied by hands-on sessions and demonstrations.

METHOD GROUPS
FOR RESEARCH DEVELOPMENT AND 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
- Preclinical

Read more about the focus of each group at p. 66-70.

TO BE OR NOT TO BE A STUDENT AT DRCMR

Every year we enroll a considerable number of students (BA, MA 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. The students come from all over the world – in 2017-18 we had students from countries as different as Hong-Kong, Norway, The Netherlands, Korea, Germany, Italy, Mexico, Turkey, Israel, Greece, Austria, Spain, Canada, Sweden, Ukraine, Iran, Portugal, China and of course Denmark.

YOU CAN MEET THREE OF OUR STUDENTS HERE:

MARTA – MA student from Portugal

Name: Marta Marques
Age: 23 years
Study: Masters student at the Faculty of Sciences, University of Lisbon, Portugal.

As part of my master's degree in Biomedical and Biophysics Engineering I decided to seek an international opportunity as a way to conduct my Master Thesis project in research and thus finalize my degree. Through an Erasmus+ program I was able to come to the colorful city of Copenhagen for 10 months. I am currently working at DRCMR on a project which aims at studying and understanding the role of cortical pathology in Multiple Sclerosis' patients using state of the art ultra-high field MRI.

Even though I've only been at DRCMR for a few months the whole experience so far has been extremely positive and as a passionate about neuroscience and magnetic resonance imaging, I don't think I could have found a better place to conduct my dissertation.

Whilst at DRCMR, not only am I able to work with the most advanced technologies, but I am also fortunate enough to be surrounded by an incredible interdisciplinary team of highly motivated and competent researchers from which I can only expect to learn and grow from throughout the next few months.

CORNELIA – Intern from Germany

Name: Cornelia Rudolph
Age: 25 years old
Study: Master student in Cognition and Communication at the University of Copenhagen, Denmark.

For four months I was an intern at the DRCMR and assisted in the reward and homeostasis research group. I chose the DRCMR as my internship place because I wanted to gain an insight into the world of research in the area of cognitive science, in particular in cognitive neuroscience. Especially the processes of conducting research – from the idea, to the funding, to the actual execution of the research project was very interesting for me since I never came in touch with it previously. My main task at the internship was to help out with the OmniSaM project (read more p. 20-21). As for my stay at the DRCMR, I really enjoyed the time there and I learned a lot. The people were very nice and helpful – thanks to the open and international working environment. And even though I do not come from the natural sciences, as most of the other employees at the DRCMR do, I never felt like I lacked something in knowledge or practice. I still belonged there and was an equal part of the institution.

ANNA – Psychology student from Denmark

Name: Anna Jacobsen
Age: 27 years old
Study: Psychology student at the University of Copenhagen, Denmark.

I wrote my master thesis at DRCMR in cooperation with a research project called Lifespan. I chose to apply to DRCMR because of the great possibility to learn about new advanced brain scanning methods and to be involved in the research process from recruiting the participants, collecting the data to sitting with the data analysis. The Lifespan project seeks to get a better understanding about the healthy aging process in many different aspects. The master thesis focused on metabolite levels in the brain, measured with MR Spectroscopy, across different age groups and their correlations with cognitive performance. It was a great experience to work with highly competent and experienced researchers from other disciplines. The interdisciplinary work environment served as a great possibility to learn how different majors seek to get a better understanding of the same object, here at DRCMR - the brain. As a student you are involved socially which was an important aspect of thriving at DRCMR. No matter how consumed you were with work, there was always time for a quick match of table soccer.

THE DRCMR STUDENT GROUP

WHO ARE WE?

The DRCMR student group consists of PhD students, Research assistants, BA and MA students, visiting Interns, and "research year" medical students. We meet on the last Friday of every month to have lunch together, have discussions and listen to talks on different subjects.

OUR PURPOSE

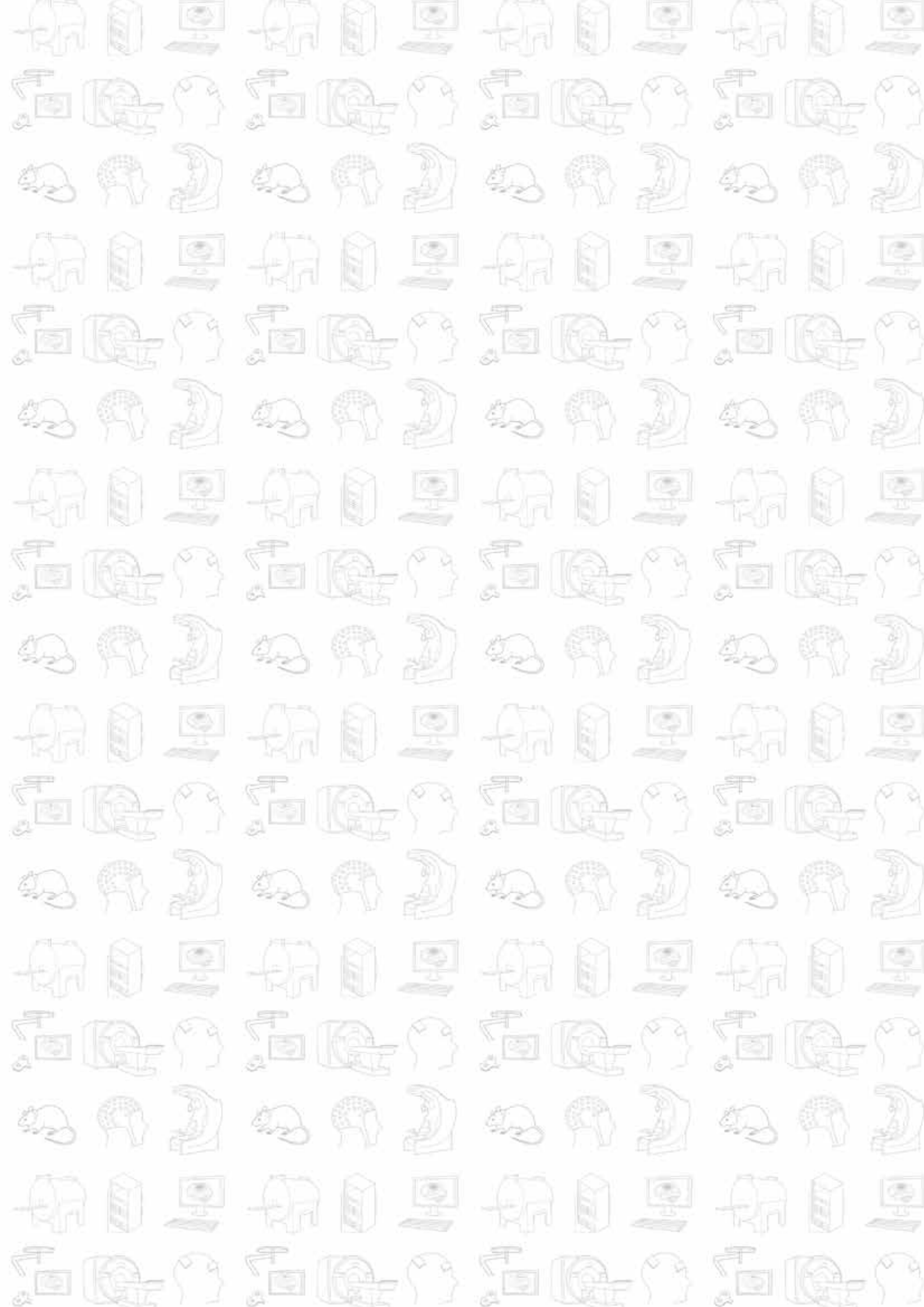
We form the basis of a student network and encourage both academic and social exchanges between students at DRCMR.

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. In example, recent 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" – we have, for example, revived the old tradition of going for after-work "Friday beers" on the same day as the student meeting.

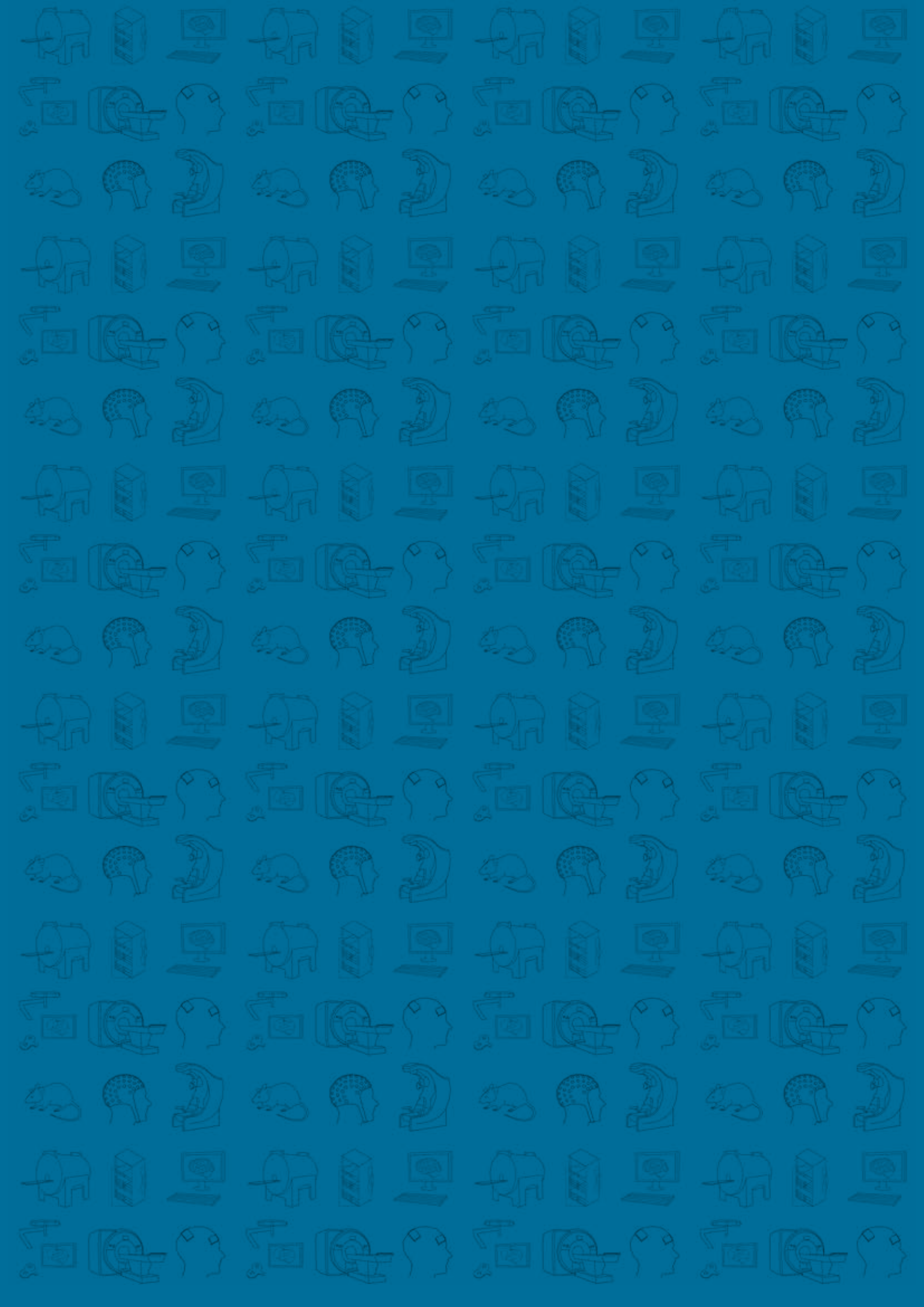
Some of the members of the DRCMR student group.



DISSERTATIONS

11 PhD candidates defended their theses at DRCMR in 2017–18.

The PhD's where done in collaboration with The University of Copenhagen, The Technical University of Denmark, University Federico II of Naples and Università degli studi di Palermo.



FUNCTIONAL BRAIN IMAGING UNDER SEROTONERGIC CHALLENGES

Bettina Hornbøll

SUMMARY

The major aim of the current study was to investigate the connections between personality traits linked to neuroticism and behavior in healthy humans with a main focus on serotonin (5-HT) measured by functional magnetic resonance imaging (fMRI). Brain activation patterns were investigated in healthy volunteers while they performed a gender discrimination task on images of fearful, angry, and neutral facial expressions during serotonergic challenges.

With this study, we have shown that structures such as the OFC, amygdala, subgenual cortex, as well as superior temporal cortex play a crucial role in the processing of aversive faces. 5-HT2A receptor mediated signaling increases the sensitivity of OFC to fearful facial expressions and regulates the strength of a negative feedback signal from OFC to amygdala. Furthermore, both lowering and increasing the serotonergic tone of the brain increased the correlation with neuroticism scores when looking at aversive faces. This supports the idea that serotonin and neuroticism are tied together in processing threatening face emotions, and that this influence is depending on an individual's personality trait. This finding may represent a neural mechanism for the variable therapeutic effect of SSRI treatment observed in clinical populations.

SUPERVISORS

Prof. Olaf B. Paulson, NRU
Prof. Hartwig Siebner, DRCMR
Postdoc Julian Macoveanu, DRCMR

UNIVERSITY

University of Copenhagen

DATE OF DEFENCE

May 8th, 2017

WORKING TODAY

Eksternal Lecturer in Neuroscience at DIS – Study Abroad in Scandinavia

GRAMMAR-LEXICON DISTINCTION IN A NEUROCOGNITIVE CONTEXT: INTEGRATING TWO THEORIES

Byurakn Ishkhanyan

SUMMARY

Recent neuroimaging techniques and lesion studies contribute to our understanding of the neurocognitive underpinning of language in the brain, while psycholinguistic studies offer models of how and in which order different components are processed. Most of those studies see language either from a modular or from a connectionist perspective. A usage-based theory of grammatical vs. lexical status (Boye & Harder, 2012) positions itself between Generative Grammar and Construction Grammar. A theory of the reorganization of elementary functions (REF-model; Mogensen, 2011; 2014) suggests a three-level organization of cognitive functions in the brain and accounts for post-injury recovery. The current thesis aims at deriving hypotheses and testing them based on these two theories, using various methods, such as pure behavioural and transcranial magnetic stimulation.The results suggest a potential for a successful integration of the two theories. The findings further provide evidence for Boye & Harder's (2012) understanding of the grammar-lexicon distinction, and for the involvement of working memory in language production, as the REF-model would predict.

SUPERVISORS

Assoc. Prof. Kasper Boye, NORS
Prof. Jesper Mogensen, UCN
Prof. Hartwig Siebner, DRCMR

UNIVERSITY

University of Copenhagen

DATE OF DEFENCE

August 31st, 2017

WORKING TODAY

The Puzzle of Danish Project, Aarhus University

A NOVEL MRI APPROACH FOR MEASURING WEAK ELECTRICAL CURRENTS INSIDE THE HUMAN BRAIN

Cihan Göksu

SUMMARY

Knowing the current flows inside the human brain is very important for various neuroscience applications, e.g. improving transcranial current stimulation. Magnetic resonance current density imaging (MRCDI) is an emerging method combining MRI with weak electrical currents to measure the current flow distributions inside the human brain. The method uses the current-induced magnetic field measurements, and the sensitivity of the measurements directly affects the accuracy of the current flow estimations. Therefore, sensitivity improvements of the underlying MRI methods are crucial for MRCDI.

In the first study of my PhD, systematic sensitivity analyses of two different MR methods, multi-echo spin echo (MESE) and steady-state free precession free induction decay (SSFP-FID), are performed to optimize them for human in-vivo brain MRCDI. The sensitivity simulations are validated by comprehensive phantom experiments. Secondly, the optimized methods are further improved for human experiments and tested in-vivo. The current flows are estimated from the field measurements and compared with the simulations based on realistic head volume conductor models.These first reliable current flow measurements pave the way for clinical use of human in-vivo brain MRCDI.

SUPERVISORS

Assoc. Prof. Axel Thielscher, DRCMR/DTU
Assoc. Prof. Lars G. Hanson, DRCMR/DTU

UNIVERSITY

Technical University of Denmark

DATE OF DEFENCE

November 24th, 2017

WORKING TODAY

Postdoc at DRCMR

IN VIVO EVALUATION OF FAST SENSORIMOTOR INTEGRATION IN THE HUMAN MOTOR HAND AREA

Raffaele Dubbioso

SUMMARY

The studies included in my thesis mainly evaluated the fast sensorimotor integration in the human sensorimotor area in vivo, by using a well-known TMS (transcranial magnetic stimulation) technique called short-latency afferent inhibition (SAI).

Section 1 reviewed current knowledge on the biological and physiological basis of fast sensorimotor integration and its role in mild cognitive impairment and dementia.

Section 2 reported two studies. The first one focuses on using an innovative central sulcus-based mapping technique of SAI. The second study mainly focuses on the role of cerebellum in the modulation of somatosensory afferent pathway.

Section 3 reported two studies where SAI has been used as a tool to investigate functional involvement of central cholinergic circuits in two different types of cognitive impairment. In the first study, we showed that patients with the adult form of Niemann Pick type C (NPC) are characterized by abnormal SAI (Dubbioso et al. 2014) whereas in the second one, we found that SAI is normal in Parkinson disease (PD) patients with Freezing of Gait (FOG) (Dubbioso et al. 2015). These results indicate that SAI can differentiate two types of dementia: cholinergic and non-cholinergic dementia.

SUPERVISORS

Prof. Lucio Santoro, UniNa
Prof. Hartwig R. Siebner, DRCMR

UNIVERSITY

University Federico II of Naples and University of Copenhagen

DATE OF DEFENCE

June, 7th, 2017

WORKING TODAY

Clinical Research fellow at University of Naples Federico II

ASYMMETRY OF SELECTIV ATTENTION IN HEALTHY SUBJECTS AND PATIENTS WITH FOCAL DYSTONIA

Gaetana Chillemi

SUMMARY

The thesis explored the role of selective attention in healthy subjects and dystonic patients employing novel paradigms which require shifts of spatial and temporal processing in response to visual and auditory cues. The results obtained in healthy subjects showed a rightward bias for auditory attention. Together with the evidence of a leftward bias for visuo spatial attention, the results support the idea of modality-specific auditory and visual attentional systems. Furthermore, the experiments provided evidence that temporal attention may be spatially driven, again, expressing a leftward bias for the visual modality and a rightward bias for the auditory modality. In contrast to healthy individuals, patients with idiopathic cervical dystonia and prominent torticollis displayed a consistent leftward bias for visual stimuli. This was also the case in patients in whom dystonia was worse on the right side of the body. Moreover, it is especially important to design rehabilitation treatment for individuals who have sustained damage to portions of the parietal-basal ganglia-cerebellum network and may be suffering from various attentional disorders.

SUPERVISORS

Prof. Angelo Quartarone, UNIME
Prof. Hartwig Siebner, DRCMR

UNIVERSITY

Università degli studi di Palermo

DATE OF DEFENCE

March 27th, 2017

WORKING TODAY

Centro Neurolesi Bonino Pulejo Messina

ENCODING OF NON-MR SIGNALS IN MAGNETIC RESONANCE IMAGING DATA

Jan Ole Pedersen

SUMMARY

Other signals than the magnetic resonance (MR) signal are often of interest during MR imaging. These can contain, for example, biomedical information such as electroencephalography (EEG) or be used for scanner monitoring and characterization to yield improved MR image quality. When acquiring such non-MR signals, care must be taken to avoid interference with the MR measurements, and to avoid scanner-induced artefacts in the non-MR signal.

In this PhD project, the feasibility of using the MR scanner to not only acquire the MR signal, but also concurrently acquire the non-MR signal, was investigated. The project focused on solving the technical challenges arising from this approach, and implementing real-time signal processing in custom circuitry to expand its applicability. The approach led to strong attenuation or elimination of the scanner-induced artefacts for the investigated non-MR signals.

SUPERVISORS

Assoc. Prof. Lars G. Hanson, DRCMR/DTU
Prof. Rong Xue, CAS
Assoc. Prof. Vitaliy Zhurbenko, DTU

UNIVERSITY

Technical University of Denmark

DATE OF DEFENCE

May 4th, 2018

WORKING TODAY

MR Clinical Scientist, Philips Healthcare

EFFECTIVE CONNECTIVITY AND GAMMA OSCILLATIONS IN A GROUP AT RISK OF PSYCHOSIS

Kit Melissa Larsen

SUMMARY

22q11.2 Deletion Syndrome (22q11.2DS) is associated with a markedly increased risk of schizophrenia. Therefore, 22q11.2DS is a homogeneous genetic liability model enabling studies on functional abnormalities that may precede disease onset of schizophrenia. These could potentially assist in the search of biomarkers for schizophrenia.

In my thesis, I investigated processes consistently found to be impaired in schizophrenia, in a cohort of 22q11.2 deletion carriers using electroencephalograpgy. Participants engaged in a roving mismatch negativity paradigm as well as an auditory steady state paradigm. Both of these paradigms are known to involve processes that are impaired in schizophrenia. I showed that individuals with 22q11.2DS have reduced ability to phase lock to 40 Hz auditory stimulation, which was associated with symptom severity in the group. I further showed that predictive processes are intact in individuals with 22q11.2DS but that the adaptive processes are reduced. The studies contribute to understanding the underlying pathology of 22q11.2 deletion syndrome and if results are confirmed by longitudinal follow-up studies, the results might contribute to the search of biomarkers for schizophrenia.

SUPERVISORS

Assoc. Prof. Morten Mørup, DTU
Prof. Hartwig Siebner, DRCMR
Prof. Thomas Werge, IBP
Senior researcher William Baaré, DRCMR

UNIVERSITY

Technical University of Denmark

DATE OF DEFENCE

May 1st, 2017

WORKING TODAY

PostDoc, Queensland Brain Institute, Computational cognitive neuroscience group, Brisbane, Australia

Kit Melissa Larsen at her PhD-defence.

THE MECHANISM BEHIND CENTRAL MOTOR FATIGUE IN MULTIPLE SCLEROSIS

Olivia Svolgaard

SUMMARY

Fatigue is one of the most common and disabling symptoms of multiple sclerosis (MS). The pathophysiological mechanism behind fatigue is unknown and the treatment is often insufficient. To advance our understanding of fatigue and to develop specific targeted treatment, objective neuroimaging biomarkers of fatigue are needed. We performed a functional magnetic resonance imaging study of 44 mildly disabled MS patients with varying degrees of fatigue and 25 age- and gender-matched healthy controls. Using a three-phase precision grip task with a pre-fatigue phase, a fatiguing phase and a post-fatigue phase, we explored the neural correlates of self-reported motor fatigue and the neural response to being fatigued. The study showed that the MS patients' subjective feeling of motor fatigue correlated with the activity in the right motor cerebellum and the fatigue-induced change in the left premotor cortex. Additionally, fatiguing the patients gave an altered response bilaterally in the dorsolateral prefrontal cortex and putamen.

This study provides solid support for the concept that motor fatigue and fatigability in MS can be mapped to functional changes in the brain. However, the role of the involved areas needs to be further explored.

SUPERVISORS

Prof. Hartwig Siebner, DRCMR
Prof. Finn Selleberg, DMSC
Postdoc Kasper W. Andersen, DRCMR

UNIVERSITY

University of Copenhagen

DATE OF DEFENCE

Februar 9th, 2018

WORKING TODAY

Pharmaceutical Medicine Programme, Novo Nordisk – Educational programme for medical doctors

PERCEPTUAL AND NEURAL RESPONSE TO SOUND TEXTURE

Richard McWalter

SUMMARY

A primary goal of sensory neuroscience is to understand how people navigate in natural environments. We sense (see, smell, taste, hear and feel) our surroundings and act upon these sensory inputs in complex ways. In my PhD, I was focused on the auditory system and how we listen in natural environments. In particular, I was interested in how we perceive background sounds, such as the sound of rain falling on a rooftop, horses galloping in a field, or the chirping of insects in a forest. These sounds – referred to as sound textures – are thought to be represented in the auditory system by a set of time-averaged summary statistics. I conducted several experiments to investigate how humans listen to sound textures, how we might average sound texture acoustic information over time, where this averaging might happen in the brain, and how texture statistics might be related to sound perception. Our findings suggest the auditory system adapts to statistical properties of sound textures and that the statistical structure of texture may be represented at a cortical level in the auditory system.

SUPERVISORS

Prof. Torsten Dau, DTU
Senior researcher Jens Hjortkjær DTU/DRCMR

UNIVERSITY

Technical University of Denmark

DATE OF DEFENCE

May 23rd, 2017

WORKING TODAY

PostDoc - Laboratory for Computational Audition, Department of Brain and Cognitive Sciences, MIT

NEURAL MECHANISMS OF FREELY CHOSEN ACTIONS

Steffen Angstmann

SUMMARY

To choose an action freely in a largely unconstrained world is an essential part of our behaviour. Such free action selection is hard to observe and to study. Experimental frameworks are often constructed as to provide a minimally constrained task space, paradoxically paired with a maximally constrained response space. Arguably, task situations have been described as an experimental confound, they are lacking crucial features of real-life situations, and stimulus-response relations can be weak.

The current thesis studied volitional actions by exploiting two very different experimental paradigms that treat task context as a meaningful part of free action selection. Such were a stream of paced rapid spontaneous decisions on the one and realistic and ecologically valid decisions on the other hand.

FMRI and TMS suggested that brain activity associated with free action selection processes differs depending on both internally generated and externally induced task strategies. Constraints, like timing or foreseeability of selection options, influence the temporo-spatial activity patterns in areas relevant for making and implementing motor decisions.

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HOMEOSTATIC CHOICE THEORY

Tobias Morville

SUMMARY

Motivation is fundamental for control in biological agents as this guides behaviour towards states of the world that are congruent with either survival, reproduction, or both. Thus, biological fitness and motivation must be intricately linked. This thesis offers a novel perspective on homeostatic control based on the free-energy principle. Put concisely, this principle suggests that all biological agents resist dissipation through the second law of thermodynamics, by restricting themselves to a limited number of states. This engenders a Bayesian perspective of (active) homeostatic control that reformulates core concepts in both classical feedback accounts of homeostasis and theories of decision-making under the framework of Active Inference.While undergoing functional magnetic resonance scanning, five subjects completed four sessions of a passive Pavlovian cue-conditioning design while subjected to glycemic flux.It is shown that signals commensurate with state modulated (reward) prediction errors are expressed differentially in midbrain, brainstem and striatum. These findings are discussed in light of both classical theories of reward and Active Inference.

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

- Henry Ford

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COMING TO DRCMR

James Olav Breen Norris

I have spent the last four years working on a Ph.D. in "Non-invasive cytometry of tumours using diffusion MRI, measuring water exchange across the cell membrane with Diffusion Exchange Spectroscopy (DEXSY)" at UCL in London.

I am looking forward to applying everything that I have learnt in the course of my studies, to a new challenge starting at the DRCMR on December 1st, 2018. I am also looking forward to getting to know everyone at the DRCMR and familiarising myself with Copenhagen. I will be working as a Postdoc in Microstructure Imaging of Hearing Loss on the UHeal "Uncovering Hidden Hearing Loss" project at the DRCMR. The aim of Uheal is to design imaging techniques and auditory methods to detect and diagnose a recently described noise induced hearing loss that a large part of the population has without really knowing it. My part of the project will be carried out at the DRCMR and is a synergistic collaboration with research teams at the Technical University of Denmark (DTU) and Harvard Medical School. I will be working as part of the Microstructure and Plasticity (MaP) group headed by Tim Dyrby.

H. Martin Kjer

After some years of research and completion of a PhD in Informatics in a "classic" academic setting, I was intrigued by an opportunity to move to DRCMR in mid-2017 as a postdoctoral researcher. My research had focused mainly on image analysis, -processing and -reconstruction. I was mostly involved on the side of method development/data analysis and rarely in the actual data collection, i.e. sample preparation, scanning etc. My work would also often feel far from the end-user and the applications. This is precisely the intriguing appeal of a place like DRCMR; the excellent MRI scanner – and lab facilities; the closeness to the clinic and patients. In such an eco-system, one can easily be involved in all aspects of research, ranging from MRI physics, sequence optimization and data acquisitions, through data processing and modelling, and all the way to clinical studies.

Currently, I am hired on a pre-clinical research project (MAX4-Imagers). Here, we use both MRI and synchrotron imaging to study the brain microstructure of both mice and monkeys. The MRI allows us to study the whole brain, although at a low resolution. We extract small samples from specific regions of the brains, which we then image with incredibly high resolution at synchrotron facilities. Analyzing and linking the data from two such vastly different modalities requires several challenging data processing steps, and this forms the core of my current work.

Søren Asp Fuglsang

I came to work as a Postdoc at DRCMR in November 2018. During my PhD studies at the Technical University of Denmark (DTU), I studied how information about sound stimuli is represented in single-trial EEG responses and how attention affects EEG responses to sound mixtures. My current project is part of a new synergy project, UHEAL ("Uncovering Hidden Hearing Loss", starting up medio 2018), with collaborators from DTU and Har-vard Medical School. In my work, I will use fMRI and EEG to study how auditory pro-cessing of sounds is affected by cochlear synaptopathy.

Working at DRCMR has been a great experience so far. DRCMR offers a collaborative and interdisciplinary work environment as well as excellent neuroimaging facilities. This makes DRCMR an exciting place to work and provides great opportunities to interact with and learn from researchers with different backgrounds and competences.

I look forward to developing my skills as well as furthering my learning skills for the next phase of my scientific career at DRCMR.

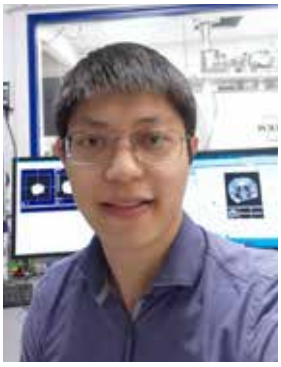
Syoichi Tashiro
田代祥一

I am a rehabilitation physician from Japan. I came to study as a post-doctoral researcher in April 2017 after having finished my PhD and a post-doctoral clinical study at the Department of Rehabilitation Medicine, Keio University School of Medicine in Japan. My PhD work was the regenerative-rehabilitation with neural stem/progenitor cells transplantation for spinal cord injury model animals, and the other clinical study was sensory evoked potentials in chronic stroke patients undergone neurorehabilitation.

My main motivation to come to the DRCMR was to find a new non-invasive transcranial brain stimulation (NTBS) method which is applicable in the clinics of rehabilitation. Currently, I am involved in the BaSiCs project under the supervision of Prof. Hartwig R. Siebner. Partly taking over research of a previous Japanese researcher Mitsuaki Takemi, I am researching transcranial alternating current stimulation (TACS) and transcranial magnetic stimulation (TMS)- Electroencephalography (EEG).

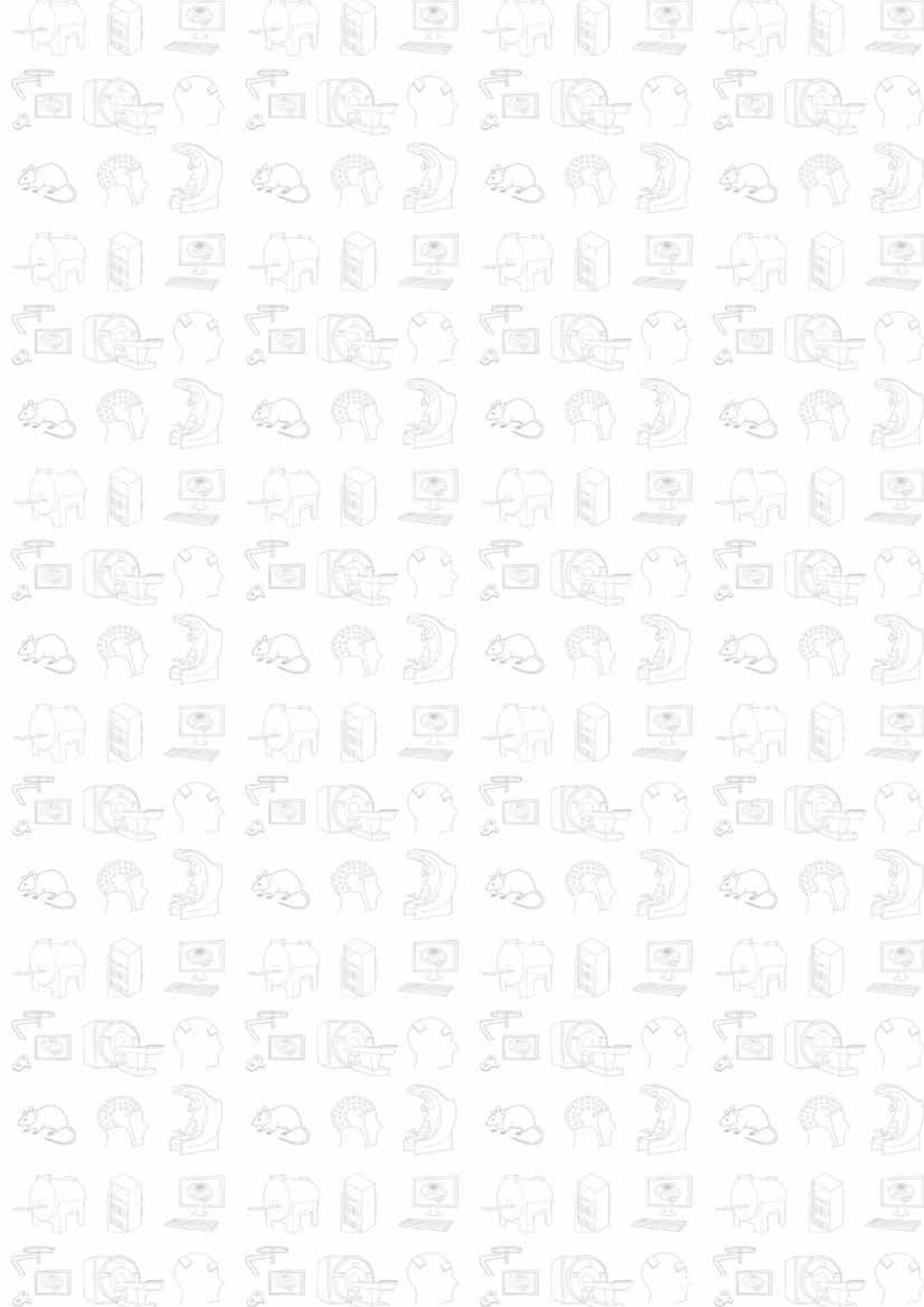
It is a great opportunity for me to join the DRCMR, not only to deepen my research idea but also to improve my clinical potential, since DRCMR has an exciting environment which international researcher with broad scientific backgrounds are using to improve their learning.

Yi He
何祎

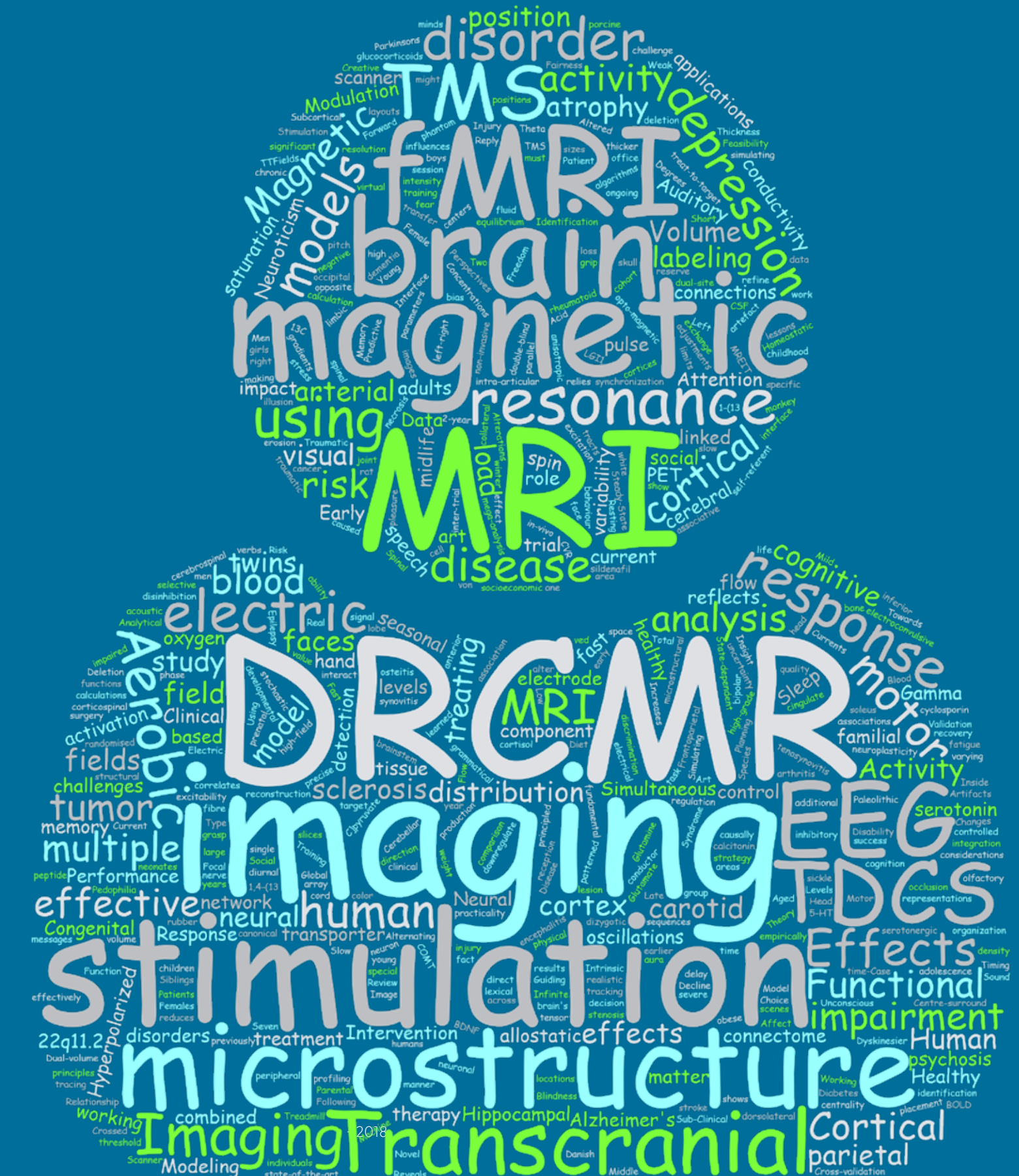


I came to work as a Postdoctoral Researcher at DRCMR in January 2018. During my Ph.D. research at Max Planck Institute for Biological Cybernetics, I focused on providing and combining functional MRI (fMRI) technical approaches with MR compatible cutting-edge tools (optogenetics, simultaneous calcium recording). Since fMRI signals originate from vessels, it is crucial to examine neural activity-induced fMRI changes in different vascular compartments. I combined them to investigate function activity and connectivity from the perspective of single vessels in rodents and humans.

After my Ph.D. training in animal fMRI, I would like to obtain the postdoctoral training in diffusion MRI and human fMRI. Then I joined the DRCMR as part of the MAX4 Imagers project. My current interest focuses on the translation of synchrotron data of brain tissue to diffusion/quantitative MRI by optimizing MRI sequence and biophysical model. I work on combining diffusion MRI and quantitative MRI with task-related fMRI, resting-state fMRI to quantitatively link functional features with microstructures in animal MS models and translate them to clinical application.



PUBLICATIONS



2018

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