

DRCMR

DANISH RESEARCH CENTRE FOR MAGNETIC RESONANCE

Biennial Report 2015–2016

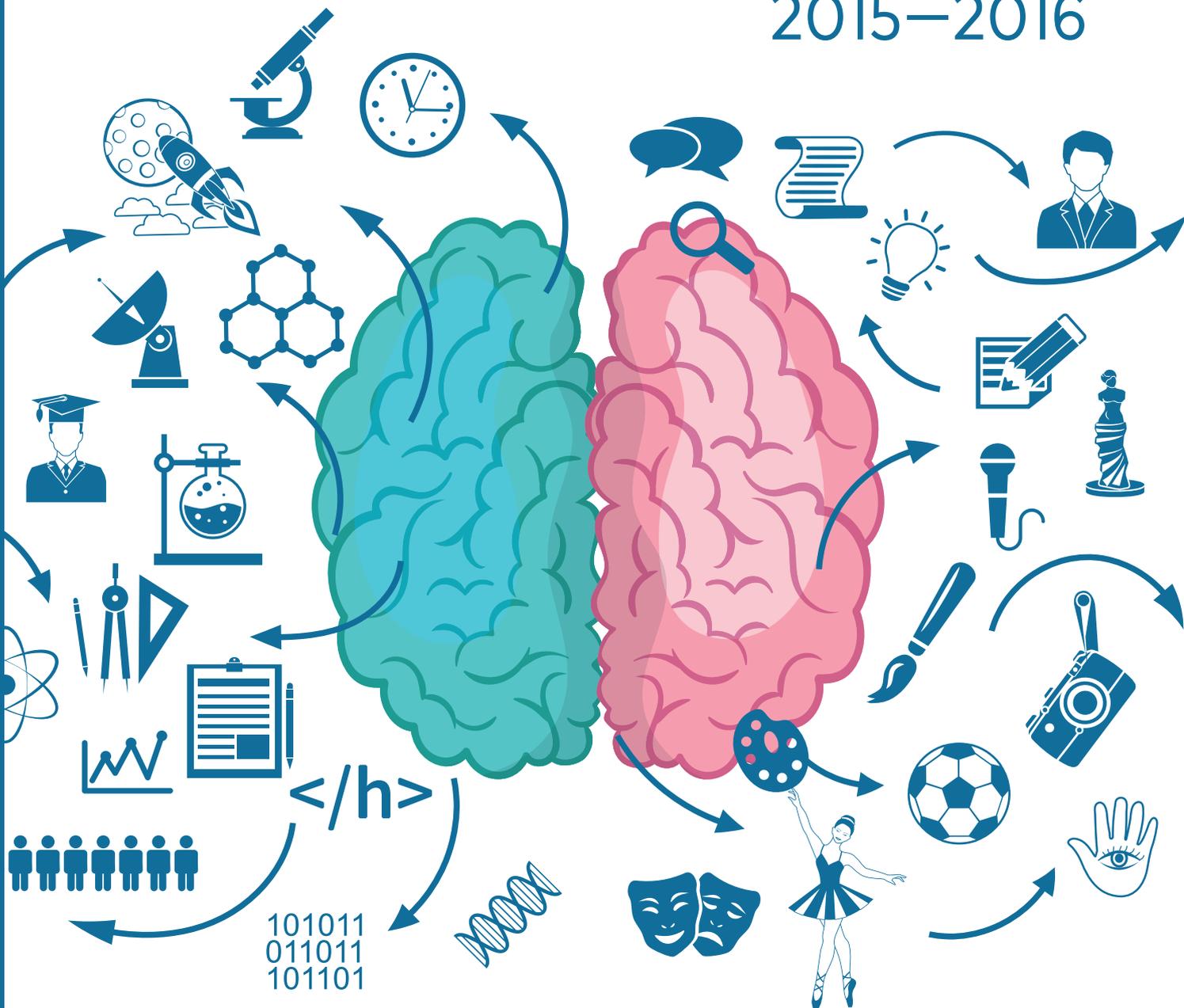


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PREFACE



Professor Hartwig R. Siebner, Head of Research at DRCMR.

During the last couple of years, the DRCMR has taken a big step forward, establishing a clearer research strategy, enlarging our collaboration and inaugurating new facilities.

We have worked in depth with our organization; the structure, the groups, and the research focus.

We asked ourselves: What do we want to achieve as a translational research centre based at a large university hospital, and how can we reach our scientific goals and ambitions?

We are committed to conduct innovative research at the highest international level. We do not intend to make our findings in a closed bubble. On the contrary, we are open-minded, engage constantly in new collaborations in Denmark, Europe and worldwide and bridge multiple disciplines.

In this biennial report, we wish to give you an overview of our work the past two years and how we plan for the future. 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 “reach for the stars”.

All the best wishes

A handwritten signature in blue ink that reads "H Siebner". The signature is fluid and cursive.

Hartwig R. Siebner

Researchers, students and support staff at the DRCMR.



HIGHLIGHTS AND MILESTONES 2015–2016

The brain continuously interacts with the body and is shaped by a complex interplay of genetic, physical, social, cultural, and environmental factors. These interactions emerge on different timescales and drive developmental cascades across the lifespan. “Brain dynamics” determine our lives. Beneficial brain dynamics secure our health and well-being. Aberrant brain dynamics may result in brain disorders, affecting our lives and causing enormous individual, societal and economic burden. At DRCMR, we use brain mapping to unravel causal dynamics in the human brain. Our mission is twofold: On the one hand, we study beneficial brain dynamics that secure physical and mental health. On the other hand, we identify detrimental brain dynamics that cause brain disorders across the lifespan. The years 2015 and 2016 brought a series of exciting new developments that added significant momentum to the science conducted at DRCMR and that opened up exciting possibilities for the future.



The participants at the 30-year symposium held on May 8th, 2015 to celebrate the DRCMR anniversary. Photo: Franck Thibault.

CELEBRATING 30 YEARS OF RESEARCH

The DRCMR was established in 1985 as a result of a very generous donation by travel magnate Simon Spies. He had been hospitalized at Hvidovre Hospital several times in 1983–84 due to liver disease and was so satisfied with the care and treatment he received at the hospital that he decided to give the hospital a gift that could benefit future patients. The gift ended up being the first Magnetic Resonance Imaging (MRI) scanner in Denmark – a 1.5 Tesla MRI scanner produced by Siemens. Large donations for research from private foundations were virtually unknown in Denmark at the time, so the 20 mill. DKK grant in 1984 (corresponding to approx. 44 mill. DKK today) was a unique opportunity for Hvidovre Hospital to establish a ground-breaking research and knowledge centre – the Danish Research Centre for Magnetic Resonance.

On 8th May 2015, the DRCMR marked its 30-year anniversary with a symposium at Hvidovre Hospital. The full-day symposium featured both historic and scientific talks by current and former staff as well as prominent international scientists. A 30-year commemorative report was also published as part of the celebration and it is available as PDF on the DRCMR website.

7T UP AND RUNNING

Finally in 2015, the preparations for the National 7T MR facility paid off. The 7T magnet was ramped up to full field in January 2015 and the scanner was officially inaugurated on February 24th 2015 by Sophie Hæstorp Andersen, the Chairman of the

Regional Council of the Capital Region of Denmark. The inauguration featured a demonstration of the strong magnetic field in the scanner and was well-attended by officials, the granting bodies, collaborators and staff. The National 7T facility was funded by the Danish Agency for Science, Technology and Innovation and the John and Birthe Meyer Foundation.

Following the inauguration, the 7T scanner still had to undergo some final calibrations by Philips, and was handed over in January 2016. A number of projects focusing on methods development are already pursued by the Ultra-high Field MR group at DRCMR, led by associate professor Esben T. Pedersen. The first neuroscientific projects have been started up and many more projects are in the pipeline. All projects are scientifically assessed by an executive committee which refers and reports to the steering committee of the National 7T MR facility.

Sophie Hæstorp Andersen, the Chairman of the Regional Council of the Capital Region of Denmark, at the inauguration of the 7T MR scanner in February 2015.



NEW PRECLINICAL FACILITIES

Preclinical research at DRCMR received an important boost, thanks to the installation of a new Bruker 7T preclinical MR scanner towards the end of 2016. The scanner replaced the former Varian (Agilent) 4.7T preclinical MR scanner of which some parts (the magnet) dated back to 1989. In parallel to the installation of the new scanner, the existing preclinical animal

research facilities were completely reconstructed and refurbished. The preclinical facilities provide an ideal platform for translational studies at ultra-high magnetic field, offering ample possibilities for synergistic studies in all major research areas being pursued at DRCMR.

BASICS

The combination of transcranial brain stimulation and human brain mapping became a research focus at DRCMR in 2008. This line of research reached a new level in 2015. Together with co-applicants Lars Kai Hansen (DTU-Compute) and Axel Thielscher (DTU-Electro), principal investigator Hartwig R. Siebner initiated a 3-year project entitled Biophysically adjusted State-informed Cortex stimulation (BaSiCs). The BaSiCs project is funded by a 15 mill. DKK synergy grant from the Novo Nordisk Foundation. This highly ambitious project aims to integrate advanced modelling of the electrical fields

induced with non-invasive transcranial brain stimulation, with real-time recording of brain states using EEG and functional MRI in order to dynamically adapt the spatiotemporal properties of non-invasive transcranial brain stimulation to the intrinsically expressed brain states. We expect that this research will yield important discoveries regarding the neural underpinnings of human brain function and dysfunction. Our ambition is to push the frontiers of non-invasive transcranial brain stimulation as an interventional tool to optimize the function of human brain networks in health and disease.

CONTACT FAREWELL SYMPOSIUM

2016 also saw the conclusion of the Control of Action (ContAct) research program led by Hartwig R. Siebner and funded through a large Grant of Excellence from the Lundbeck Foundation (25 mill. DKK). Starting in 2011, the research program was designed to gain a better understanding of the neural mechanisms mediating the flexible control of actions. A core hypothesis of ContAct research was that the brain achieves the flexible control of voluntary actions by dynamically adjusting the functional interactions within and across specialized motor brain

networks. To identify and understand these temporo-spatial brain dynamics of motor control, the Contact group integrated multimodal brain mapping, non-invasive brain stimulation, and computational modelling. The research program was concluded with a 2-day international farewell symposium held in November 2016 at the Elsass Institute in Ordrup, where ContAct researchers and collaborators shared and discussed the main outcomes of the program.

ASSOCIATE PROFESSORSHIPS

DRCMR has for many years had an intensive collaboration with the Technical University of Denmark, including numerous shared PhD-students. The Capital Region of Denmark initiated a strategic collaboration with DTU at the end of 2014 that has enabled us to set up several new shared associate professorships with DTU in 2015 and 2016. Within this framework, three senior researchers at DRCMR have received 5-year part-time positions (20 %) at DTU as associate professors while

maintaining the majority of their work-time at DRCMR. These collaborations have been setup with the Department of Applied Mathematics and Computer Science (DTU-Compute) and the Department of Electrical Engineering (DTU-Electro) at DTU. Apart from enabling the senior researchers to be main supervisors for DTU PhD-students, the appointment as associate professor is a significant step forward in their careers and will greatly facilitate the already existing collaborative ties with DTU.

METROPOLITAN UNIVERSITY COLLEGE

2015 and 2016 have also seen an increasing collaboration with the Metropolitan University College (Metropol) in Copenhagen. Metropol and DRCMR joined forces and co-founded a

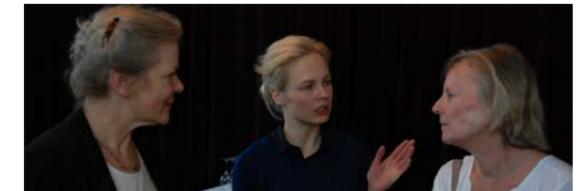
PhD project. Radiographer and PhD student Christian Bauer embarked on an ambitious MRI project to identify structural correlates of fatigue in patients with multiple sclerosis. In 2016,

senior researcher Kathrine Skak Madsen was appointed associate professor at the Metropolitan University College and continues a strategic research and education collaboration with DRCMR. The two institutions have also jointly invested in an MR-Simulator ("Mock-scanner") that is placed at DRCMR

and can be used to train subjects, especially children, in going through an MRI scan. The objective of this approach is to reduce the need for anaesthetizing children that need to have an MRI scan without compromising image quality due to subject motion during the scan.

PRIZE FOR MULTIPLE SCLEROSIS RESEARCH

PhD. Student and Medical doctor Olivia Svolgaard received the "Torben Fogs and Erik Tries Fond" prize in 2016 for her research within Multiple Sclerosis. Olivia's research was done within the frame of a comprehensive multi-modal brain mapping study, where the aim was to delineate abnormalities in brain function and structure that lead to fatigue in patients with Multiple Sclerosis.



Olivia Svolgaard receiving the prize.

A CLEARER STRATEGY

During 2015 and 2016, researchers at DRCMR have been working on defining a clearer research strategy and improving outward communication and branding of DRCMR. This strategic process was greatly facilitated by Chief Research Consultant Lene Cividanes who joined the DRCMR in 2015. DRCMR got a new logo which conveys our overarching research theme. We have identified five research areas that cover the bulk of our research: Precision Neuroimaging of Brain Disorders, Cognitive and Computational Neuroscience, Life Span Imaging, MR Physics and Analyses, and Transcranial Brain Stimulation. A coordinator has been assigned to each research area to coordinate the activities carried out by the research groups within each area. A new website was launched in 2016 which reflects our new research strategy and describes the five main areas of research.

Imaging brain dynamics across the human life span is a keystone of research at DRCMR and has received special attention in 2016. We have been particularly active in the European population neuroscience arena. Due to our active participation, the Capital Region of Denmark has now joined the Big Data Value Association, and we have had increasing interaction with the European Brain Council. Our efforts culminated in an international population neuroscience symposium that was held as a satellite to the European FENS Forum 2016 in Copenhagen. Furthermore, our strategic work in the area resulted in us being part of a European consortium, Lifebrain, whose main objective is to identify determinants of brain, cognitive and mental health at different stages of life by integration, harmonisation and enrichment of major European neuroimaging studies of age differences and changes. The project was funded through the EU Horizon 2020 framework program with 10 million Euros.



New Bruker 7T preclinical MR Scanner, 7T Scanner, public outreach and summer party at the DRCMR.

CELEBRATING 30 YEARS

On May 8th, 2015, the DRCMR celebrated its 30th birthday with a scientific symposium at Hvidovre Hospital. The 30-year anniversary symposium featured both historic and scientific talks by current and former staff at DRCMR as well as prominent international scientists. A 30-year commemorative report was published as part of the celebration, marking the highlights and milestones of the first three decades of DRCMR's history. The report can be found on the DRCMR website.

Ulf Joel Jensen reports from the celebration.

The first head of DRCMR, Ole Henriksen, and Janni Spies at the inauguration of the "Spies scanner" on May 10th 1985. Source: Polfoto.

DRMCR — 30 YEARS OF MRI

DRCMR celebrated its 30th anniversary in 2015. It has been 30 years of continued development — 30 years of research with studies that have changed diagnostics and treatment of several severe diseases. But it all started with a terminally ill — and yet very grateful — Danish benefactor ...

By Ulf Joel Jensen



Participants at the DRCMR 30-year anniversary symposium held on May 8th, 2015. Photo: Franck Thibault.

30 years ago only a few people had heard about the newest imaging technology, MRI — even fewer had worked with the actual machinery. Nonetheless, when the Danish patron, Simon Spies, who had earned a significant fortune in the travel industry, in the mid 1980'ies wanted to donate a large sum of money to Hvidovre Hospital, the management and the leading physicians of the hospital designated the MR scanner as a possible technology of tomorrow.

Simon Spies was terminally ill with cirrhosis and had experienced several painful liver biopsies during his months in Hvidovre Hospital in 1983–84. Thus he was concerned about investing some of his means in a technology that could prevent the same painful experience for future patients. And even though MRI can't replace liver biopsies, it certainly is a non-invasive and completely painless examination.

In May 1985, one year after Simon Spies passed away, the first 1.5 Tesla MR scanner in Scandinavia was inaugurated at Hvidovre Hospital. Being such a new technology research was needed and the MR scanner came with a contract stating that the machine had to be used 25% in the clinic, scanning patients from the entire country, and 75% of the time for research purposes. And that was the early beginning of the Danish Research Centre for Magnetic Resonance — DRCMR.

HIGHLY QUALIFIED INTERNATIONAL RESEARCH TEAM

Fast forward to May 2015: Professor, MD, DMSc Hartwig R. Siebner is the third head of DRCMR — and the proud host of a scientific symposium celebrating the 30th anniversary of DRCMR. In his speech, Professor Siebner expressed gratitude to Simon Spies and his ability to think big and embrace the future. But he also thanked the people who are DRCMR — the researchers from the early days in the 1980'ies and their successors of today:

"DRCMR is turning 30. We have grown up as an organization and have matured — but we are not old or over the hill. We are just at the top. Earlier this year we inaugurated the new 7 Tesla scanner for research purposes only. We are very excited about this new large scanner — but as important as all our machines might be, they are nothing without the people running them. And the DRCMR has over the years always been very fortunate to have some dedicated and highly qualified researchers. As the head of DRCMR, I am confident about our highly international team of researchers. DRCMR is indeed a Danish research environment. Nevertheless half of our staff are foreigners — which I consider a big strength."

LEARNING BY DOING

When you look at the research infrastructure of DRCMR today, the numerous research groups, the staggering number of scientific articles published by researchers from DRCMR — not to mention the literally countless patients going through MRI at Hvidovre Hospital, it is hard to imagine the situation in 1985.

"It was very much a case of learning by doing: The so-called 'Spies-Scanner' was one of only three 1.5 Tesla scanners in Europe at that time and there was only little experience — or none at all — of the clinical use of these new machines," remembers Margrethe Herning, MD at DRCMR from 1985 to 2006.

The experience was made and founded as the patients were scanned and — maybe even more so — as research projects were completed and published. In these early years of DRCMR,

Professor Freddy Ståhlberg, Director of the Lund University Bioimaging Center, talks at the DRCMR 30-year anniversary symposium about how his research career started as a PhD-student at DRCMR in the 80's. Photo: Franck Thibault.



headed by late Ole Henriksen, this relatively small research environment actually was among the most active worldwide. As a result of this, international researchers and hospital directors took a natural interest in the Danish research group at Hvidovre Hospital. Colleagues from all over the world came to visit DRCMR, thereby creating a kind of foundation for the later highly international profile of DRCMR. But in the early years, almost the entire staff was still Danish.

AN EVER-GROWING SUM OF TESLA

During the 1990'ies the DRCMR management initiated several new funding projects to supply the centre with new and more powerful scanners. In 1995 the original 1.5 Tesla scanner, donated by Simon Spies, was replaced by two new and modern scanners – respectively 1 and 1.5 Tesla. And a few years later the very first 3 Tesla scanner in Denmark was taken in use at DRCMR. *“As early as 2003 I started the process of financing a 7 Tesla human scanner. But it took a lot of work to secure the funding for such a large investment. I have personally used more than a total of 1.5 FTE's on this process alone,”* explains Professor Olaf Paulson, head of DRCMR 1995–2010.

But the mission was finally completed, the means were found and in 2015 the first 7 Tesla human scanner in Scandinavia was inaugurated at DRCMR. By then Olaf Paulson had retired from DRCMR – but is still an active neurology researcher at Rigshospitalet today.

A STRONG INTERNATIONAL PROFILE

As he mentioned in his speech at the anniversary symposium Professor Hartwig R. Siebner is highly concerned about DRCMR's international network. Today 19 different nationalities are working at DRCMR and the many highly active research

groups at DRCMR are collaborating with colleagues from all over the world.

“There is a very close connection between the research in Cambridge and the neurological research environments in the Copenhagen Area. Our collaboration has already resulted in numerous spectacular and internationally recognized scientific articles. In one of our remarkable collaborations, researchers at DRCMR established a novel MRI paradigm, that makes us capable of understanding and predicting some of the complications when treating Parkinson's disease. Thus the connection and friendship between Cambridge University and DRCMR grow day by day,” states Dr. James Rowe, reader at Cambridge University and Senior Research Fellow at the Wellcome Trust. Looking to the future the plan for DRCMR is already made to a certain point: It's about strengthening the research profile of the centre and keeping up-to-date with the new technical equipment. Karam Sidaros, PhD and research coordinator at DRCMR, explains:

“At DRCMR we already have several experienced and highly qualified senior researchers. But we need more than one professor affiliated to DRCMR. We need a stronger affiliation to the universities in order to attract larger appropriations to the centre and in order to supervise the many PhD-students we have at DRCMR.”

With the new 7 Tesla scanner, DRCMR is the host of a national Danish collaboration: The National Danish 7 Tesla Project. In a way, this closes a circuit – in 1985 DRCMR was the MRI centre for the entire country receiving patients from all over Denmark. Today the center is to embrace and host R&D projects from all of the 5 Danish regions.

Professor Hartwig R. Siebner looks forward to this next challenge – along with other scientific frontiers to be explored

– in collaboration with both Danish colleagues and colleagues from abroad.

“We wish to break the barrier between our research environment and the rest of the world. We want to connect our research with the immense amount of data about human behaviour modern technology can provide us. With the smartphone you

are able to map your sleeping habits, your exercise – but also your ways of communication. How is your social life? What kind of music do you listen to – and how often? If we can combine this information with our neurological knowledge and science we will be able to open entirely new areas of investigation. And that is where we are headed!”

DRCMR KEY FIGURES

27 nationalities

DRCMR is a part of the Capital Region of Denmark and host of the National Danish 7 Tesla Project. But indeed it also has an international profile: In 2015 researchers from 19 different nationalities worked at DRCMR – making it one of the most international research centres in the Capital Region of Denmark.

887 peer-reviewed articles

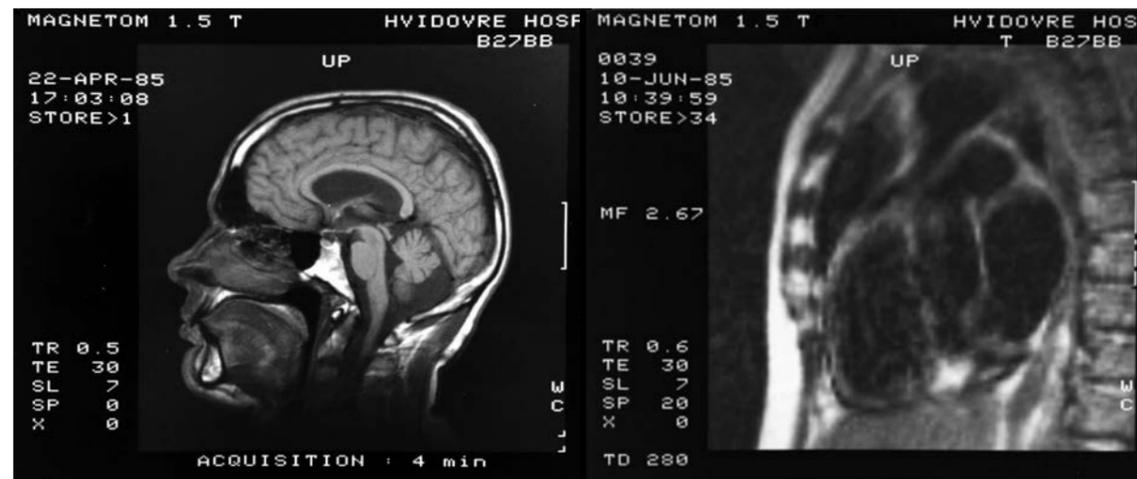
From the beginning in 1985 until 2014 the researchers at DRCMR authored or co-authored no less than 887 peer-reviewed articles. For several years the centre was among the most active MRI-research centres worldwide.

75 theses

From 1985 to 2014 a total of 66 PhD theses and 9 DMSc theses have been made by researchers based at DRCMR.

27 tesla

With the inauguration of the new 7 Tesla scanner from Philips, the total sum of magnetic force in DRCMR grew from 1.5 tesla in 1985 to 27 tesla in 2015.



Examples of the first MR images acquired with the “Spies scanner” in 1985. Top: brain. Bottom: heart.

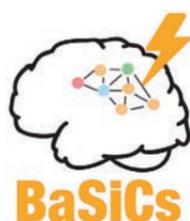


KEY PROJECTS

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 2015–2016.

BASICS

BIOPHYSICALLY ADJUSTED STATE-INFORMED CORTEX STIMULATION



BASICS is an interdisciplinary collaboration between DRCMR, DTU Compute and DTU-Electro with the goal to synergistically combine non-invasive brain stimulation, brain mapping, electric field modelling and machine learning. By combining computational and neurobiological expertise our vision is to design efficient and novel brain stimulation applications, tailored to individual brain anatomy and activity and to establish a scientific framework for biophysically adjusted and state-informed stimulation.

The BASICS research group is supported by a Novo Nordisk Foundation Synergy Grant awarded to Hartwig Roman Siebner (Main Applicant), Axel Thielscher and Lars-Kai Hansen (Co-applicants).

The BASICS team pursues two main lines of research:

- I **Biophysically adjusted NTBS:** We perform advanced modelling of the electrical fields that are induced by non-invasive stimulation in individual brains. We use this information to adjust intensity and spatial arrangement of brain stimulation to optimally target the cortical network of interest.
- II **State-informed NTBS:** We use electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) to identify the spatiotemporal signatures of functional and dysfunctional brain states at an individual level. EEG and fMRI also enable us to trace the dynamic expression of these “state signatures” during non-invasive brain stimulation. We use this information to adapt stimulation to these signatures in the healthy and diseased human brain.

NOVO NORDISK SYNERGY GRANT

Grant Recipients	Hartwig R. Siebner Lars-Kai Hansen Axel Thielscher
Grant Size	15 mill. DKK
Funding Period	June 2015 – June 2018
Funding Agency	Novo Nordisk Foundation Inter-disciplinary Synergy Program
Grant Number	NNF14OC0011413

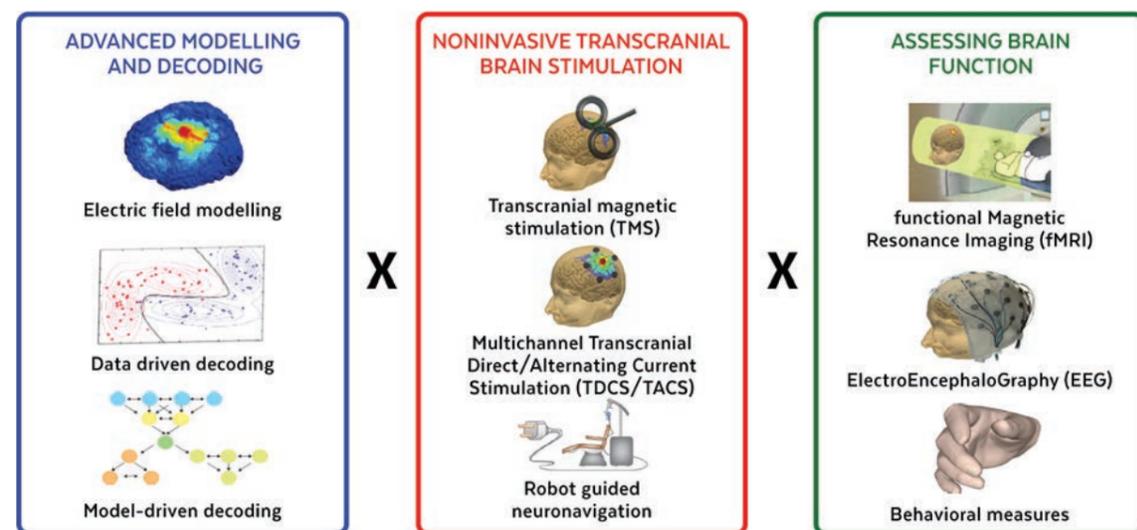
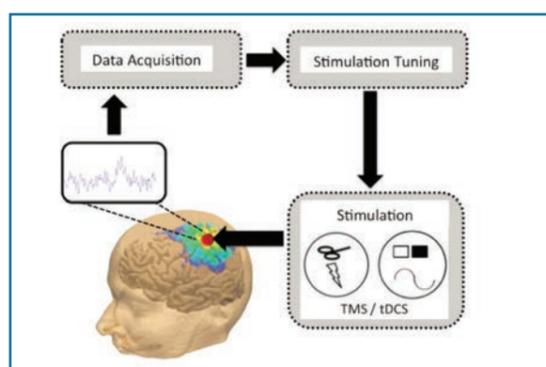


Illustration of the synergistic integration of the complementary methods used in BaSiCs.

WORK PACKAGES

WP1 – BIOPHYSICAL MODELLING, DTU-Electro

WP-leader: Axel Thielscher

WP1 pushes the methods for realistic field estimates to the level that they can reliably inform non-invasive brain stimulation. This is achieved by: (1) Modelling stimulation hardware and bi-directional information exchange between the field calculation software and the experimental setups. (2) Building advanced solutions for individual head models that can deal with structural changes in disease populations (e.g. patients with chronic stroke). (3) Developing novel targeting approaches both for TMS and TDCS/TACS fully based on individual head models, enabling optimal stimulation and “dose estimation”.

WP2 – MACHINE LEARNING, DTU Compute

WP-leader: Lars Kai Hansen

WP2 works on optimizing non-invasive brain stimulation by detecting individual brain states with the help of advanced machine learning methods. This approach generates models that can predict the brain reaction to stimulation protocols and allow for optimized stimulation planning. WP2 uses a Bayesian framework to systematically improve robustness of spatial targeting in non-invasive brain stimulation. We expect that this approach will allow linking the effects of stimulation to specific brain motifs in the future.

WP3 – Modulation of the healthy brain, DRCMR

WP-leader: Hartwig R. Siebner

WP3 harvests the methodological developments made by WP 1 and 2 to establish biophysically precise, state-informed brain stimulation in healthy individuals. WP3 uses a variety of stimulation methods to selectively influence cortical brain activity by using stimulation patterns that resemble natural task-related activity and connectivity patterns. State-dependent stimulation is used to reinforce patterns that boost motor brain function and to construct individually adjusted protocols that are optimally tuned to intrinsically expressed network motifs.

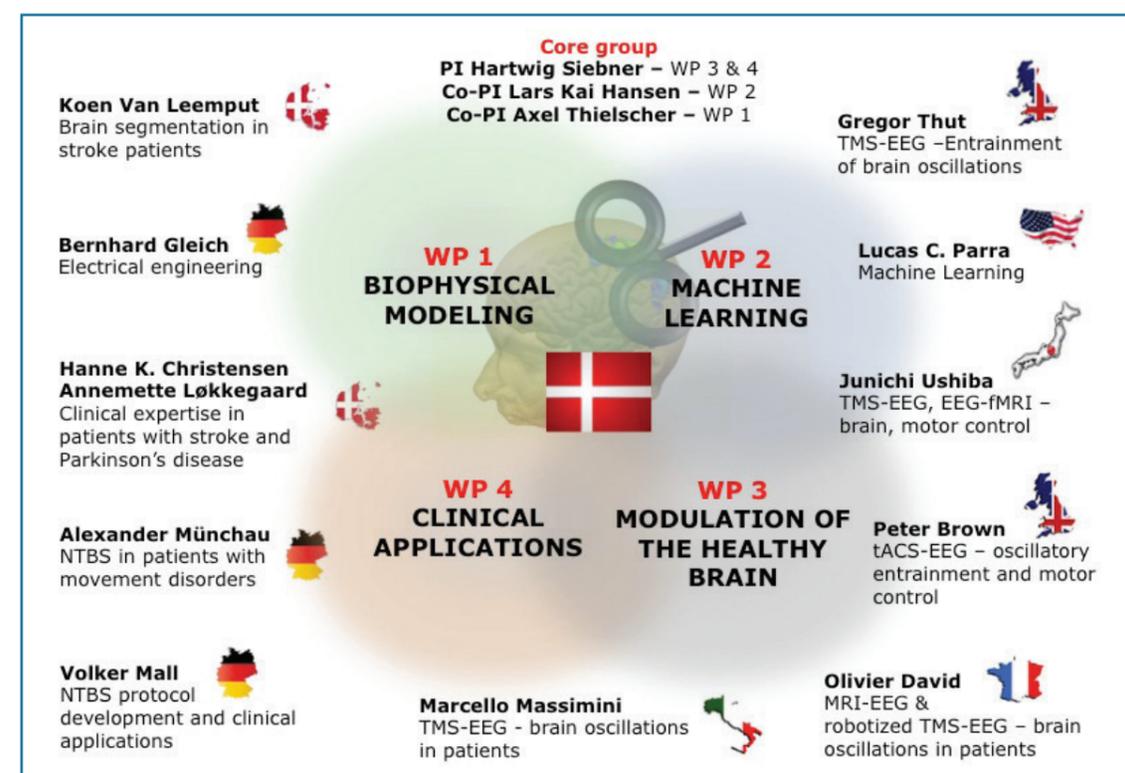
WP4 – Clinical applications, DRCMR

WP-leader: Hartwig R. Siebner in collab. with clinical partners

In WP4 the knowledge gathered in proof-of-principle studies in healthy individuals will be extended to proof-of-efficacy studies in patients with Parkinson’s disease or motor stroke. Building on the other work packages we want to boost the efficacy and reliability of therapeutic non-invasive brain stimulation and pave the way for individualized brain-stimulation treatment.

International Network

The research project is imbedded in a strong international network of medical doctors, engineers and neuroscientists who closely contribute to and interact with our group.



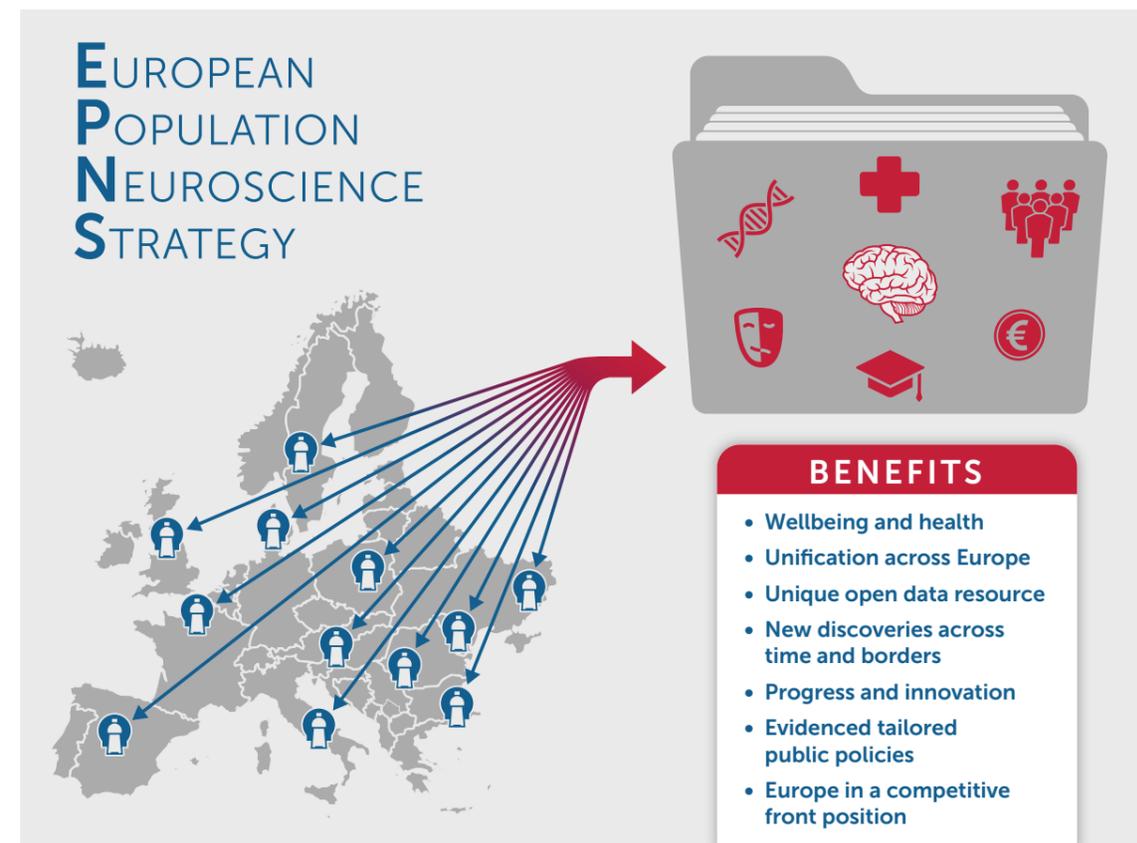
POPULATION NEUROSCIENCE STRATEGY

The DRCMR is advocating a long term European Population Neuroscience Strategy (EPNS), in close collaboration with CreoDK (Copenhagen EU office in Brussels) and the European Brain Council (EBC). The core objective of this strategy is to model the complex interplay of multidimensional factors (e.g. cultural, social, environmental, biological, physical and mental health, brain and body) across the life span in cohorts across Europe. These cohorts have to be representative of the general populations in terms of their genetic makeup, age and sex distributions, social-economic and health status, and culture. The EPNS builds on neuroimaging- based “read-outs” of individual brain function, metabolism, and structure. These neuroimaging measures derived from structural, functional and neurochemical imaging of the brain and body along with biological, behavioral and cognitive measures will provide insights into brain-related mechanisms through which environmental exposures cause behavioral and health outcomes. The strategy is detailed in the figure.

The EPNS was launched at a successful event in November 2015 in Brussels that included high level EU policy and research representatives, international scientists as well as public and private stakeholders, to highlight the importance of prioritizing European Population Neuroscience. In July 2016, we held an inspiring cross-disciplinary, scientific symposium in Copenhagen. The symposium was held as a satellite event of the FENS FORUM 2016 and addressed the scientific potential and key challenges of an EPNS (see figure). The talks triggered a lively discussion. As it is currently not feasible to assess and follow individuals from the cradle to the grave, prospective population based studies need to account for historical cohort effects e.g. older people might have experienced different physical environments and educational factors than younger individuals. Newly discovered relationships and patterns of age-related changes in brain and body should prompt in-depth studies in selected sub-populations that address and test specific

research questions together with experimental in vivo and in vitro studies designed to elucidate possible mechanisms underlying observed relationships and patterns. A successful European Population Neuroscience strategy requires a joint effort that bridges different scientific disciplines as well as inspiring and transparent interactions between scientific, public, legal, and private stakeholders across Europe and most importantly with the general population. In the autumn of 2016, we had constructive discussions, in Brussels, with respectively the board of the EBC and representatives of the European Commission – Directorate-General for Research, Health. We are committed to drive the EPNS agenda and organize new events in the years ahead.

WHAT?	EUROPEAN POPULATION NEUROSCIENCE RESEARCH <i>Understand how brain and behavior in health and disease are shaped throughout life</i>
WHY?	<i>Promoting health and wellbeing Avoid and minimize disease Prediction and prevention, Diminish risk, Precision medicine Stimulate growth, innovation, and productivity</i>
OBSTACLES	<i>Low reliability, generalizability, limited reproducibility and applicability of current research findings Fragmented knowledge base Lack of uniform infrastructural, legal, and financial frameworks</i>
HOW?	<i>Prospective study of large groups of people, across national borders, representative of general populations Accumulating unbiased evidence based on reliable and reproducible multi-dimensional markers that are predictive of physical and mental health, potential, resilience, risk, and treatment outcome across the life span e.g. healthy ageing starts in the womb</i>
WHO?	<i>Unified focused effort of Citizens and patients, Scientific disciplines, and Political, Legal, Public & Private Stakeholders across national borders</i>
WHY EUROPE?	<i>Strong focus on citizens and patients rights and involvement Unifying privacy, and data security policies. Capitalizing on European initiatives e.g. Horizon 2020, Joint Programming Initiatives, Innovative Medicines Initiative, and Research Networks e.g. Human brain project. Maturity of the BIG data community, initiatives and capabilities Health records and registries e.g. Nordic countries Global collaborations</i>



The first EPNS meeting was organised in Brussels in November 2015.



Organizers (**bold**), and speakers (*italics*) at the EPNS symposium held in Copenhagen in July 2016. From left to right: **Hartwig R. Siebner**, *Tomáš Paus*, **William Baaré** (back), *Marcus Munafò* (front), **Lene Cividanes** (back), *Kristine Walhovd* (front), **Keith W. Kelley** (front), *Erich Schweighofer* (back), **Mark Tittgemeyer** (front), *Thomas Werge* (back), *Lars Kai Hansen*. Missing on photo: *Erik Lykke Mortensen*, *David Nutt* and *Andreas Brandmaier*.

CONTACT

THE CONTROL OF ACTIONS



In our everyday life, we need to flexibly adjust our actions to the challenges imposed by our environment, our internal state and last but not least the social context a situation is embedded in. Here motor control and decision making play a key role to guide and shape our behavior. Using multimodal brain mapping, non-invasive brain stimulation and computational modelling, the ContAct Group and its international collaborators aimed to reveal the underlying neural mechanisms and motor-networks mediating these flexible actions. While the funding period has ended, the ContAct Group is still an active research group with regular weekly meetings to discuss project ideas and data.

MAJOR RESULTS

During the 6 years of funding, the ContAct group has produced more than 60 publications in high-ranking journals – and counting. The research program was divided into three methodologically and three neurobiologically oriented work packages. The methodological line of research was centred around diffusion MRI (measuring the diffusion of water-molecules in order to map white matter tracts), transcranial magnetic stimulation (TMS) and advanced connectivity methods. Our work has led to the development of several new techniques, such as new diffusion MRI methods that increase the resolution and are more sensitive to changes in white matter pathways in multiple sclerosis. We were the first to show the advantages of TMS stimulation optimized to individual brain physiology and tested advanced measures of brain connectivity.



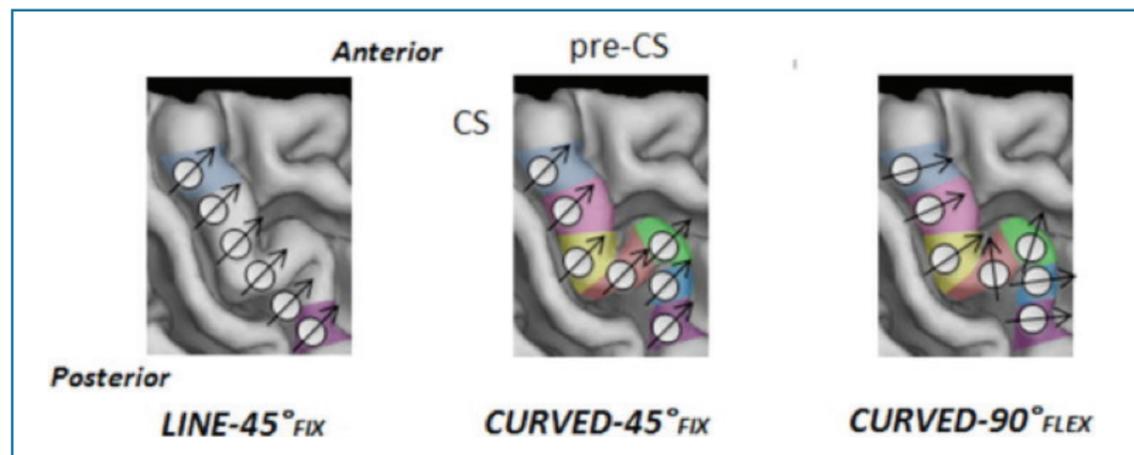
ContAct was funded by a large “Grant of Excellence” awarded by the Lundbeck Foundation to Hartwig R. Siebner (25 Mill DKK 2010–2016) for salary, experimental equipment and the construction of laboratory facilities.

The neurobiologically oriented packages have provided insight into fundamental neuroscientific and clinical questions pertaining to action control, such as the neural encoding of surprise (prediction errors) in healthy subjects and Parkinson’s disease patients or the neural dynamics involved in action inhibition and in voluntary action control in Parkinson’s disease.

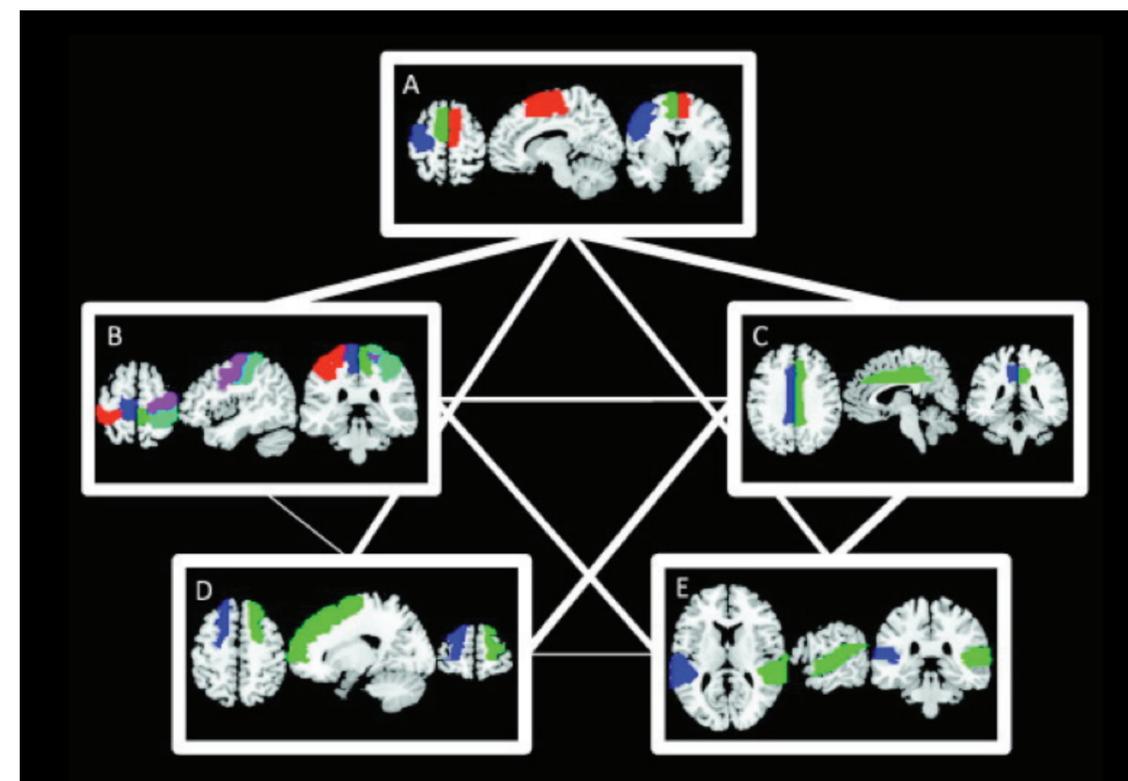
Besides tangible research results, the funding has provided indispensable support to a number of research careers, leading to the establishment of research groups and permanent positions, such as the Associate professorships at DTU awarded to Tim Dyrby and Kristoffer Madsen. It also made it possible to recruit highly profiled international researchers like Associate professor Axel Thielscher and Senior researcher Oliver Hulme.

CONTACT LABORATORIES

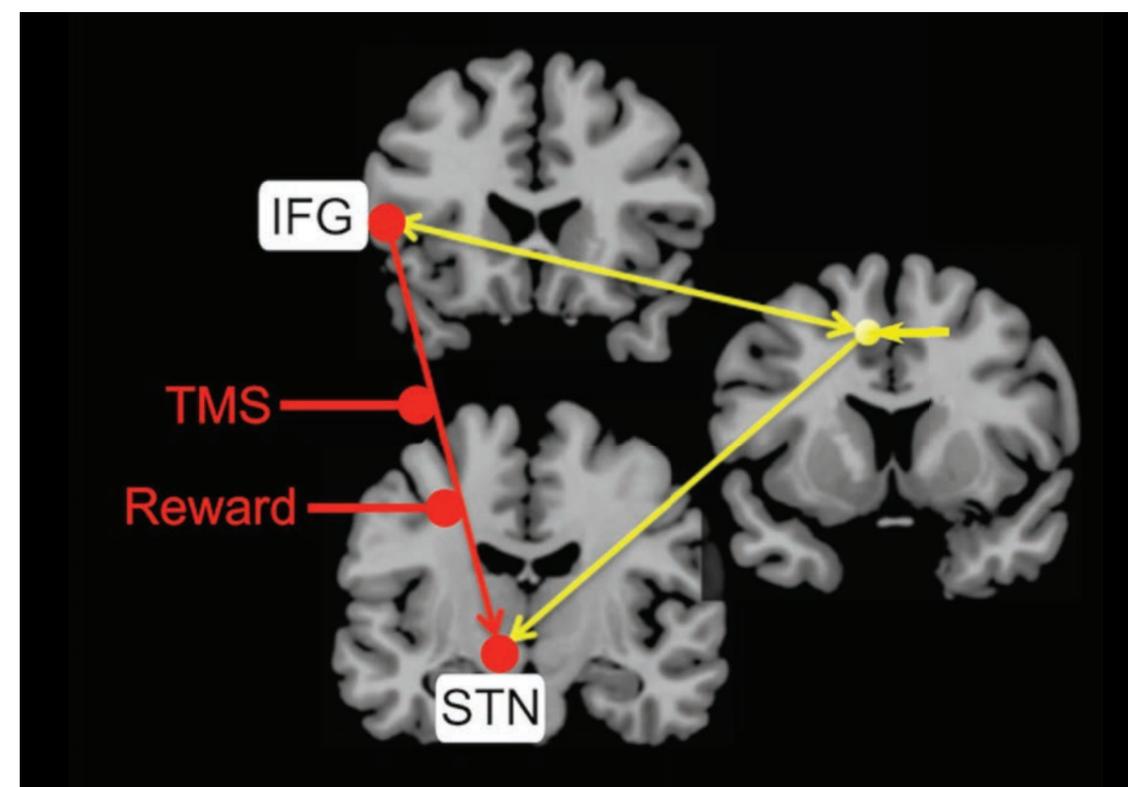
Our state-of-the-art ContAct laboratories provide a cutting-edge infrastructure to perform TMS experiments (guided by neuronavigation) and EEG studies. A key-hole surgery simulator allows the detailed investigation of complex motor skill acquisition.



Only the precise orientation of the TMS coil along the individual shape of each subject’s central sulcus (right) allows the mapping of separate finger representations.



Non-parametric Bayesian graph models can reveal the connectivity between different brain regions’ activity while subjects lie relaxed in the scanner without any explicit task instruction.



Only the combination of MR-imaging of brain activity, advanced connectivity analysis and TMS can reveal that stimulation can have wide-spread effects. Here, TMS stimulation over the pre-SMA (yellow circle on the right) led to an increase in connectivity between two other regions (IFG and STN, red line).

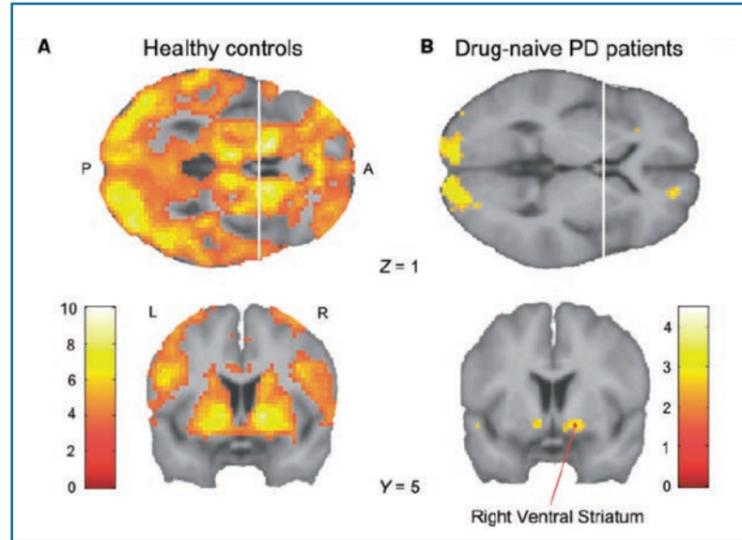
HIGHLIGHTS

Providing a science platform such as ContAct also requires exchange of knowledge and collaboration with national and international partners. These efforts successfully led to 3 international workshops on TMS organized by ContAct in order to introduce neuroscientists to non-invasive brain stimulation techniques. Furthermore, world-leading neuroscientists presented their research at our regular ContAct presentation series.

FAREWELL SYMPOSIUM

On November 24th and 25th, 2016, the ContAct group held a “Farewell Symposium” at the Elsass Institute in Ordrup, marking the end of the funding period. The productive years of research made possible due to the ContAct research group found a fitting closure in a two-day scientific symposium with presentations of excellent scientific findings and inspiring debate. For the members of the ContAct group, it was a satisfying and motivating experience to see a two-day summary of the impressive array of research they had generated over the course of six years. In the course of six sessions, the symposium gave the possibility to hear about the results from the projects performed in the context of the different work packages, spanning from structural

brain connectivity to computational modelling, non-invasive brain stimulation, learning, inhibitory control and motivation. Each session started out with keynote lectures by high-profile international and local researchers that put the presented research into context and revealed how the research performed in ContAct had made valuable contributions to the questions asked in the scientific community. The beautiful Elsass Centre provided an inspiring setting where scientific ideas were debated and the potential for future collaboration was probed in the course of several coffee and lunch breaks.



The neural response to rewarding outcomes (winning money) is greatly reduced already in newly diagnosed Parkinson's patients (figure above).

Group photo from the farewell symposium.



WOMAN STUDY WOMEN WITH MIGRAINE AND AURA NEUROIMAGING

The WOMAN study used the national Danish twin registry and advanced brain scanning to clarify the question whether migraine with aura is associated with structural lesions and morphology changes of the brain. An association between migraine with aura and risk of silent brain infarcts and white matter hyperintensities (WMH) has previously been reported in females. Prompted by these findings, the group decided to investigate these relations in a population-based sample of female twins. More than 380 twins were invited for a state of the art MRI-scan of the brain, including structural, functional and quantitative MRI, blood samples, physical assessment, and various questionnaires. Based on our extensive experience with lesion assessment, a detailed analysis of vascular changes – including WMH rating and quantification – was performed on 172 cases, 34 co-twins, and 139 control subjects. Although cases had slightly larger WMH volume compared to controls this did not reach sta-

Migraine with aura and risk of silent brain infarcts and white matter hyperintensities: an MRI study, David Gaist*, Ellen Garde*, Morten Blaabjerg, Helle H. Nielsen, Thomas Krøigård, Kamilla Østergaard, Harald S. Møller, Jacob Hjelmborg, Camilla G. Madsen, Pernille Iversen, Kirsten O. Kyvik, Hartwig R. Siebner, Messoud Ashina. *BRAIN* 2016 Jul; 139(7): 2015–2023

*These authors contributed equally to this work.

tistical significance. In July 2016, the main outcome of the study was published in the journal *BRAIN*. Our large population-based study of female twins did not confirm the notion that female patients suffering from migraine have more silent infarcts and WMHs than females without this headache disorder. This is good news for affected patients, but also shows the importance of large population-based neuroimaging studies to establish or dismiss relationships between brain disorders and alterations in brain structure.

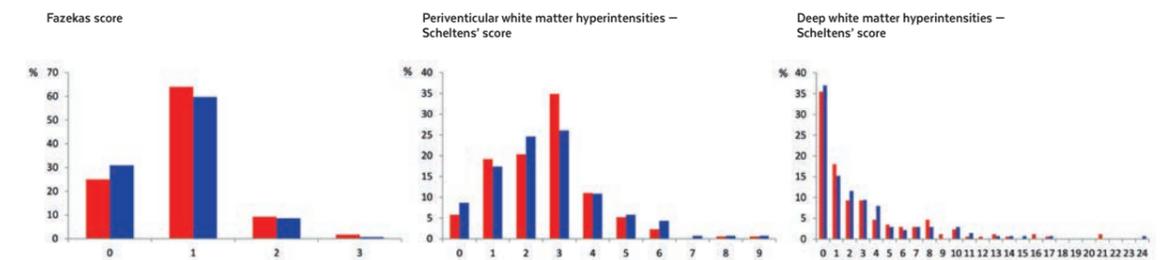
THE WOMAN STUDY IS A COLLABORATE EFFORT

PARTNER INSTITUTIONS

- Department of Neurology, Odense University Hospital & Institute of Clinical Medicine, Faculty of Health Sciences, University of Southern Denmark
- Danish Headache Center, Department of Neurology, Glostrup Hospital, University of Copenhagen
- Danish Research Centre for Magnetic Resonance, Copenhagen University Hospital, Hvidovre
- Danish Twin Registry, University of Southern Denmark

GROUP MEMBERS

- Professor David Gaist
- Professor Hartwig R. Siebner
- Professor Kirsten Kyvik
- Professor Messoud Ashina
- Consultant Camilla Gøbel Madsen
- Associate professor Ellen Garde
- Associate professor Kristoffer Madsen
- Associate professor Tim Dyrby
- Associate professor Lars Hansson
- Research Medical Laboratory Technologist Sussi Larsen



White matter hyperintensity scores assessed by visual rating scales in 172 females with migraine with aura (cases) and 139 migraine-free female control subjects. None of the scores revealed a difference in white matter hyperintensities between twins who have migraine with aura (red columns) and control subjects without migraine (blue columns) as published in *Brain* (*BRAIN* 2016 Jul; 139(7): 2015–2023).

THE NATIONAL 7T FACILITY IS UP AND RUNNING



Efforts to establish a **National 7 Tesla MR Facility** for whole-body scanning of human volunteers reached two significant milestones when the first Danish 7T scanner was inaugurated in 2015 and the first subject was scanned in 2016. This ambitious project secures Denmark's lead position in biomedical MR research. It is an important strategic achievement, which will gather researchers from both eastern and western Denmark. There is already a lot of research carried out on the scanner with projects from several Danish institutions. In addition, several international collaborations have already been established with other 7T MR research sites in and outside of Europe. The executive committee of the Danish National 7 Tesla MR Project has processed and accepted close to 20 projects from across the country, pinpointing the instant success and the urgent need for an ultra-high field imaging facility in Denmark.

To make the best use of this advanced equipment, a **dedicated 7 Tesla MR research group** has been established at the DRCMR. The group develops and advances MR methodology to maximally exploit the benefits offered by the ultra-high field MR system. The group actively participates in local and national 7T MR projects to ease project planning and execution.

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 MR scanner is a "whole-body" scanner that allows cutting-edge imaging of the human brain but also other organs.

Equipped with the latest hardware, the 7T MR system will keep Denmark in a leading position within *in vivo* MR imaging and spectroscopy. The setup fosters close collaborations across centers, both nationally and internationally, and the good synergy will therefore ensure a fast progress, not only within the imaging field but also in basic science and clinical research. To ensure equal access and a high scientific standard, a **steering committee**, chaired by Professor Jørgen Frøkiær from Aarhus University, oversees the scientific content and progress of the facility. An **executive committee** coordinates and ensures the scientific quality of the proposed 7T projects according to the guidelines set by the steering committee.

The scanner is a state-of-the-art Philips Achieva 7.0 T actively shielded magnet. It is ideal for ultra-high resolution functional and structural imaging at submillimeter isotropic resolutions not possible on common clinical scanners. The ultra-high field also results in a significant improvement of MR-based spectroscopy, which is used to assess the metabolic profile of tissues. Also, a new hardware lab has been established in connection with the 7 Tesla project, making it possible to develop, test and repair coils and other equipment, which is often needed in ultra-high field systems. Particularly for imaging outside the brain, it is often required to design dedicated coils for the organ of interest. In addition, the system is fit for multi-nuclear imaging and spectroscopy (other nuclei than protons, e.g. phosphorus, carbon or sodium), which benefit much from the higher field strength.

The magnet was lifted and rolled to its current location in March 2014. After a series of unfortunate quenches during the process of ramping up the magnetic field to 7T, the magnet was finally on field in January 2015. A quench happens when the superconducting magnet becomes resistant and thereby boils off the liquid helium within a very short time period. The remaining part of 2015 was used for adjustment and calibration of the system.



In summary, an important strategic research infrastructure is now fully functional at DRCMR. The first clinical research study, led by Dr. Henrik Lundell and supported by a prestigious SAPERE AUDE grant of the Danish council for Independent Research, has already started with very promising preliminary results. This is just the beginning. Many more exciting studies taking full advantage of the ultra-high field MRI system will start in the years to come. A new era has begun for Danish biomedical imaging with unprecedented possibility for scanning the human brain!

The National 7 Tesla MR Facility is financed by the The Danish Agency for Science, Technology and Innovation and The John and Birthe Meyer Foundation.



The national steering committee in August 2015.

ULTRA-HIGH FIELD MAGNETIC RESONANCE COLLABORATION WITH THE KOREA BASIC SCIENCE INSTITUTE

In 2015 we generously received a 200.000 DKK framework grant from The Danish Agency for Science, Technology and Innovation for an International Network Programme titled: "Ultra-High Field Magnetic Resonance Collaboration with the Korea Basic Science Institute".

The Korea Basic Science Institute (KBSI) has a 7T MR system that is identical to the one we have at DRCMR, and this framework grant facilitated a very fruitful collaboration between our two institutes. The focus of the collaboration particularly lies on advanced spectroscopic imaging and several exchange visits of both senior and junior researchers to and from South Korea have been made. Moreover, this collaboration and common academic interests have led to the signing of a Memorandum of Understanding (MoU) between Hvidovre Hospital/DRCMR and KBSI. The aims of this MoU include working together on basic scientific research and student exchange opportunities, and strengthening the academic ties between our two countries.

BRIEF HISTORY OF THE DANISH NATIONAL 7T MR PROJECT

2003

The first initiatives were taken by professor Olaf B. Paulson on behalf of a national consortium.

2009

The Ministry of Higher Education and Science donates 27.4 million DKK to the project.

2010

The John and Birthe Meyer foundation donates 38.6 million DKK to realise the project.

2014

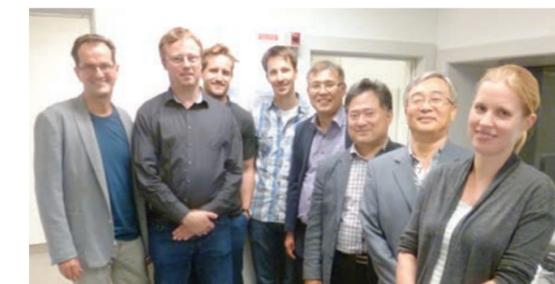
The 7 Tesla magnet arrives at Hvidovre Hospital and installation starts.

2015

The scanner reaches the 7 Tesla field strength and is inaugurated by the Chairman of the Regional Council Sofie Hæstorp Andersen.

2016

The system is handed over from Philips to Hvidovre Hospital and the first human study starts on the 7T scanner, led by Henrik Lundell.



Group photo during a visit of the senior researchers from the Korea Basic Science Institute in September 2016.

NEW RESEARCH POSSIBILITIES THANKS TO NEW PRECLINICAL FACILITIES

AN ERA COMES TO AN END

Preclinical facilities have existed at the DRCMR since 1989 when the preclinical 4.7T Agilent MR scanner was installed. The gradient set of the scanner as well as its supporting hardware were continually upgraded ensuring a powerful scanner setup. The last hardware upgrade was in 2008, including the installation of state-of-the-art 600mT/m gradients, which was kindly supported by the Lundbeck Foundation. The research focus then turned towards hyperpolarized Carbon-13 (C-13) metabolic and advanced microstructural imaging. In recent years, the need to replace the existing MR scanner became more and more pressing after the scanner vendor Agilent announced in 2013 a stop to all MRI-related activities.

Several ongoing projects needed to be concluded before removing the old 4.7T MRI scanner – the final scans were only a few minutes before the magnet was turned off by a controlled quench in August, 2016. The old 4.7T Oxford preclinical magnet had been on field for 27 years.

LOOKING FORWARD

Different options for replacing the Agilent scanner were considered. In the end, we decided to realize our vision of establishing a translational imaging facility at DRCMR that complements our preclinical research better to our clinical research. We therefore aimed for a state-of-the-art preclinical MR system that would be comparable to the newly installed whole-body ultra-high field 7T MRI system for biomedical imaging in humans. The decision landed on a Bruker 7T BioSpec MRI scanner.

At the same time, it was decided to expand and refurbish the preclinical laboratories to enable advanced stereotaxic microsurgery as well as optogenetic and pharmacogenetic brain stimulation. These techniques will be used as basic research approaches to complement our highly-profiled non-invasive brain stimulation research in humans.



The new lab facility consists of a large lab (picture) and a smaller lab especially designed and approved for stereotaxic operations and optogenetic work with rodents.



In the new scanner room the magnet is placed in a room together with the Hypersense and the new lab is placed next door.

PRECLINICAL RESEARCH – V. 2.0

The new Bruker scanner arrived mid-November, 2016. The pre-clinical 7T magnet, weighting “only” 3 tons, was transported and pushed in place by a regular pallet lifter. Already the following day the magnet was on field, and two weeks later the scanner installation and testing was completed.

In addition to housing the Bruker scanner, the new scanner room still houses the HyperSense, which allows for the investigation of e.g. tumors and cellular metabolism using hyperpolarized C13-imaging. The old scanner room has now been separated into two laboratories, a larger multi-purpose laboratory including an electrophysiology setup, and a smaller laboratory, classified as biosafety level II, intended for working with viruses and stereotaxical surgery.

The new preclinical facilities are run by a dedicated research group led by Associate professor Tim Dyrby, but are meant to allow basic preclinical research by all DRCMR research groups and key collaborators.



The new preclinical magnet is not as big as our 7T human magnet and it can easily fit inside a medium sized truck and only three strong men were needed to push the magnet into place. After a day the magnet was on field and ready.

MAJOR FUNDING RECEIVED

We are very grateful for the substantial economic support we receive every year from a great number of funding bodies – private, national and international funders. Without this funding we would not be able to conduct cutting-edge research. Our largest ongoing project is BASICS funded by an Inter-disciplinary grant of 15 million DKK from The Novo Nordisk Foundation (read more page 14). Here, we present two selected projects funded by prestigious grants.

SAPERE AUDE RESEARCH TALENT AWARD

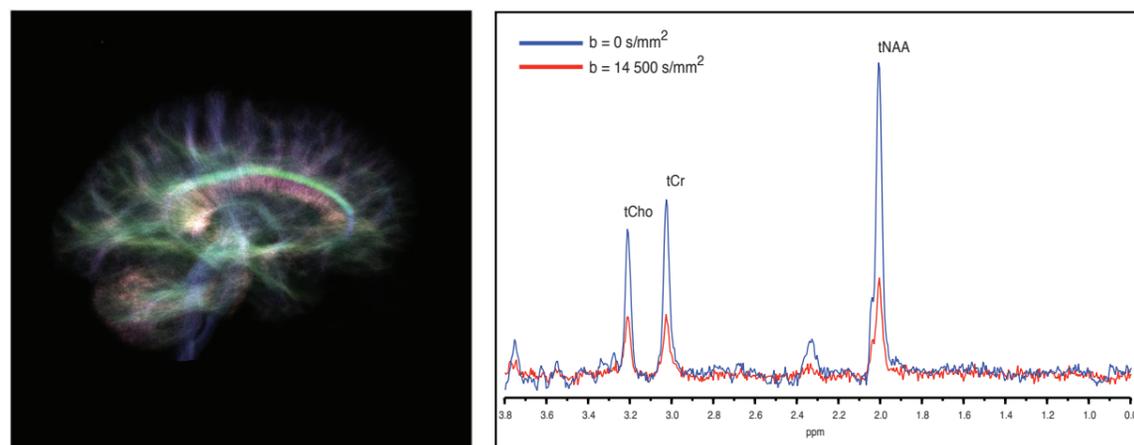
Postdoc Henrik Lundell was awarded a Sapere Aude research talent award from the Danish Council for Independent Research for his postdoc project on ultra-high-field imaging of multiple sclerosis (MS). The award is aimed at providing researchers in the beginning of their careers a platform for developing their research profile and international network.

In Denmark almost 15.000 people are affected by the neurodegenerative disease multiple sclerosis and MRI is an important tool for diagnosis. Conventional clinical MRI methods used today are sensitive in identifying pathologies but provide little insight into the underlying disease mechanisms and their functional implications for the individual.

Improving and simplifying cutting-edge MRI methods towards clinical routines is a major motivation for Henrik. His approach in this ongoing project is to develop a hybrid technique called diffusion weighted spectroscopy (DWS) to merge the benefits and resolve the individual shortcomings of already established methods. The recently installed national 7T scanner at DRCMR

has been a prerequisite for conducting this project. DWS has been pioneered by key collaborator, Professor Itamar Ronen at the Leiden University Medical Centre, The Netherlands. The project also extends on the long-term collaboration with the Danish Centre for Multiple Sclerosis at Rigshospitalet. Besides from this, Henrik is leveraging the expertise from the Neuroimaging in Multiple Sclerosis group, the 7 Tesla group and the Microstructure and Plasticity group at DRCMR.

The initial methodological optimization has spun off novel techniques integrated in the second and ongoing part of the project performed on individuals with multiple sclerosis. An important addition made possible by the award is the evaluation of DWS with 3T MRI available at most hospitals today. A grant from the Danish Multiple Sclerosis Foundation has made it possible to expand the protocol with an advanced brain stimulation protocol to map out relations between function and structure. Besides from the honor and acknowledgement, the Sapere Aude award has given the project a great momentum and helps to establish the 7 Tesla MRI and MS research fields at DRCMR in an international context.



CAPTION: Diffusion weighted MRI gives the possibility to infer microstructure from the mobility of water trapped in the hindering barriers of cells. From data, axonal white matter pathways can be estimated (left) and subtle changes can be detected. However, with water abundant in all tissue compartments the interpretation is unspecific to cell types. With the combination of diffusion weighting and MR spectroscopy the mobility of cell specific metabolites can be assessed.

THE WORLD'S BEST X-RAY IMAGES – SEEING INTO NANOSTRUCTURES

Tim Dyrby and collaborators have been awarded 4.5 million DKK from The Capital Region Research foundation for Healthcare as part of the strategic focus area on the potentials of synchrotron imaging.

Just outside the city of Lund in the southern part of Sweden an enormous building has been established consisting of two circular shaped buildings having diameters of 528 and 96 meters, respectively. These buildings contain today the world's most powerful x-ray source and equipment, the MAX IV synchrotron. Researchers from the Capital Region have been granted access to the best x-ray source ever seen in the world. The MAX IV synchrotron opens a new horizon in medical imaging because it is possible to obtain 3D CT-scanning images of anatomical structures in such a high image resolution not possible with any other existing imaging technology. Hence it will open new insights for research, and can change the way we today think of diagnosis and treatment of patients. However, the unique anatomical rich data sets call for new advanced algorithms that can handle the enormous amounts of data (terabytes) that each synchrotron image consists off.

INTERNATIONAL LEADING

The project is led by Associate Professor Tim Dyrby (DRCMR, DTU-Compute) and is a synergistic collaboration between Hvidovre Hospital and Rigshospitalet as well as the University of Copenhagen and the Technical University of Denmark. The research focus is on developing new image analysis algo-



The newly installed synchrotron MAX IV in Lund, Sweden is today the world's most powerful x-ray source and will provide images in nanometer resolution. Tim Dyrby and collaborators will be collecting medical images of soft and hard tissue in nanometer resolution and develop algorithms to process the enormous data sets.

gorithms making it possible for both researchers and clinicians to understand the highly detailed patterns in synchrotron images. In four proof-of-principle projects, researchers will investigate the microstructure of brain tissue, sperm movement patterns, muscle structures and bone structures and strive to leverage the full potential of synchrotron imaging, ranging from basic science to diagnostic healthcare.

The project will be seminal for forming an international leading competence cluster in the Sund region which excels in the clinical use of synchrotron imaging. This will give the hospitals in the Capital Region a platform for being at the international forefront of this line of research. Furthermore, the results yielded by the four proof-of-principle projects can directly be applied to clinical projects and thereby provide the first steps integrating the potential of synchrotron imaging for improving patient care.

CONSORTIUM MEMBERS

CAPITAL REGION HOSPITAL PROJECT PARTNER

(PI) Associate professor Tim B. Dyrby
DRCMR, Hvidovre Hospital, DK

Professor Hartwig R. Siebner
DRCMR, Hvidovre Hospital, DK

Professor Fin Biering-Sørensen
Department of Spinal Cord Injuries,
Rigshospitalet, DK

Professor Peter Schwarz
Department of Endocrinology,
Rigshospitalet, DK

Senior researcher Kristian Almstrup
Department of Growth and Reproduction,
Juliane Marie Centret, Rigshospitalet, DK

Postdoc Jessica Pingel
Department of Nutrition, Exercise and Sports,
University Of Copenhagen, DK

EXTERNAL PROJECT PARTNERS

Professor Mads Nielsen
DIKU, University of Copenhagen, DK

Professor Rasmus Larsen
DTU compute, Technical University of Denmark (DTU), DK

Professor Robert Feidenhans'l
European XFEL, GE

Associate professor Martin Beck
MAX IV, SE

THE ART OF INTER-DISCIPLINARY RESEARCH

Cross-disciplinary research is at the heart of DRCMR. Engineers, psychologists, physicians, biologists, radiographers, linguists and many other professions work together to provide cutting-edge research by merging knowledge, research designs and methods from different disciplines. Merging competences and knowledge yields solid advantages, such as providing the most suitable methods optimized to answer the scientific question at hand, but it is also challenging, because each field has its own ways of thinking, its own methodological approaches and nomenclature. The same scientific issue often has different names or is thought of quite differently. Here three researchers, who are part of DRCMR's interdisciplinary environment, reveal some of their thoughts on working at the crossroads of several scientific fields.

OLIVER HULME

Coordinator of the research area "Cognitive and Computational Neuroscience"



"Interdisciplinarity is one of those virtues that funding agencies encourage, and is often achieved through collaborations between people in different disciplines. I have found it very stimulating to try to become more interdisciplinary myself, mainly by trying to ignore the concept of disciplines and focusing predominantly on my research problems."

"To answer questions I just try to grab whatever I need from wherever I can find it. Some might call this transdisciplinarity. In my work on homeostasis I borrow from economics, physiology, neuroscience, philosophy, mathematics, statistics, physics and so on. There are so many disciplines that are able to contribute to almost any question."

"One advantage is that it becomes relatively easy to come up with new ideas, or new perspectives, just by trying to join the dots between equivalent concepts. The disadvantage is that you perhaps have less time to develop very specific and focused expertise within a small niche."

VIOLAINE MICHEL LANGE

Postdoc, part of the ProGram project which investigates the neuro-cognitive basis of grammar



"The challenge of interdisciplinary research is that people from different fields of research do not always respect each other's work. They might think that other researchers working in the middle of two fields of research never become experts because you have to account for the wishes of both fields, making it difficult to familiarize to a large extent with knowledge from each field."

"You often only read one type of articles about a subject, but interdisciplinary research allows you to use another field of research to falsify a well-established theory and review problems which were not apparent before."

"The advantage of interdisciplinary research is that it provides a new angle to research. Interdisciplinary research integrates theories and empirical data to examine a common question."

"We are going to build a wall protecting us from the MDs, and we will make the radiographers pay for it. It will be incredible. Believe me. The social scientists are fake news, and the engineers are crooked. (They are) total losers. We, the physicists, have the best words. It is true."

ASSOCIATE PROFESSOR LARS HANSON

Group leader of Acquisition technology and physicist



"I like the challenge of teaching groups of people having very different backgrounds, e.g. engineers, medical doctors and psychologists. Despite differences in education, different groups can respond well to similar teaching, if it is adapted. It all boils down to common sense, which is needed to understand any complicated subject. This exists in all groups, independent of mathematical skills, for example. The average engineer may be better at describing problems mathematically than the average radiographer, but not necessarily better at understanding relevant mechanisms. An intelligent mix of well-educated persons can outperform an average group of people operating within their own field of expertise."

"There are plenty of pitfalls and challenges when working with MRI. Some are of practical nature, while others relate to physics, chemistry, physiology, psychology or statistics, for example. No person has sufficient insight into all aspects needed for conducting good science. Hence, collaboration is a necessity. The individual researcher needs sufficient insight to identify the coworkers needed to conduct a scientific project, and skills to communicate effectively with those. To avoid pitfalls, this typically requires broad knowledge far beyond what a standard education gives."

"When teaching MRI physics, I sometimes refer to persons as bags of protons. It is probably good that I have non-physicist colleagues to add perspective."

MERGING JOURNALISM AND NEUROPSYCHOLOGY – NEURO-JOURNALISM?

Can the effect of journalism be examined with the use of neuropsychology? Journalist and Master student Morten Thomsen thought so, and despite several obstacles in merging the two fields his master thesis provided unique knowledge to the field of journalism.

Looking back at my master thesis it was all worth it. Setting my own footprints, somewhere between the road of journalism and neuropsychology. Providing much needed and unique knowledge for the field of journalism. And receiving an award for best master thesis of 2016 at Center for Journalism, University of Southern Denmark.

Forgetting for a moment the working nights and the sweating in how to combine the two very different scientific fields: Journalism with its emphasis on ecological validity, and neuropsychology with its emphasis on internal validity.

In the summer of 2015, I began working as a volunteer at DRCMR. The idea of examining journalism with methods of neuropsychology had been with me for some years, and after taking courses in neuropsychology, I needed practical experience. At the same time I began preparing the master thesis for the spring.

Journalism is a field much based upon tradition and gut feeling and our knowledge about the effect of journalistic communication is sparse. Therefore, it is unknown how journalists communicate their message in a manner that facilitates attentional, perceptual and memory processes.

This is the first study known to Center for Journalism to merge these two fields, and I therefore chose a subject which could encompass both journalistic research and neuropsychology:

Examining how emotional words change how headlines are processed.

During the next six months of master thesis writing, I encountered both advantages and disadvantages in conducting interdisciplinary research.

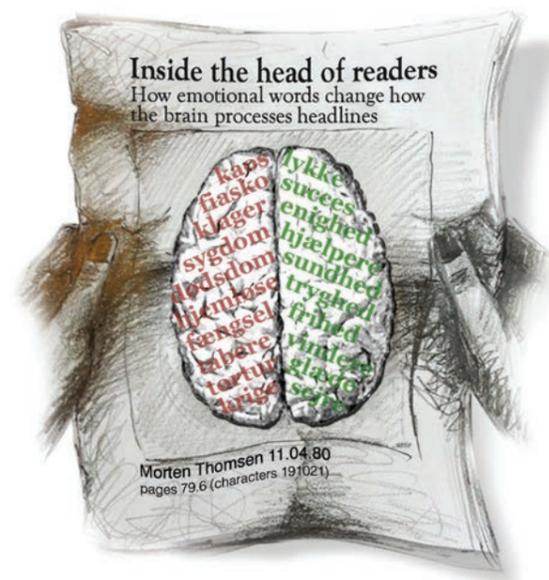
For instance, the academic methods of journalism differed from that of neuropsychology, thus most software, statistics and EEG-methods had to either be learned from scratch or I had to rely on supervisors' aid.

But the most difficult process was to determine stimuli. Whereas neuropsychology mainly relies on simple stimuli, controlling each possible variable, journalism mainly relies on stimuli that resemble real life. Thus, it required many discussions, thoughts and later pilot studies to determine the final stimuli.

However, the main advantage of conducting such interdisciplinary research is the amount of practical and theoretical experience in the team of researchers provided by DRCMR and Center for Journalism. Almost all difficult issues can be solved, and feedback can help improve the study by a mile.

Thus, input from both research fields can provide synergistic effect, maximizing the output of the study and providing much needed knowledge.

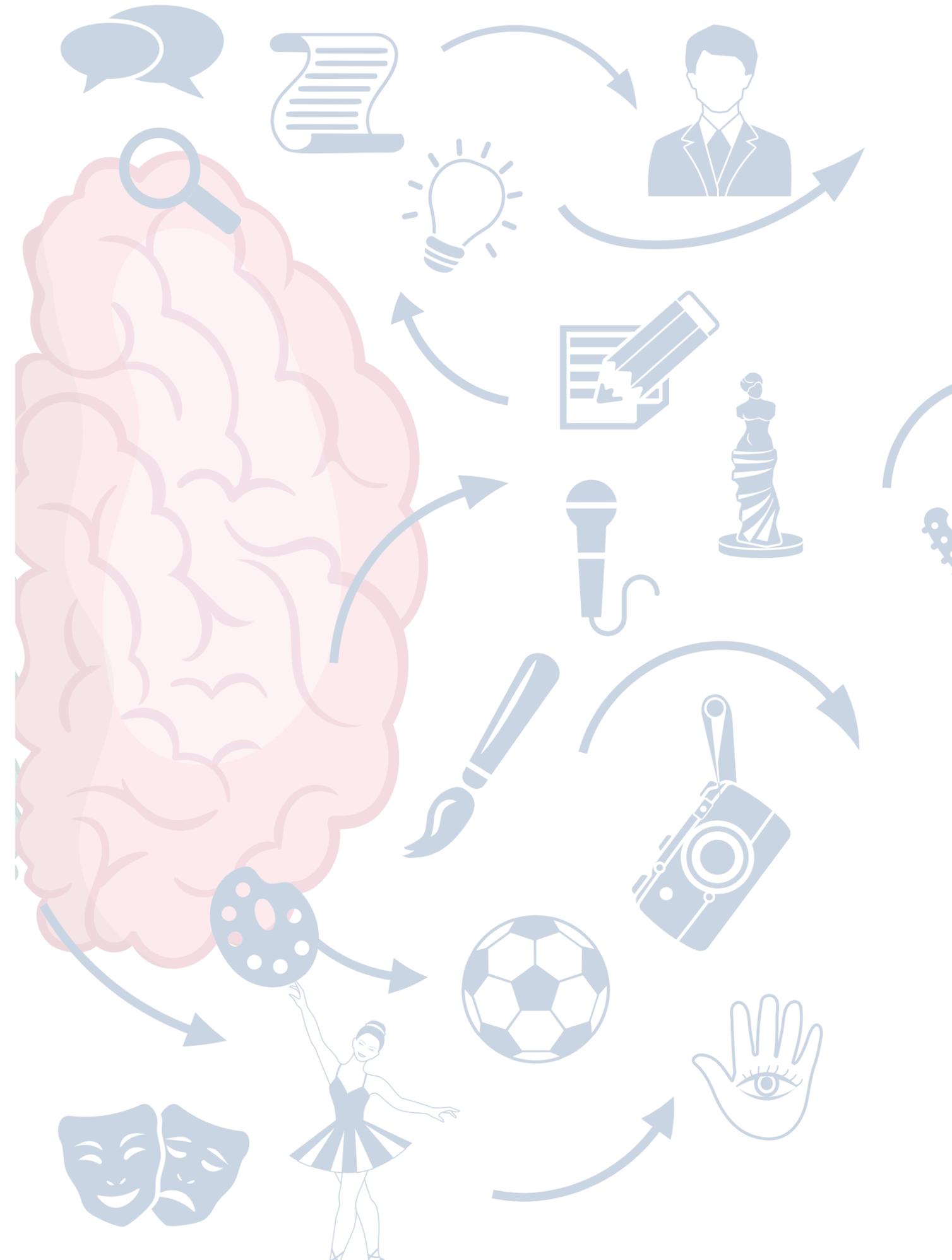
This is why all the sweating and working nights were all worth it.



Front page, Morten Thomsen's master thesis: "Inside the head of readers".

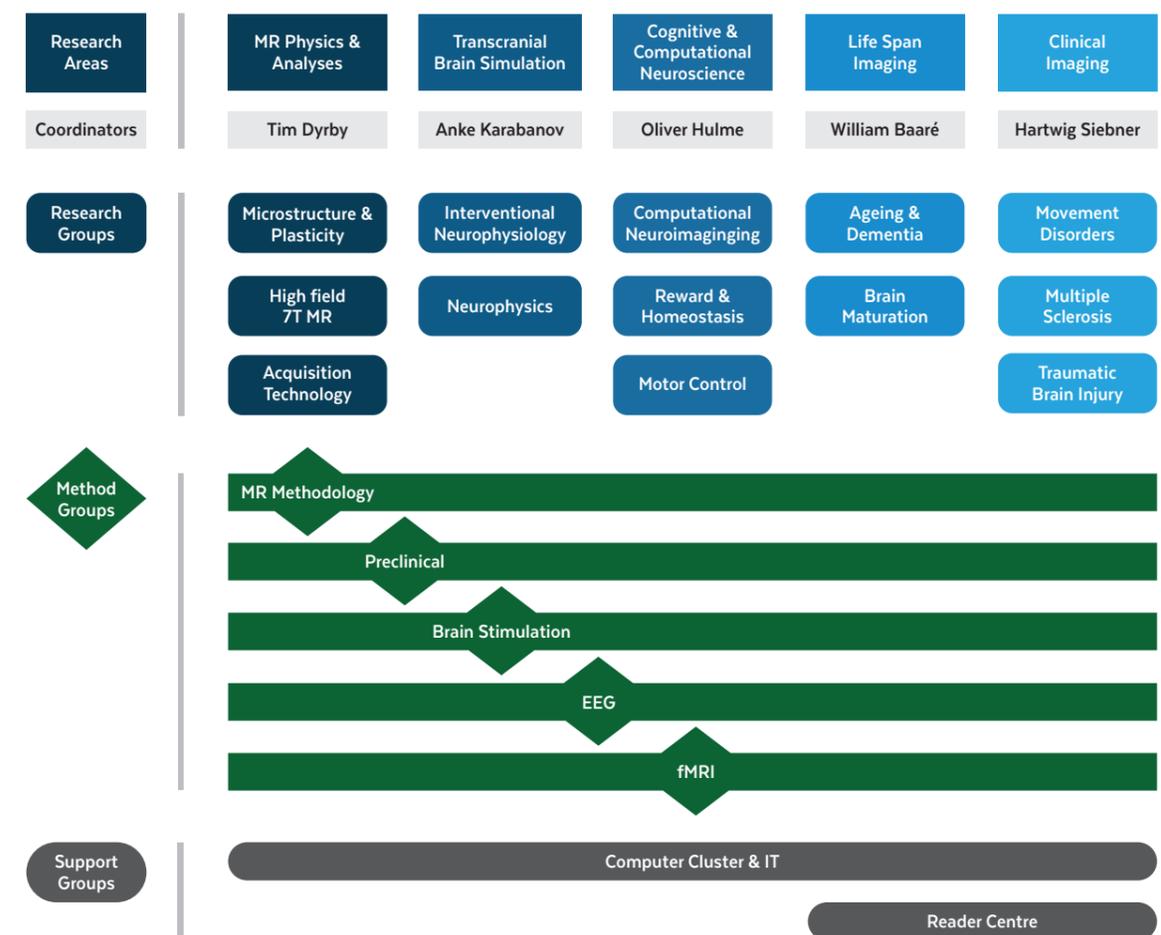


Journalist and Cand.Public. Morten Thomsen receiving an award for best master thesis of 2016 at Center for Journalism, University of Southern Denmark.



STRATEGY AND ORGANISATION

During the last two years we have focused on reconsidering and implementing our research strategy, including vision and mission. In parallel, we worked in depth with our organization –the way we organize our research, secure a robust state-of-art infrastructure, and nurture transdisciplinary education and training. We identified five research areas which will constitute our main lines of research in the years to come (see figure). The Clinical Imaging research area plays a central role in our research strategy. The Clinical Imaging area is strongly intertwined with and capitalizes on the specific expertise and outcomes of the MR Physics & Analyses, Transcranial Brain Stimulation, Cognitive & Computational Neuroscience and Life Span Imaging research areas.



It is all about the BRAIN

Although brain research has made remarkable advances, the human brain remains largely a mystery. It is made up of more than 80 billion nerve cells, called neurons, forming a giant dynamic network. The brain generates electrical signals that travel along the neurons, and jump from one neuron to the next by release of neurotransmitter chemicals in synapses. These patterns of electrical and chemical signals make us feel, think, and move and produce such amazing phenomena as consciousness, empathy, intelligence, and creativity.

Better BRAINs make better LIVES

The brain continuously interacts with the body and is shaped by a complex interplay of genetic, physical, social, cultural, and environmental factors that emerge on different timescales and drive developmental cascades across the lifespan. These “brain dynamics” determine our lives. Beneficial brain dynamics secure our health and well-being. Aberrant brain dynamics can result in brain disorders affecting our lives and causing enormous individual, societal and economic burden.

We are committed to conduct innovative research at the highest international level leading to new brain mapping methods, analyses and biomedical applications. We use advanced multimodal brain mapping technologies to study functional, metabolic, and structural properties of the brain networks and how they are altered by brain disorders. Focusing on causality, we use a range of interventional approaches such as pharmacological challenges, transcranial brain stimulation, and training to identify network dynamics that promote, maintain or recover efficient integration and hereby optimize brain function. Our clinical focus is on promoting the use of innovative MRI technology in clinical practice and research for the benefit of individual patients and society.

Education and inspiration

We have a strong focus on thorough in-house education to provide young scientists with necessary knowledge, skills, and confidence to conduct cutting-edge research. We foster an inspiring international and multi-disciplinary research environment through openness and respect in order to unfold the scientific potential and secure the well-being of each member of our staff.

OUR VISION

Mapping brain dynamics to promote health, understand disease, and 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 advanced brain mapping techniques 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 make major contributions to future efforts to boost public and individual health, potential, and well-being.*
- *This knowledge will also help to tailor therapeutic interventions in the brain dynamics expressed in individual patients (precision medicine).*

MR PHYSICS AND ANALYSES

Our research is geared to improve the basic understanding of the brain's structure and function by means of novel MR-based imaging and spectroscopic technologies. MRI is unique in the sense that a single scanner modality provides many different imaging contrasts. New and improved sequences continuously emerge and continue to advance the field of MR-based brain imaging. Today, MRI delivers not only exceptional structural information, but also detailed information about function, metabolism and microstructural organization of the tissue. The field moves with an amazing speed where technical barriers are broken almost as fast as they appear and ultrahigh field MRI has become a locomotive for innovation in experimental and clinical research. We pursue this endeavor by developing innovative data acquisition techniques and advancing

analytic methods to optimally extract the information from the acquired MR. Our main MRI modalities of interest are diffusion MR, perfusion MR and MR spectroscopy. By keeping in front with the latest MRI technologies and by combining the information with other modalities, such as non-invasive transcranial brain stimulation, we enable high-level basic science and foster research synergies among internal research groups and external collaborators. The MR infrastructure at DRCMR includes a 7T whole-body MR system for human use, a hardware lab, three 3T MR scanners, and a preclinical 7T MR system plus an attached animal research facility. This infrastructure is housed within a large university hospital, offering unique possibilities for translational bench-to-bedside research.



Microstructure & Plasticity

High field 7T MR

Acquisition Technology

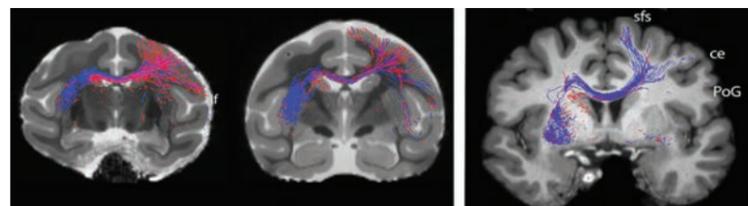
MICROSTRUCTURE AND PLASTICITY

In 2016, the “Diffusion Imaging” Group changed its name into “Microstructure and Plasticity” (MaP) group. 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 2015, the head of the group, Tim Dyrby, was appointed Associate professor in Multi-Modal Medical Imaging Analysis at the Technical University of Denmark (DTU). In 2016, he organised an ISMRM workshop “Breaking the Barriers on diffusion MRI” in Lisbon.

The group continued its work on multi-modal validation [6, 36, 68]. Together with Giorgio Innocenti (Karolinska Institute), we described for the first time the existence of direct projections from the cortex to contralateral striatum, with the help of tracer studies in monkeys and tractography in both monkeys and humans [68]. The existence of this projection was later confirmed in a post-mortem study by another group using the Klingler dissection technique.

We are active in designing innovative gradient waveforms for diffusion MRI that enable insight into a new type of microstructural features. Tim Dyrby and Henrik Lundell were part of an international group writing a review on double diffusion encoding (DDE) [111]. Samo Lasic (CR Development AB, Sweden) worked on developing DDE as part of his Marie Curie project in the MaP group, which highlights both the academic as well as the industrial relevance of those new methods. Apart from DDE, the group is also active in the development of ways to capture ultra-short diffusion times as done with the oscillating gradient spin echo (OGSE) method.



Contralateral corticostriatal projecting axons found with invasive tracer in monkey supported by corresponding tractography projections — emanated from nucleus caudatus (red) and putamen (blue) in the macaque (left), vervet (middle) and human (right).

GROUP MEMBERS

- Associate Professor Tim B. Dyrby
- Postdoc Henrik Lundell
- Postdoc Samo Lasic
- Postdoc Kasper W. Andersen
- Postdoc Nina Reisle
- Postdoc Helle Sickmann
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EXTERNAL COLLABORATORS

- Professor Giorgio Innocenti
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- Professor Maurice Ptito
- Professor Daniel Topgaard
- Professor Daniel Alexander
- Professor Geoff Parker
- Professor Roberto Caminiti
- Professor Kristine Krug
- Professor Mads Nielsen
- Associate professor Simon Eskildsen
- Associate professor Sune Jespersen
- Associate professor Morten Mørup
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- Associate Professor Itamar Ronen
- Assistant professor Mark Burk
- Associate lecturer Markus Nilsson
- Dr. Ivana Drobnajk
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PUBLICATIONS

13, 72, 85, 115

ULTRA-HIGH FIELD MR

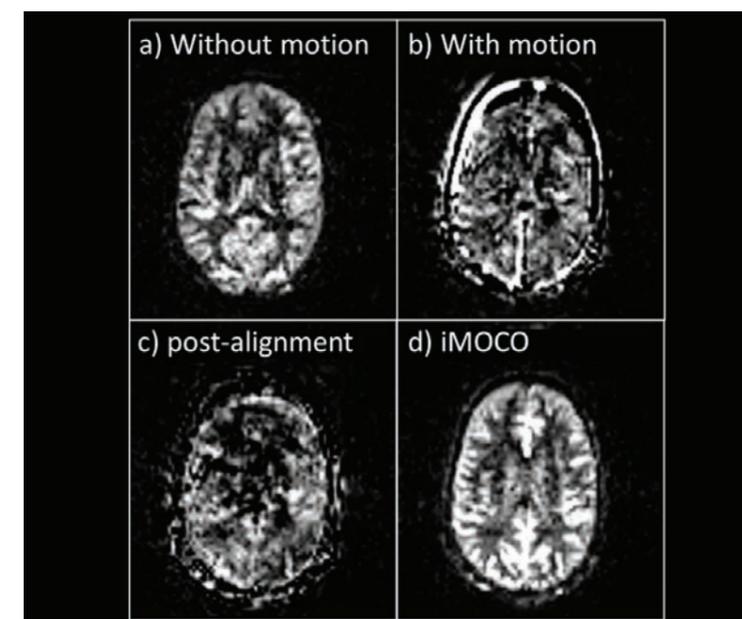
The Ultra-High Field MR group strives at providing state-of-the-art sequences and protocols, which take full advantage of the 7T system available at DRCMR. MR systems operating at fields of 7 tesla or above pose a series of technical challenges in reaching the full potential. We therefore work on both software and hardware solutions in order to optimise the system, including the use of navigators for motion correction and fast acquisitions schemes for reduction of scan time and thereby the chance of motion artefacts. We also work on new RF and coil designs which will improve the homogeneity in the acquired images.

The technical innovations, made by the group, are available and applied to all clinical studies performed on the system. The group’s clinical interest ranges from high-resolution structural, functional and quantitative imaging to advanced spectroscopic editing and imaging. We apply these techniques to ageing studies, studies of neurodegenerative diseases, in particular Parkinsonism, neuropsychiatric research and research on various other diseases. Examples of ongoing or upcoming projects typically conducted in synergy with other groups within or outside DRCMR are listed below:

“Diffusion weighted magnetic resonance spectroscopy at ultra-high field: Unravelling microstructural changes in cerebral white matter in patients with multiple sclerosis” by Henrik Lundell

“Brain metabolite changes across the lifespan: a 7T MR study” by Anouk Marsman and Anna Lind Hansen

“A generalised prospective motion correction framework for improved spectroscopy, structural and angiographic imaging” by Mads Andersen and Vincent Boer



Arterial spin labeling perfusion imaging is sensitive to motion (compare a,b). Retrospective coregistration does not improve (c). Using an innovative motion correction scheme (iMOCO) the original data quality is restored despite subject motion (d).

GROUP MEMBERS

- Associate professor Esben Thade Petersen
- Postdoc Vincent Boer
- Postdoc Anouk Marsman
- Postdoc Mads Andersen
- Senior Researcher Peter Magnusson
- PhD Student Anna Lind Hansen
- PhD Student Morten Gørtz Jønsson
- Associate professor Lars G. Hanson
- Postdoc Henrik Lundell
- Postdoc Kasper Winther Andersen
- PhD Student Jan Ole Pedersen

EXTERNAL COLLABORATORS

- Professor Birte Yding Glenthøj
- Professor Lene Juel Rasmussen
- Professor Erik Lykke Mortensen
- Professor Freddy Ståhlberg
- Professor Jeroen Hendrikse
- Professor Andrew Webb
- Professor Gyunggoo Cho
- Professor Chulhyun Lee
- Associate professor Egill Rostrup
- Associate professor Dennis Klomp
- Associate professor Matthias van Osch
- Associate professor Itamar Ronen
- Senior researcher Brian Villumsen Broberg
- PhD student Kirsten Borup Bojesen
- Associate professor Gunther Helms
- Dr. Karin Markenroth Bloch
- Nam Lee, MSc

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www.drcmr.dk/7t

PUBLICATIONS

21, 61, 62, 68, 73, 117

ACQUISITION TECHNOLOGY

Our aim is to improve MR acquisition speed, robustness, sensitivity or specificity, drawing on fundamental physics and advanced data processing to optimally extract the measured MR parameters of interest. The targets include imaging, spectroscopy, and multi-modal acquisition for advancing research and clinical practise.

Non-MR signal recording during scanning is challenging due to extreme conditions near a scanner. We have shown that high-quality EEG can be recorded using the scanner itself. This principle is now used for recording sound almost free of scanner-induced noise that would dominate normal recording. This is useful for patient surveillance. In MSc Jan Ole Pedersen's PhD project, newly developed hardware capable of real-time signal processing was used for implementing a novel "k-space sensor" that transmits information for image calculation to the scanner. This allows for general image reconstruction corrected for imperfections. This collaboration with the Chinese Academy of Sciences was funded by the Sino-Danish Center and the Technical University of Denmark (DTU).

Motion results in MR image errors for patients that are not able to lie still. This was the focus of Mads Andersen's PhD project which he successfully defended in 2016. The study was conducted in collaboration with the 7T MRI centers in Leiden and Utrecht, the Netherlands.

Fast spectroscopic imaging was improved in several projects. Some were aimed at efficiently improving the spatial localization. Methods for ultra-high field were developed with co-workers in the 7T group. Efficient imaging of hyperpolarized substances was a focus.

MRI education was given at DRMR and elsewhere, and the material is used widely. Our YouTube videos have been seen over 120.000 times. A new web-based simulator was developed for introducing MR. The corresponding CompassMR app was installed over 500 times.

GROUP MEMBERS

- Associate professor Lars G. Hanson
- Senior researcher Peter Magnusson
- PhD student Jan Ole Pedersen
- Postdoc Mads Andersen
- Associate professor Kristoffer Hougaard Madsen
- Student Carlos Dieste
- Student Andreas Nexmann
- Student Mikkel Marcussen
- Student Søren Bohøj

EXTERNAL COLLABORATORS

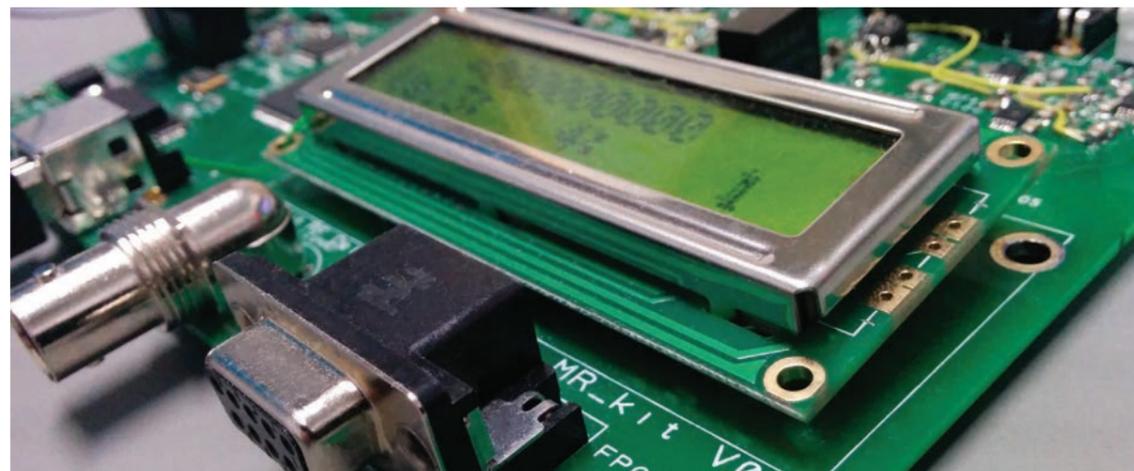
- Professor Rong Xue
- Associate professor Gunther Helms
- Professor Jan Henrik Ardenkjær-Larsen
- Dr. Marten Versluis
- Professor Andrew Webb
- Professor Dennis Klomp
- Christian G. Hanson

HOMEPAGE

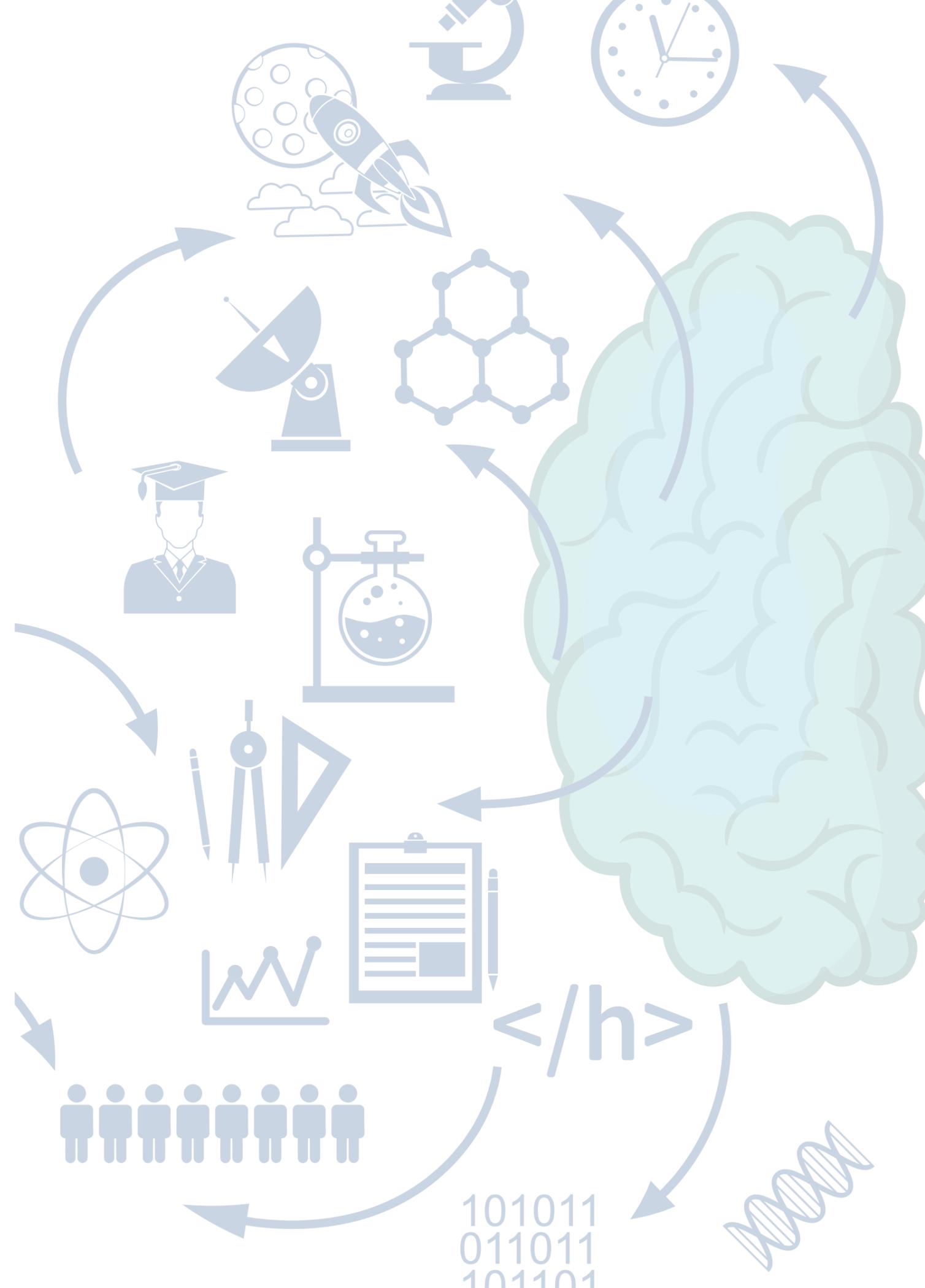
www.drcmr.dk/acquisition

PUBLICATIONS

7, 12, 62, 88



Some activities in the group involve hardware development. The picture shows unique electronics developed by Christian G. Hanson for real-time processing of signals acquired during MRI. This is used for combining MR and non-MR data.



TRANSCRANIAL BRAIN STIMULATION

Moving towards causal neuroscience

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.

Mission and Vision

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 Modelling to decipher the underlying physiological and biophysical mechanisms needed to improve the effects of TBS.

A unique infrastructure for brain stimulation

The DRCMR houses a unique infrastructure, including five state-of-the-art laboratories where all NTBS 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.



Interventional
Neurophysiology

Neurophysics

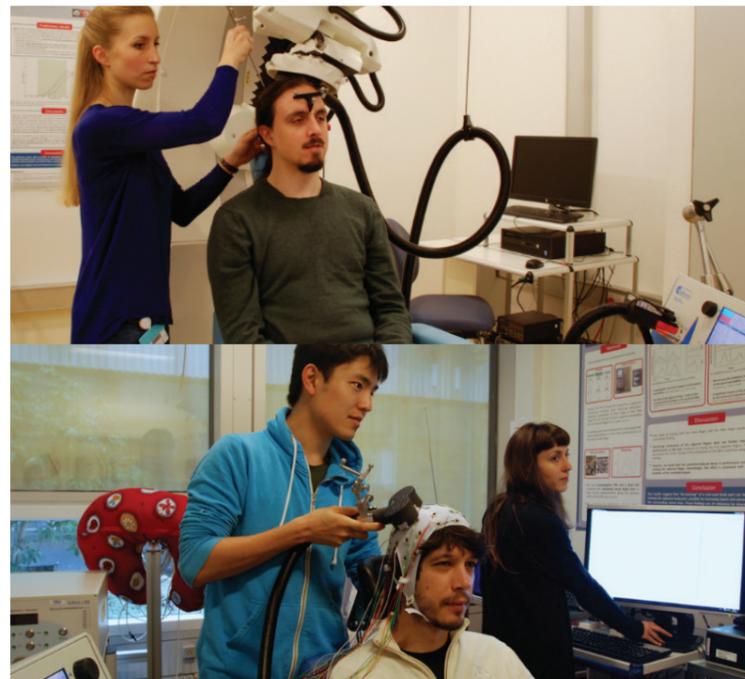
INTERVENTIONAL NEUROPHYSIOLOGY

The Interventional Neurophysiology group studies the physiological effects of non-invasive brain stimulation on the human brain with a focus on the sensorimotor system. We examine how noninvasive brain stimulation interacts with the brain, locally and globally, by combining electrophysiological readouts (MEP, EEG) with advanced brain mapping techniques (MRI, MRS) and behavioral measures.

A better understanding of the physiological mechanisms is critical for future efforts to enhance the efficacy and reliability of non-invasive brain stimulation as a scientific and therapeutic tool. Our research will also be of key importance for the development of new, biologically informed stimulation protocols that interact with natural activity patterns generated by the brain itself.

During 2015–2016 the group has published several landmark papers showing that Noninvasive Transcranial Brain Stimulation (NTBS) can trigger a homeostatic plasticity-like effect in the human motor cortex, and can produce lasting effects on sensorimotor processing and action selection by changing effective connectivity in sensorimotor networks. We also developed a novel mapping technique that allows tracing brain plasticity in the human motor cortex for individual muscle representations.

The Interventional Neurophysiology group is headed by Professor Hartwig R. Siebner and is a main contributor to the ongoing BASICS project funded by the Novo Nordisk Foundation. We have tight interactions with the research groups “Neurophysics”, “Motor control” and “Computational Neuroimaging”.



Top image: Registering a participant in the newly acquired TMS-robot that allows for precision targeting and mapping. // Bottom image: TMS-EEG experiment

GROUP MEMBERS

- **Professor Hartwig R. Siebner**
- Senior researcher Anke Ninija Karabanov
- Postdoc Leo Tomasevic
- Postdoc Virginia Conde
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- Postdoc Til Ole Bergmann
- Professor Volker Mall
- Research group leader Gesa Hartwigsen
- Professor Vincenzo Di Luzzo
- Senior researcher Franca Tecchio

HOMEPAGE

www.drcmr.dk/neurophysiology

PUBLICATIONS

16, 18, 29, 34, 36, 49, 51, 59, 64

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 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. 1B). To validate the predictions of the biophysical models, we are also working on novel MR methods to measure the current flow patterns induced by TBS (MR current density imaging; Fig. 1C). 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 biophysical research by measurements of the impact of TBS on brain activity using neuroimaging methods such as functional MRI (Fig. 1A) and EEG. We also use this combination as a powerful tool to assess causally the interaction in brain networks. We apply it to study human sensorimotor integration and motor control, which set the neuroscientific scene in which we employ our TBS methods. 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

- **Associate professor Axel Thielscher**
- Postdoc Oula Puonti
- PhD student Cihan Göksu
- PhD student Guilherme Bicalho Saturnino
- PhD student Cristina Pasquinelli
- PhD student Mürsel Karadas
- PhD student Sofie Johanna Nilsson
- PhD student Jesper Duemose Nielsen
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- Medical student Peter Jagd Sørensen

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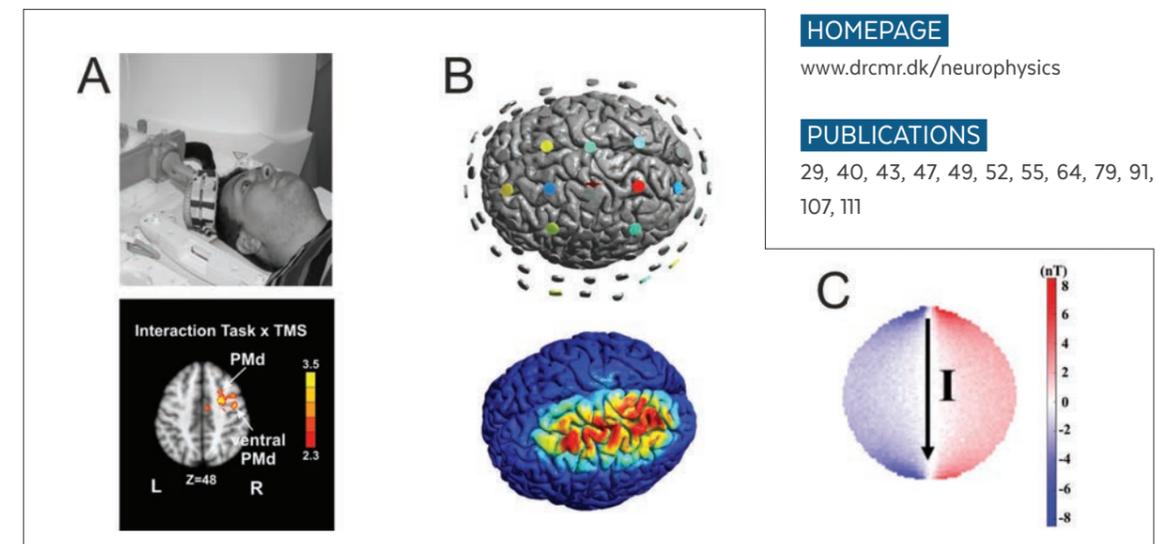
- Professor Ulrik Lund Andersen
- Associate professor Alexander Huck
- Associate professor Koen van Lempuut
- Specialist registrar in neurosurgery Anders Rosendal Korshøj
- Professor Dr. Klaus Scheffler
- Assistant professor Hyunjoo Jenny Lee

HOMEPAGE

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PUBLICATIONS

29, 40, 43, 47, 49, 52, 55, 64, 79, 91, 107, 111



A Combination of TBS methods with concurrent functional MRI to image how TBS modulates brain activity. B Novel computational methods for targeted stimulation. C Novel highly sensitive MR method to directly measure the current flow induced by TBS.

COGNITIVE & 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 motor control 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 modelling and analysis of neuroimaging data from EEG, to fMRI, as well as diffusion & structural data.



Computational
Neuroimaging

Reward &
Homeostasis

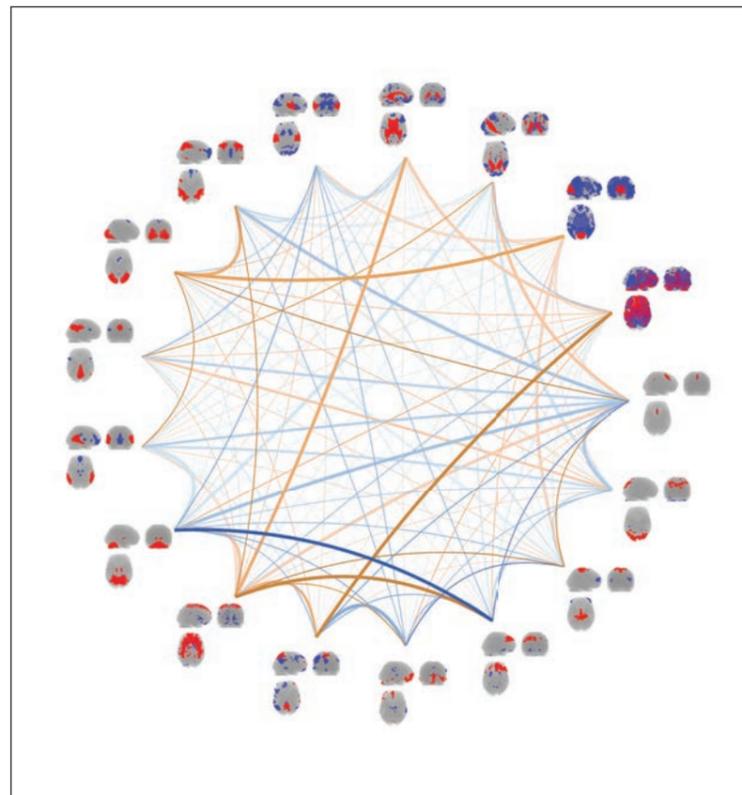
Motor Control

COMPUTATIONAL NEUROIMAGING

The group uses machine learning methodology to improve the sensitivity and interpretability of brain imaging data through sophisticated modelling and analysis methods. A major focus is on multivariate classification of task labels and subject phenotypes based on functional magnetic resonance imaging (fMRI) data. We investigate how optimized models can be used to extract features for reliable prediction. Within the field of fMRI data analysis, we have lately worked on 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. One example is a Bayesian formulation of Independent Vector Analysis for modelling of functional networks across subjects in the presence of limited inter-subject variability.

Additional research efforts are within Bayesian nonparametric modelling of fMRI data and investigations of predictability and reproducibility of unsupervised decomposition methods using resampling techniques.

Other recent research includes the development of setups for online analysis of neuroimaging data enabling state-dependent stimulation and brain-computer interfaces, and accurate modelling of electric fields for transcranial magnetic stimulation.



The figure illustrates how functional connectivity estimated by fMRI can be decomposed into subnetworks via parallel factor analysis. Subnetworks are indicated by the 17 brain illustrations, and the lines between them indicate coupling strength.

GROUP MEMBERS

- Associate professor **Kristoffer H. Madsen**
- Postdoc Kasper W. Andersen
- Postdoc Albert Vilamala
- PhD student Jesper Duemose Nielsen
- PhD student Rasmus Røge
- PhD student Søren Føns Vind Nielsen
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- Research assistant Mads Gylling Safeldt

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- Professor Lars Kai Hansen
- Associate professor Morten Mørup
- Professor Rong Xue
- Postdoc Nathan W. Churchill
- Professor Tülay Adalı
- Group leader Moritz Grosse-Wentrup

HOMEPAGE

www.drcmr.dk/computational-neuroimaging

PUBLICATIONS

25, 32, 67, 81, 82, 104

REWARD & HOMEOSTASIS

The reward and homeostasis group aims to address some apparently simple, but surprisingly difficult problems. Why do we find some things rewarding but not others? And why do we find those some things rewarding only some of the time?

These key problems of value-based decision making can be formulated in more neurobiological terms: What are the evolutionary origins of reward value? What role does reward valuation play in our homeostasis? How are homeostatic states and reward values computed by the brain? And what function does this all ultimately serve?

The framework we work from makes one key assumption from which several other theoretical predictions can be made. The principal role of reward valuation is to shape behavior toward optimizing homeostatic states of the body, which in turn optimizes long-run survival. The work we do is thus partly theoretical and partly empirical.

We seek to derive theories of reward that are grounded on fundamental principles of homeostatic dynamics and their evolution. We draw on concepts, tools, and results, from a diversity of fields, including economics, ecology, physiology, and computational biology. And we use these to build computational models of reward and homeostasis. One major result of this approach is the discovery that economic phenomena can be derived from known statistical features of homeostasis, thus providing a unifying and evolutionarily grounded theory of simple homeostatic decision making.

From these models we can derive falsifiable predictions for behavioral, physiological, and neural responses. In human subjects, we triangulate between computational modelling, fMRI, physiological monitoring, and economic behavior.

GROUP MEMBERS

- Senior researcher **Oliver Hulme**
- Postdoc David Meder
- PhD stud. Tobias Morville
- Student Line Pedersen
- Student Magnus Koudahl
- Student Finn Rabe

EXTERNAL COLLABORATORS

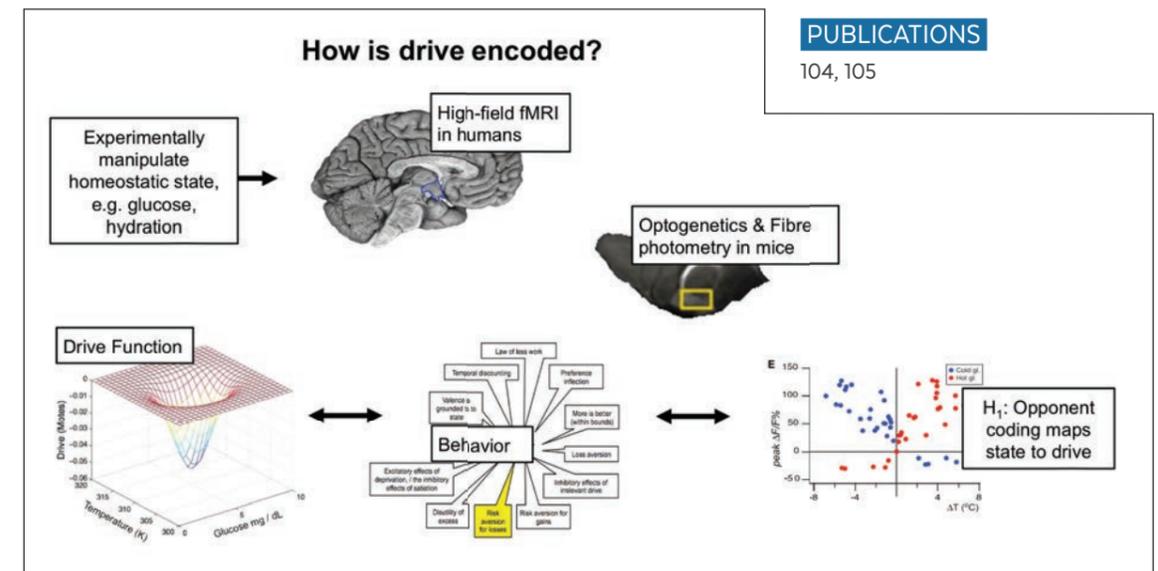
- Professor MSO Anders Sjoden
- Professor Derek Byrne
- Postdoc Barbara Andersen
- Resident Physician Kirstine Bojsen-Møller
- Professor Jens Juhl Holst
- Professor Sten Madsbad
- Associate professor Louise Whiteley
- Professor Morten Overgaard
- Visiting professor Boris Gutkin
- Professor Alexander Sebald

HOMEPAGE

www.drcmr.dk/reward-and-homeostasis

PUBLICATIONS

104, 105



Schematic depicts a research strategy of the group, investigating how homeostatic motivations (drives) are encoded. The strategy is to pursue research that spans across species, by triangulating between models, neural data and behavior.

MOTOR CONTROL

The aim of the Motor Control group is to unravel the neural mechanisms through which the brain selects and controls volitional actions. The brain is the interface between our senses and our actions, but how does the brain transform the input provided from our senses into appropriate actions? How does the brain predict the outcome of volitional actions and where in the brain does the will to act emerge? To address these questions, the group adopts a triple-M approach, which combines multimodal brain MAPPING with computational MODELLING and non-invasive neuro-MODULATION to decipher the causal neuro-dynamics in motor-related brain networks.

Sequential decision making: In a recent functional MRI-study, healthy volunteers performed a dice game, known as “pig”. The brain’s “stopping” network, consisting of the pre-supplementary motor area (pre-SMA), right inferior frontal gyrus (rIFG), and right subthalamic nucleus (STN), became gradually more active, when subjects continued to engage in sequential gambles under increasing risk. Effective connectivity analyses additionally revealed that the STN increased its coupling with pre-SMA and rIFG (Figure). Our results suggest that the “stopping” network also serves as a mental “break” during sequential gambling that is geared to increasing risk. We are now applying this dice game to better understand abnormal gambling behavior in ludomania and Parkinson’s disease.

Other research projects addressed the neural underpinnings of motor proficiency (dexterity), handedness (preferred use of a hand), bimanual motor control and motor skill learning.

The group received major funding from the Lundbeck Foundation awarding a “Grant of Excellence” to Hartwig R. Siebner (CONTrol of ACTION, 2011–2016). Additional funding was granted by the Danish Council for Independent Research.

GROUP MEMBERS

- Professor Hartwig R. Siebner
- Senior researcher Anke Ninija Karabanov
- Senior researcher Jens Hjortkjær
- Postdoc David Meder
- Postdoc Leo Tomasevic
- Postdoc Mitsuki Takemi
- Postdoc Violaine Michel Lange
- Postdoc Virginia Conde
- PhD student Allan Lohse
- PhD student Janine Kesselheim
- PhD student Melissa Larsen
- PhD student Morten Gørtz Jønsson
- PhD student Sofie Johanna Nilsson
- PhD student Steffen Angstmann
- Research assistant Oliver Naaby

EXTERNAL COLLABORATORS

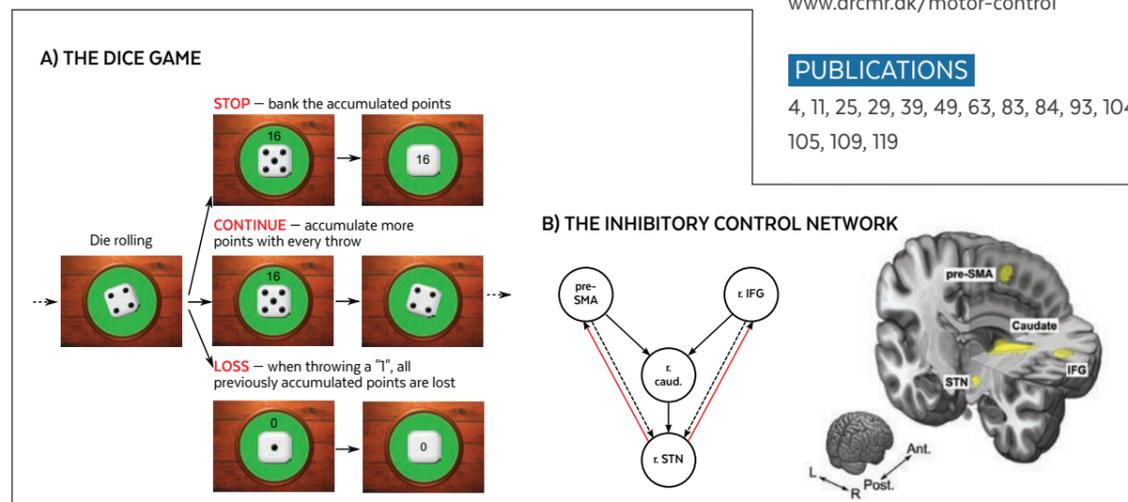
- Professor Jens Bo Nielsen
- Associate professor Mark Schram Christensen
- Professor Olivier David
- Postdoc Estelle Raffin

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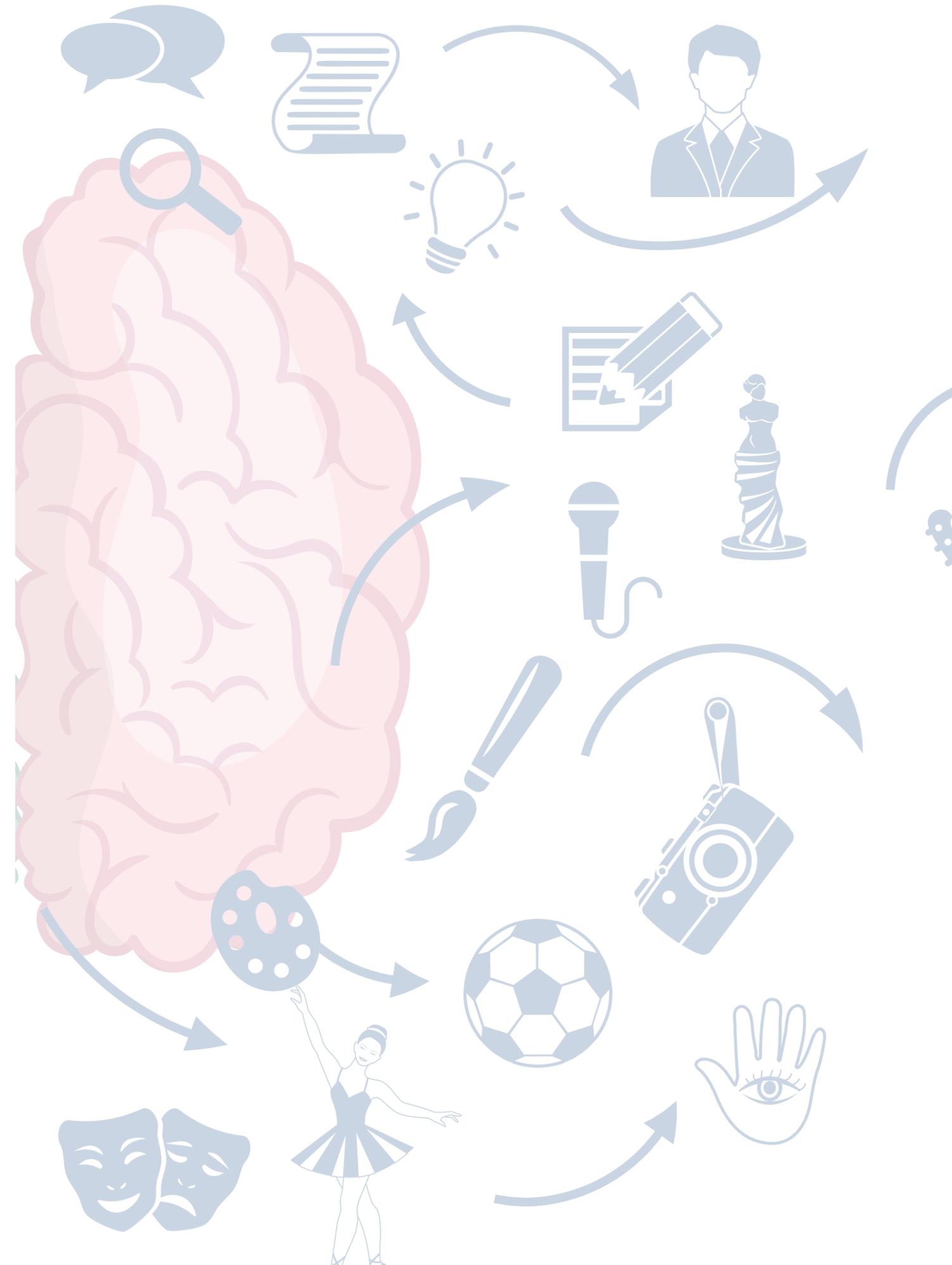
www.drcmr.dk/motor-control

PUBLICATIONS

4, 11, 25, 29, 39, 49, 63, 83, 84, 93, 104, 105, 109, 119



Left: Under increasing risk (continuing to throw the die), right subthalamic nucleus increases its coupling with pre-supplementary motor area and right inferior frontal gyrus (red arrows). Right: Anatomical location of the core-areas in the inhibitory motor control network.



LIFESPAN IMAGING

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.

Unravelling the developmental cascades across the human lifespan will give us unique insights into the complex inter-relations between “exposures” and “outcomes”. We will focus on the developmental underpinnings of neurodevelopmental disorders and approach neurodegenerative disorders and normal ageing from a lifespan perspective. Obtained insights will provide important clues to design “health interventions”, which can promote physical and mental health and prevent the emergence of illness.

Our current efforts are centered on the longitudinal assessment of typically-developing children and adolescents and interventional studies in healthy elderly populations, but also on cohorts at high risk for developing schizophrenia and specific patient cohorts suffering from multiple sclerosis and Alzheimer. We have established expertise and research infrastructures for detailed cross-sectional and longitudinal assessments of large cohorts and nurture active and elaborative national and international collaborations. Most recently we became partner in the EU horizon 2020 funded Life-brain study (www.lifebrain.uio.no). Lifebrain aims 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. We continue to expand our research to cover the entire age range and actively seek and engage in new collaborations. Furthermore, we strive to strengthen and expand our interventional research and our physical assessment with e.g. mobile sensing techniques, in depth measures of sleep patterns, diet, gut microbiome, biomarkers and body tissue composition.



Ageing &
Dementia

Brain
Maturation

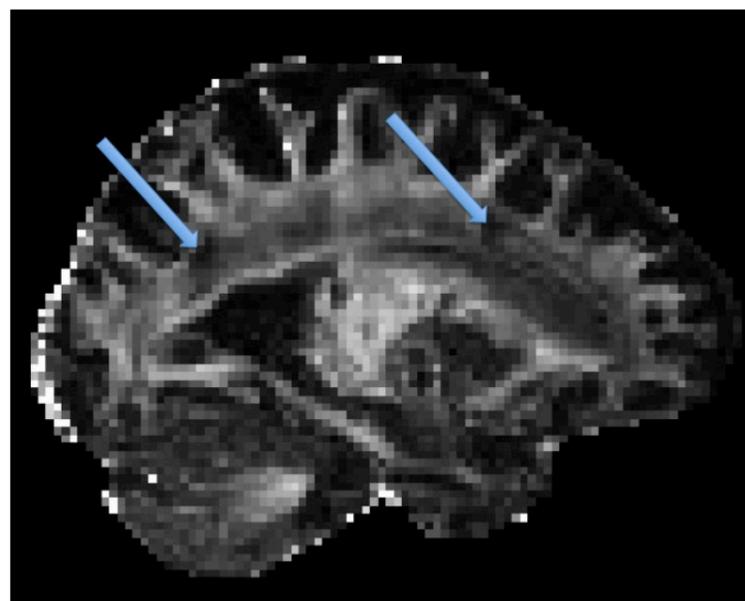
AGEING AND DEMENTIA

The main focus of the Ageing and Dementia Group is to identify structural and functional reorganization related to decline and well-being in ageing populations. Our approach encompasses large cohort and population-based projects as well as intervention studies in healthy elderly and patients.

We investigated the impact of physical activity in patients with Alzheimer's disease in the ADEX study led by the Memory Disorders Research Group, Rigshospitalet and in healthy younger and older adults in a collaboration with Concordia University, Montreal. Results from the latter study suggest that preservation of vessel elasticity may be one of the key mechanisms by which physical exercise helps to alleviate cognitive ageing. A successful grant application supports future collaborations.

The Live active healthy ageing (LISA) study: The LISA study was initiated with Bispebjerg Hospital and Center for Healthy Ageing, University of Copenhagen and includes 450 community-dwelling healthy individuals aged 62–70 years. The LISA study is the first randomised and supervised one-year strength training study performed on older adults close to retirement age with a planned long-term follow-up. Annual MRI scans of the brain and thighs are performed at DRMR, complementing extensive physical and cognitive assessments performed at Bispebjerg Hospital.

The Early Life Determinants of Midlife Mental Development and Brain Structure (LifeMabs) study: Our most recent project aims to understand the effect of early-life exposures and developmental aspects on age-related changes at midlife. In collaboration with Department of Public Health and Center for Healthy Ageing, 300–400 middle-aged individuals from The Copenhagen Perinatal Cohort (CPC) with detailed information on the life course and health status undergo psychological assessment and high-resolution quantitative MRI of the brain.



Diffusion imaging: hypointense FA regions within the white matter tracts.

GROUP MEMBERS

- Associate professor **Ellen Garde**
- Postdoc Nina Højland Reislev
- PhD student Nayome Rey Calvo
- PhD student Dinne Skjærlund Christensen
- Visiting professor Carl-Johan Boraxbekk
- Research medical laboratory technologist Sussi Larsen

EXTERNAL COLLABORATORS

- Associate professor Claudine Gautier
- Professor Erik Lykke Mortensen
- Associate professor Trine Flensburg-Madsen
- Professor Gunhild Waldemar
- Professor Steen Hasselbalch
- Professor Michael Kjær

HOME PAGE

www.drcmr.dk/ageing-and-dementia
www.lifemabs.dk

PUBLICATIONS

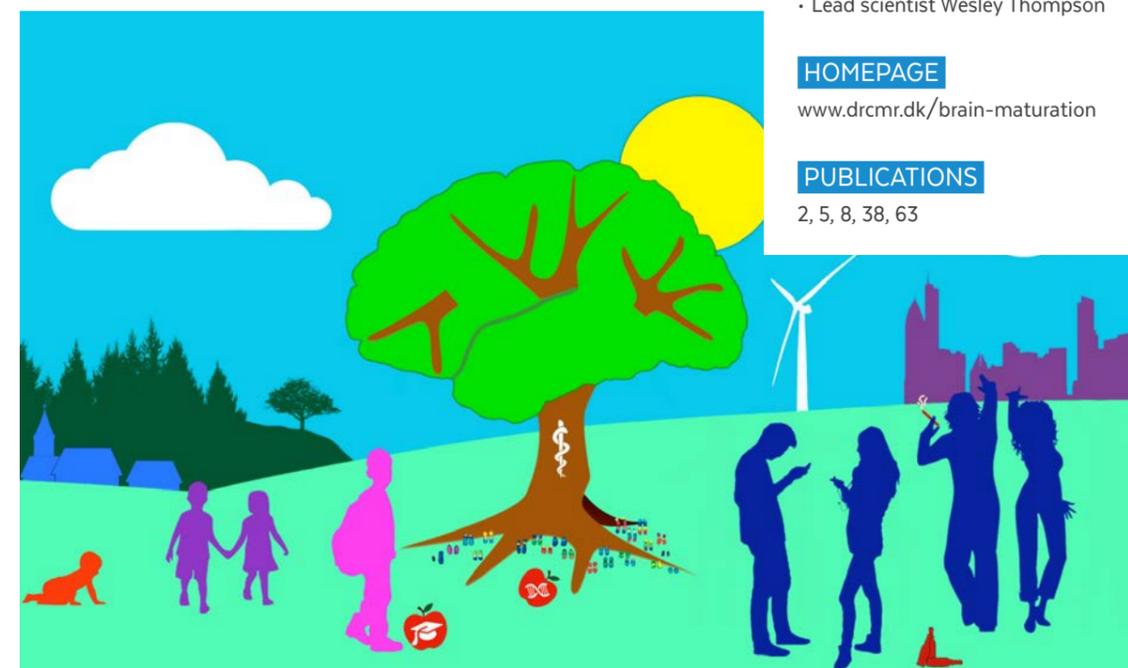
3, 24, 42, 70, 77, 76, 89

BRAIN MATURATION

All behaviour originates from the brain. 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 employs multimodal magnetic resonance imaging (MRI) techniques to investigate the structural and functional development of the brain during childhood and adolescence. By linking MRI derived markers of brain maturation to intrinsic (e.g. genetic make-up, hormones), environmental (e.g. alcohol use, diet, physical activity and stress), cognitive and clinical variables we address critical questions regarding the factors that place young people at risk for e.g. developing cognitive or emotional problems. Moreover, it allows us to identify potential factors of resilience.

A key project is the HUBU ("Hjernens Udvikling hos Børn og Unge": Brain maturation in children and adolescents) project. The HUBU project is a unique longitudinal study investigating typically-developing children that started in 2007. Children and adolescents, 7 to 13 years of age at study initiation, were assessed 12 times. The first 10 of these were done at six months' intervals. The 12th assessment was concluded in 2016. The HUBU project is part of the EU horizon 2020 funded Lifebrain study (www.lifebrain.uio.no) in which we are partners. Lifebrain will integrate data of several existing large prospective brain imaging cohorts ranging in age from 4 to 90 years. This allows to build a solid knowledge foundation for understanding how brain, cognitive and mental health can be optimized through the lifespan. Lifebrain starts January 1st, 2017.



GROUP MEMBERS

- Senior researcher **William Baaré**
- Associate professor Kathrine Skak Madsen
- Postdoc Louise Barué Johansen
- PhD student Sara Krøis Holm
- PhD student Martin Vestergaard Götzsche
- PhD student Jonathan Holm-Skjold
- Research Medical Laboratory Technologist Sussi Larsen
- Student Amalie Sofie Ekstrand
- Student Thilde Elena Kofoed Sørensen
- Student assistant Mads Stehr

EXTERNAL COLLABORATORS

- Professor Terry Jernigan
- Associate professor Alexander Leemans
- Professor Sven Kreiborg
- Dr. Mark Lyksborg
- Professor Peter Uldall
- Lead scientist Wesley Thompson

HOME PAGE

www.drcmr.dk/brain-maturation

PUBLICATIONS

2, 5, 8, 38, 63

CLINICAL 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 MR scanning in optimizing clinical decision-making through MR-based finger printing. Our mission is to develop and validate novel MR-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 pickup 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.



Movement Disorders

Multiple Sclerosis

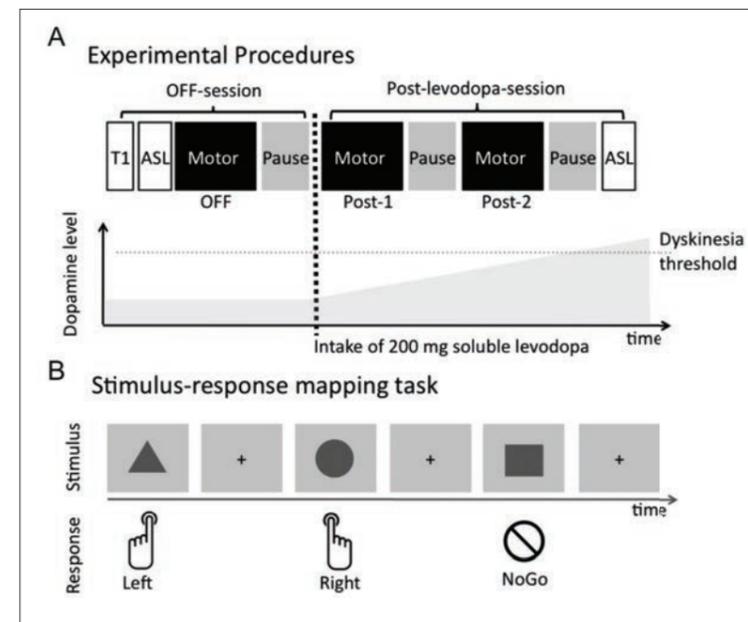
Traumatic Brain Injury

NEUROIMAGING OF MOVEMENT DISORDERS

The NiMoDis group is situated both at DRMR and the Department of Neurology at Copenhagen University Hospital Bispebjerg. Our research primarily focuses on Parkinson's disease and dystonia.

The mission of the NiMoDis group is to use advanced brain mapping techniques to investigate how movement disorders alter the brain's function, structure and metabolism and affect motor, cognitive and limbic systems. We are not only interested in studying primary dysfunction directly caused by the movement disorders, but also secondary dysfunctions of brain networks that are associated with therapy.

Current research focuses on reward processing in patients with Parkinson's disease, especially in those patients who develop impulse control disorders under dopamine replacement therapy. Another project employed functional MRI to delineate the abnormal network dynamics in the motor system driving dopamine induced dyskinesia. We are starting to exploit the unique possibility of ultra-high field MRI to image the small nuclei in the brain stem in Parkinson's disease. Neurodegeneration in these nuclei is thought to play a pivotal role for pathogenesis in Parkinson's disease. We wish to exploit this knowledge to advance personalized medicine and precision treatment. Our research projects have received generous support from the The Danish Council for Independent Research and the Danish Parkinson's Association.



Mapping brain activity during inhibitory action control in dyskinetic PD patients. Although MRI is susceptible to movement, we were able to map the abnormal activity in dyskinetic PD patients by imaging the pre-dyskinetic period.

GROUP MEMBERS

- Professor Hartwig R. Siebner
- Associate professor Annemette Løkkegaard
- Postdoc David Meder
- Postdoc Damian Herz
- Postdoc Brian N. Haagensen
- PhD student Allan Lohse
- Research year student Birgitte Liang Chen Thomsen

EXTERNAL COLLABORATORS

- Professor Bente Pakkenberg
- Senior researcher Susana Aznar
- Senior researcher Tomasz Brudek
- Professor Stéphane Lehericy
- Professor Angelo Quartarone
- Professor James Rowe
- Associate professor Anders Christensen
- Professor Hanne Christensen

Homepage

www.drcmr.dk/movement-disorders

PUBLICATIONS

32, 81, 97

NEUROIMAGING IN MULTIPLE SCLEROSIS

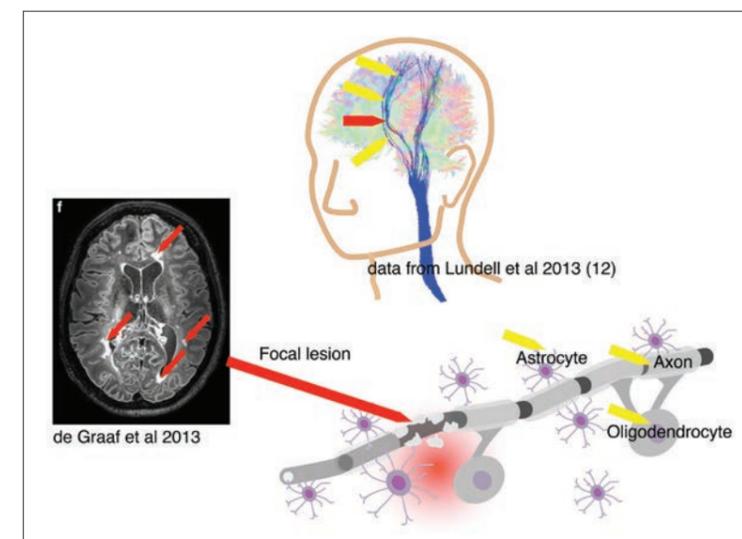
Multiple Sclerosis (MS) is an autoimmune neurodegenerative disease that diffusively attacks the central nervous system. The disease affects the neural transmission that eventually leads to several disabling symptoms. Magnetic resonance imaging (MRI) is the most sensitive imaging tool for diagnosing and monitoring the progression of MS.

The aim of the group is to expand the frontiers of MRI techniques to capture disease related alterations and the underlying pathophysiological mechanisms. We apply a wide range of MRI techniques including functional MRI (fMRI), magnetic resonance spectroscopy (MRS), and diffusion weighted imaging (DWI). We have pursued several lines of neuroimaging research focusing on tissue abnormalities in normal appearing white matter and atrophy patterns in the spinal cord. The overall theme in our research is to elucidate how MS alters the functional and structural connectivity in the brain and how these changes in the brain's connectome lead to clinical disability among MS patients.

We have initiated the first clinical ultra-high field (7T) MR study in Denmark, where we combine MRS and DWI to shed new light on how MS affects the microstructure in major white matter motor tracts. Ultra High field MRI will provide new knowledge of the intracellular and extracellular compartments in the MS brain.

In another key project we identify functional and structural changes in the brain that contribute to disease-related motor fatigue. We recently discovered that MS patients reporting fatigue exhibit a functional over-activation in the motor cerebellum during a non-fatiguing task compared to patients not reporting subjective motor fatigue. This suggests that enhanced sensorimotor processing in cerebellum may play a pivotal role in motor fatigue in MS patients.

Our research was generously supported by the Danish Multiple Sclerosis Association.



By combining conventional MRI and DWI, patterns of focal lesions (red arrow) and microstructural changes (yellow arrow) are mapped in major white-matter pathways to delineate how MS affects functional disability.

GROUP MEMBERS

- Professor Hartwig R. Siebner
- Associate professor Tim B. Dyrby
- Associate professor Ellen Garde
- Associate professor Kristoffer H. Madsen
- Senior researcher Anke N. Karabanov
- Postdoc Henrik Lundell
- Postdoc Kasper W. Andersen
- PhD student Olivia Svolgaard
- PhD student Christian Bauer
- Research assistant Irina Akopian
- Research assistant Silas H. Nielsen
- Research radiographer Hanne Schmidt
- Research medical laboratory technologist Sascha Gude
- Research medical laboratory technologist Sussi Larsen

EXTERNAL COLLABORATORS

- Professor Per Soelberg Sørensen
- Professor Finn T. Sellebjerg
- Professor Christian Dettmers
- Senior consultant Morten Blinkenberg
- Associate professor Kathrine Skak Madsen
- Associate professor Morten Mørup
- Research leader Jesper Bencke
- Associate professor Itamar Ronen
- Consultant Anne-Mette Leffers
- Consultant Camilla Gøbel Madsen

Homepage

www.drcmr.dk/multiple-sclerosis

PUBLICATIONS

58, 110, 114, 117

TRAUMATIC BRAIN INJURY

The “ABC in TBI” or Traumatic Brain Injury group combines advanced brain mapping techniques to shed light on how TBI alters the brain’s connectome. The acronym “ABC in TBI” stands for “Alterations in the Brain’s Connectome in patients with severe Traumatic Brain Injury”. Our overarching research hypothesis is that TBI fundamentally impairs the integrative properties of the brain’s structural and functional connectivity (i.e., its connectome). The trauma-induced impairment of brain connectivity determines the patients’ functional deficits. Likewise, restoring functional integration within the brain connectome determines recovery of consciousness and other brain functions.

Using a multimodal brain mapping approach, our group is currently conducting a prospective observational study in which patients with severe TBI are assessed at three time points during their in-patient stay at the TBI unit, with an additional assessment one year after their TBI incident. Data collection is still ongoing. The study is designed to identify predictive markers of recovery by prospectively comparing patients who recover and patients who do not recover from a TBI-induced disorder of consciousness.

The ABC in TBI group is headed by Professor Hartwig R. Siebner (DRCMR) and Associate professor Ingrid Poulsen (RUBRIC), and consists of an interdisciplinary group of researchers from the DRCMR and the Research Unit on Brain Injury Rehabilitation Copenhagen (RUBRIC). RUBRIC is administratively part of Rigshospitalet, but placed at Hvidovre Hospital.



Example of an experimental session with a patient with TBI and concomitant disorder of consciousness. An interdisciplinary team of researchers and clinical personnel actively work together to ensure data quality and patient comfort.

GROUP MEMBERS

- Professor Hartwig R. Siebner
- Associate professor Ingrid Poulsen
- Consultant Christian Pilebaek Hansen
- Associate professor Lars Peter Kammergård
- Associate professor Kristoffer Hougaard Madsen
- Associate professor Tim Dyrby
- Postdoc Virginia Conde
- Postdoc Karine Madsen
- Postdoc Kasper Winther Andersen
- Postdoc Tue Hvass Petersen
- PhD student Sara Hesby Andreasen
- Nurse Karen Busted Larsen
- Consultant Camilla Gøbel Madsen

EXTERNAL COLLABORATORS

- Professor Marcello Massimini
- Professor Lars Kai Hansen
- Professor Jesper Mogensen
- Postdoc Til Ole Bergmann

Homepage

www.drcmr.dk/traumatic-brain-injury

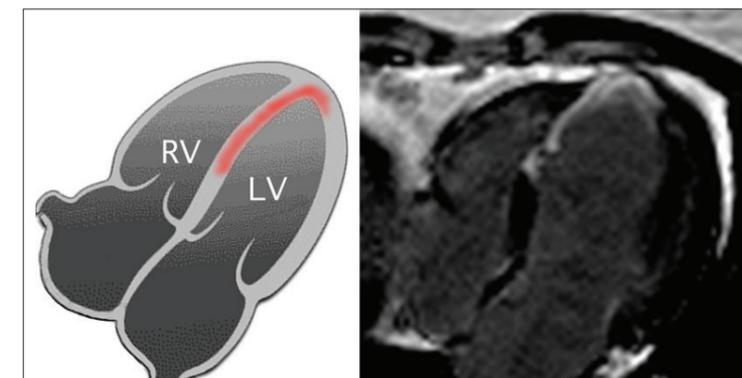
CARDIOVASCULAR IMAGING UNIT

Our intention is to develop a strong clinical cardiac MRI unit based on a profound research program. In recent years, cardiac MRI has been well established as a unique imaging modality in several areas:

- To characterize and distinguish known hypertrophic and/or dilated cardiomyopathies
- To distinguish viable from fibrotic myocardium in ischaemic cardiomyopathy
- For non-invasive examination of regional myocardial blood perfusion
- For examination of patients with complicated valve- and myocardial diseases including patients with valve regurgitation

The CIU also entails a comprehensive list of other imaging modalities as cardiac CT, advanced echocardiography (3-dimensional echo and speckle-tracking analysis) and cardiac Positron Emission Tomography (PET). Specialists in radiology, nuclear medicine and cardiology are involved in the multimodal cardiac imaging approach. Various metabolic diseases are associated with cardiovascular disease often through direct influence on cardiac metabolism with associated influence on cardiac systolic and diastolic function, and such interactions are cornerstone in the research at Hvidovre Hospital. Among others, we follow a cohort of patients with cirrosis and we plan to study the influence of obesity and diabetes mellitus and the effect of treatment with novel anti-diabetic drugs. Also, we have a study on patients diagnosed and treated for carcinoid tumours. We have a strong objective towards the development of novel cardiovascular magnetic resonance imaging (CMR) analysis tools and collaborate closely with several other DRCMR groups to achieve this goal. Perfusion studies and studies of myocardial fibrosis, and regional wall motion using strain imaging are under development. Recently, we have focused on the measurement of organ perfusion during various disease states.

Our incentive is to investigate the influence of various diseases on the cardiac hemodynamics and organ (kidney, liver, gut, etc) perfusion. We intend to optain this goal through a strong collaboration with external partners.



Late-enhancement image of the heart showing a large fibrotic area in the septum. This technic has been further developed to enable quantification of disperse fibrosis. Red colour: localisation of the fibrosis (white on the MR-image). RV: right ventricle, LV: left ventricle.

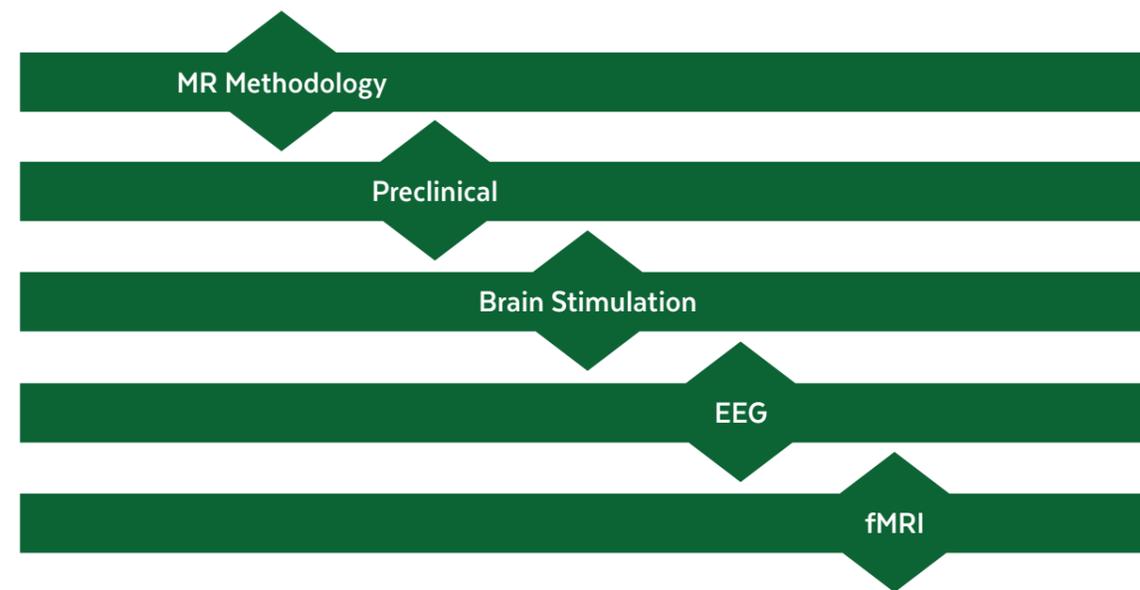
GROUP MEMBERS

- Consultant Jens D. Hove
- Chief consultant Claus Leth Petersen
- Professor Hartwig R. Siebner
- Senior researcher Tim B. Dyrby
- Professor Andreas Kjær

EXTERNAL COLLABORATORS

- Professor Søren Møller
- Professor Flemming Bendtsen
- Professor Steen Madsbad
- Chief physician Ulrich Knigge

METHOD GROUPS

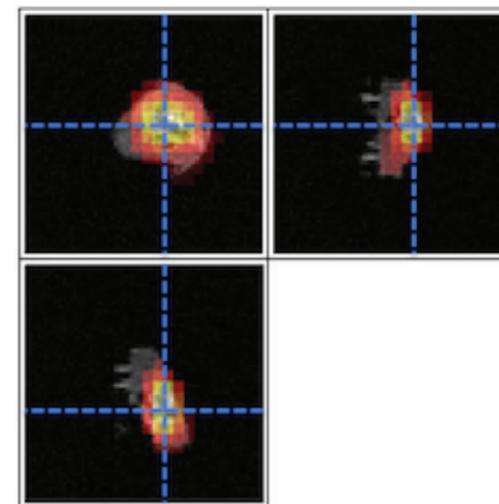


PRECLINICAL GROUP

The preclinical research facilities underwent complete refurbishment in 2016, including the installation of a new 7T preclinical Bruker scanner and the establishment of novel animal laboratories.

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. Helle Sickmann continued her postdoc project that was supported by the Danish National Advanced Technology Foundation and the Lundbeck Foundation. Helle evaluated the established prenatal stress (PNS) animal model and collected ex vivo diffusion MRI for investigating the impact of PNS on microstructure compared to normal controls.

Histology of sentinel lymph node ex vivo tissue samples is used in clinical routine for diagnosis of breast cancer metastasis. This histological procedure requires time consuming manual sample analysis. However, 3D MR Spectroscopic Imaging (MRSI) of a hyperpolarized compound can potentially speed up the diagnosis. The Hypemet project in collaboration with Albeda Research continued in 2015. Peter Magnusson performed methods research on a rapid 3D MRSI pulse sequence that efficiently utilizes the hyperpolarized magnetization. The technique presented well spatially resolved signal distributions of the injected compounds in tissue with high signal-to-noise-ratios (Figure X). The sequence was further developed to accommodate new hyperpolarized substrate approaches and the sequence was furthermore adapted, transferred and tested on a corresponding 9.4T preclinical system at Skejby Hospital, Aarhus, to ultimately be applied to human samples.



Images acquired with a rapid MRSI sequence of a single resonance hyperpolarized compound, after injection into a lymph node. Images of the hyperpolarized injected compound are displayed as color-coded overlays on corresponding structural images.

GROUP MEMBERS

- Associate professor **Tim B. Dyrby**
- Senior researcher Peter Magnusson
- Postdoc Henrik Lundell
- Postdoc Helle Sickmann
- Postdoc Samo Lasic
- PhD student Christian Skoven
- Phd student Andreas Ettrup Clemmensen
- Phd student Abubakr Eldirdiri
- Research Medical Laboratory Technologist Sascha Gude

EXTERNAL COLLABORATORS

- Professor Hans Stødkilde-Jørgensen
- Associate professor Sune Jespersen
- Professor Jan Henrik Ardenkjær-Larsen
- Assistant Professor Mark Burk
- Professor Giorgio Innocenti
- Professor Maurice Ptito
- Professor Daniel Alexander
- Dr. Mathilde Lerche
- Professor Daniel Topgaard
- Dr. Ivana Drobnajk
- Dr. Gary Zhang
- Professor Geoff Parker
- Professor Kristine Krug

HOME PAGE

www.drcmr.dk/preclinical-research

PUBLICATIONS

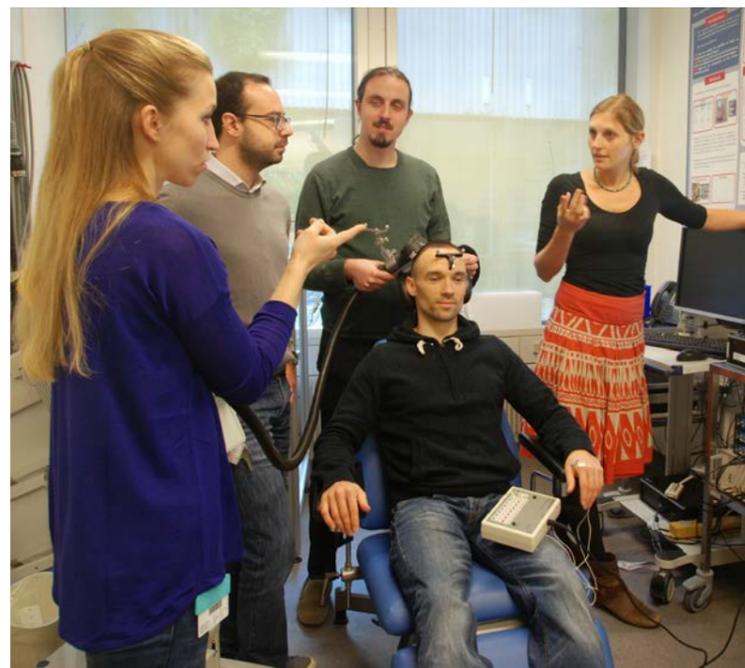
41, 85, 53, 72

BRAIN STIMULATION

Transcranial Brain Stimulation (TBS) is a versatile neuroscientific and therapeutic tool. Many researchers use TBS to shape brain activity and to evaluate brain function in health and disease, for instance in patients with movement disorders, multiple sclerosis, or 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 TBS protocols by considering the individual anatomy or the functional brain state expressed at the time of stimulation. We also develop in-house tools for easier and faster detection of common electrophysiological “read-outs” such as Motor Evoked Potentials (MEPs) and Cortical Motor Threshold (CMT). We assist with the establishment of current state-of-the-art protocols (e.g. Triple Stimulation Technique for evaluation of corticomotor function in Multiple Sclerosis). We also pioneer novel stimulation protocols to push the frontiers of TBS (e.g. robotic TMS, closed-loop EEG-informed TMS). The group also has a strong educational focus: We provide training in brain stimulation techniques at in-house workshops or international graduate-level teaching courses. Over the last three years more than 80 participants from 16 different countries have participated in our workshops.

We also perform outreach activities to inform the general public about TBS. At the “KulturNatten 2016”, more than 300 citizens took part in a “brain stimulation” event jointly performed with the Medical Museion. The TBS methods group meets every second week and welcomes all researchers at DRCMR who wish to use TBS in their research.



Discussions during a teaching session.

GROUP MEMBERS

- Senior researcher Anke Karabanov
- Postdoc Virginia Conde
- Postdoc Mitsuaki Takemi
- Postdoc Violaine Lange
- PhD student Raffaele Dubbioso
- PhD student Sofie Johanna Nilsson
- PhD student Janine Kesselheim
- PhD student Byuraken Ishkhanyan
- PhD student Allan Lohse
- Research assistant Morten Gørtz Jønsson
- Research assistant Irina Akopian
- Research assistant Lærke Krohne
- Research assistant Mads Gylling Safeldt
- Student Peter Jagd Sørensen

EXTERNAL COLLABORATORS

- Dr. Estelle Raffin
- Professor Angelo Quartarone

HOMEPAGE

www.drcmr.dk/tms-group

PUBLICATIONS

15, 17, 28, 33, 34, 35, 61, 47

ELECTRO-ENCEPHALOGRAPHY

The focus of the EEG group is to develop and advance methods for EEG data analysis and to provide DRCMR researchers with the most updated know-how about EEG methodology and data analysis.

EEG offers excellent temporal resolution and can thus trace ongoing event-related and spontaneous brain activity (e.g. brain oscillations). Moreover, there is a growing interest in using EEG in combination with non-invasive transcranial stimulation techniques, such as TMS or TDCS. We develop methods that can identify “brain states” in real time and use this information to guide the timing of brain stimulation (temporal neuronavigation). The goal is to establish EEG-controlled closed-loop brain stimulation approaches that can enhance human brain function.

Therefore, the EEG group develops existing EEG methodology in two principal directions:

- 1 EEG data cleaning in acquisitions with concurrent brain stimulation: there are still no reliable methods to retrieve brain activity covered by artefacts due to magnetic or electric stimulation.
- 2 Real-time brain state identification: the application of stimulation in correspondence with defined brain states could be crucial to improve the efficacy of the plasticity inducing protocols.

GROUP MEMBERS

- Postdoc Leo Tomasevic
- Postdoc Mitsuaki Takemi
- Postdoc Virginia Conde Ruiz
- Postdoc Violaine Michel Lange
- PhD student Melissa Larsen
- PhD student Janine Kesselheim
- PhD student Raffaele Dubbioso
- Research assistant Irina Akopian
- Research assistant Oliver Naaby
- Research assistant Mads Gylling Safeldt

HOMEPAGE

www.drcmr.dk/eeeg



EEG enables us to map the brain activity with a very high time resolution, up to milliseconds.

FUNCTIONAL MRI & STATISTICS

We run an informal weekly methods clinic and discussion forum, consisting of all members who are using or interested in using functional MRI. We also welcome members with more general interest in statistics, mathematics, and computational modelling. The clinic is also open for all collaborators of DRCMR.

The clinic is usually held after the research meeting every Friday. Therefore, discussions arising at the research meetings can spill over into discussions in the clinic. The format typically centers around ad hoc questions pertaining to anything related to fMRI, statistics, or computational modelling. Attendees are free to bring any question of any level of sophistication, from the practical to the theoretical.

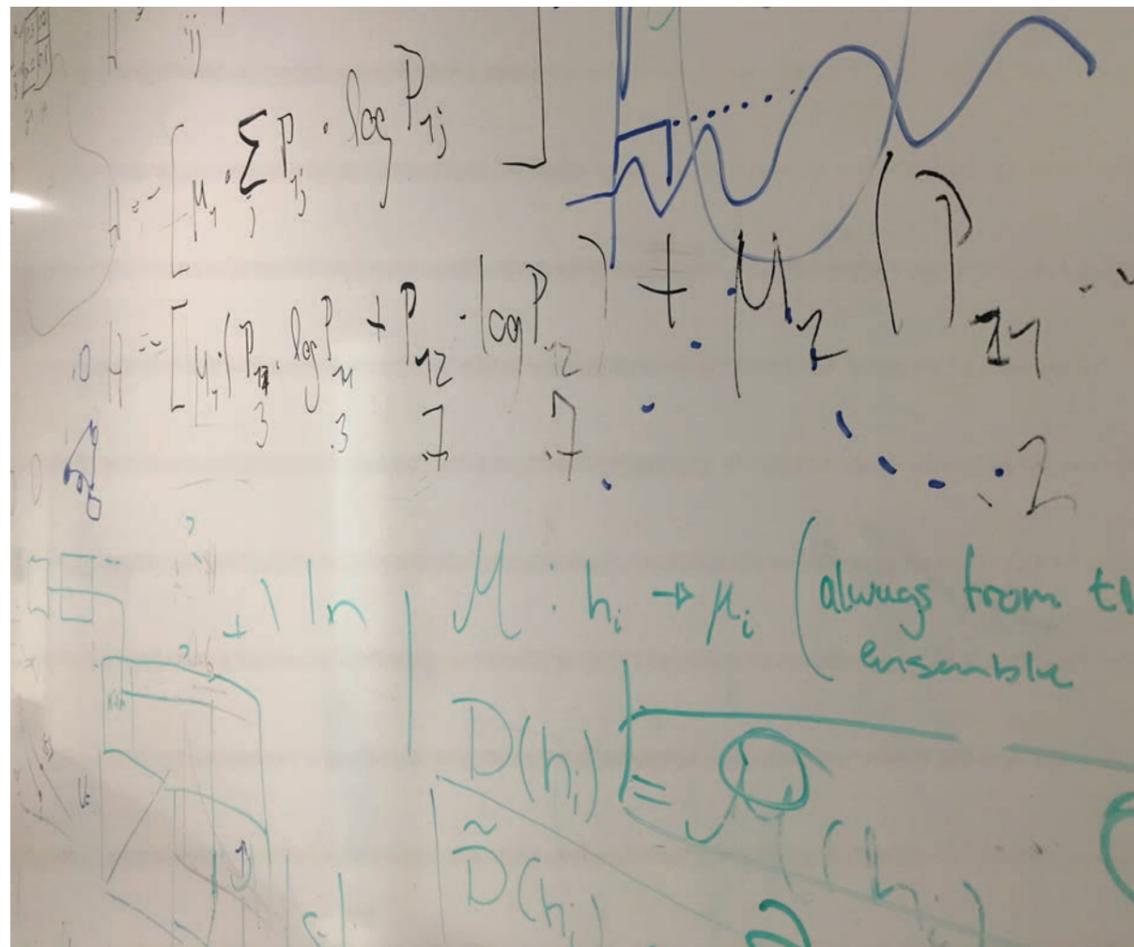
We can help with practical tasks such as methods reporting, grant writing, responding to reviewer's comments, and much else besides. We also occasionally hold journal clubs on papers, video talks, or reports of general interest to functional MRI and related issues. Attendees are also encouraged to bring data and "half-baked analyses" for discussion. Adequately baked cakes are unlikely to be rejected by the group.

GROUP MEMBERS

The meetings are chaired and organized by Ollie Hulme, Kristoffer Madsen, and Jens Hjortkjær. Attendance is voluntary but recommended for anyone engaged in fMRI research, computational modelling, or is anyway confused by something of a statistical nature. Collaborators are also welcome to attend.

HOMEPAGE

www.drcmr.dk/fmri



One of the many whiteboards decorating the walls of DRCMR.

READER CENTRE

Large cohort studies, clinical trials, and biomedical research demand effective data management and ever 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 scans logistics, big data handling, delineation of Regions-of-interest (ROIs) and focal lesion, 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 towards the needs of the individual study.

The Reader Centre is partner in several investigator driven, clinical studies. Most studies concern patients with multiple sclerosis, reflecting a strong collaboration with the Danish Multiple Sclerosis Center. In these studies, patients are scanned multiple times at our facility and scanning sequences and image processing procedures are adapted accordingly.

In recent years, the Reader Center engaged in large cohort studies, in which several hundred individuals are scanned using multimodal MR protocols. These studies build on in-house expertise in study coordination, logistics and big data handling. One of these large MRI studies was recently concluded – Women with Migraine Aura Neuroimaging (WOMAN) study. The study included participants from the Danish Twin Registry and was carried out in collaboration with David Gaist (Odense University Hospital) and Messoud Ashina (Rigshospitalet Glostrup). In 380 women we found no evidence of an association between women with migraine with aura and white matter hyperintensities or silent infarcts. The reader centre also supports two large ongoing studies on normal ageing which involve healthy participants and are conducted by the Ageing & Dementia group (LifeMaps study and LISA study).

GROUP MEMBERS

- Manager, Pernille Iversen (2015)
- Manager, Karam Sidaros (2016)
- Clinical manager, Associate professor Ellen Garde
- Postdoc Nina Højland Reislev
- Postdoc Henrik Lundell
- Research radiographer Hanne Schmidt
- Research medical laboratory technologist Sascha Gude
- Research medical laboratory technologist Sussi Larsen

EXTERNAL COLLABORATORS

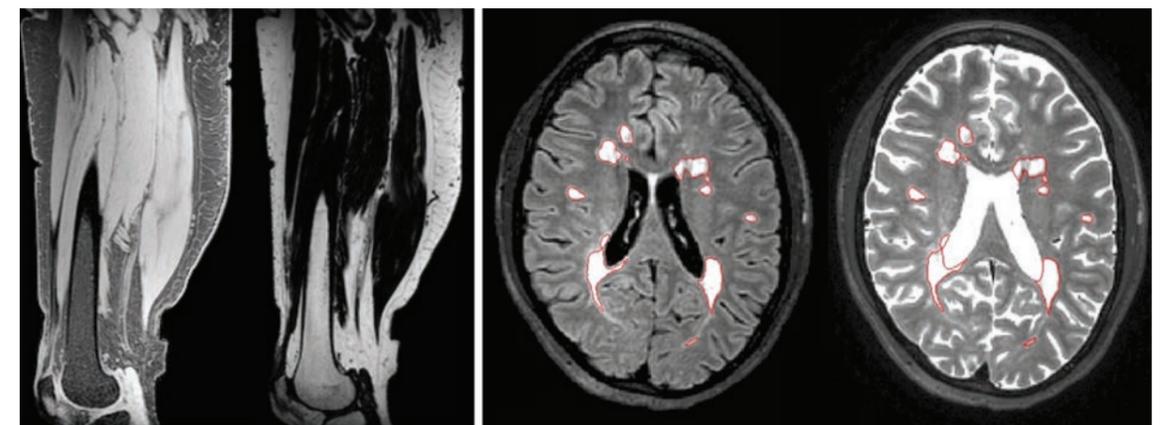
- Danish Multiple Sclerosis Center, Rigshospitalet
- Center for Healthy Ageing, University of Copenhagen
- Danish Headache Center, Rigshospitalet – Glostrup

HOMEPAGE

www.drcmr.dk/reader-centre

PUBLICATIONS

24, 70, 74, 76, 110, 114, 117



Left: Water and fat 3D images of thigh muscle. Right: Delineation of MS lesions on FLAIR images. The lesions are also visible on T2-weighted images.

PUBLIC OUTREACH

NEW DRICMR HOMEPAGE AND LOGO

2016 was a year with emphasis on strategy at the DRICMR. We worked extensively with the way we organize ourselves, how we present ourselves and how we communicate with the world. As part of this process we developed both a new webpage and a new logo.

THE HOMEPAGE

The homepage has been completely redesigned and we have worked in depth with the content. It has been very important for us to keep a simple line with a broad appeal and limit content to our main research, news and necessary practicalities. Please have a look at www.DRICMR.dk

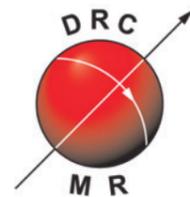


THE NEW LOGO



The logo reflects the research focus of the DRICMR, but also the centre as such.

The **arrows** symbolise the spinning the hydrogen proton, which is often used for imaging purposes as it is abundant in water and fat. The single proton can be thought of as our planet, spinning on its axis, with a north-south pole. In this respect, it behaves like a small bar magnet. The spinning effect also bridges to our former DRICMR logo.



Former DRICMR logo

The **brain** – at DRICMR it is all about the brain! Our research is focused on the brain which continuously interacts with the body and is shaped by a complex interplay of factors such as genetic, physical, social, cultural, and environmental across the lifespan. The **group of people** signifies that our research vision is to create knowledge that benefits people and can be used to optimize treatments in individual patients and to boost public and individual health, potential, and well-being. Together with the brain, our logo reflects our interest in studying interactions between the brain and the body. Finally, the group of people expresses our research culture at DRICMR; to study the brain as a multi-disciplinary and international research team.

KULTURNATTEN 2016

It is very important for us to communicate our results to the general population. DRICMR researchers therefore regularly appear in Danish media, give public lectures, etc. – here are some of the stories we have told in 2015–2016.

“A melancholic autumn night” was the topic of the “2016 CULTURE NIGHT” arrangement at Medical Museion. Researchers, novelists and Museion staff invited visitors on a nocturnal journey to discover the brain, melancholia and sleep. Research assistant Morten Gørtz Jønsson and Senior researcher Anke Karabanov explained how electric and electromagnetic brain stimulation is used to treat depression and to boost cognitive abilities. Interactive show-and-tell displays of scientific and clinical brain stimulation equipment were accessible to the visitors throughout the night.

These hands-on demonstrations provided an ideal setting for informal dialogue between citizens and researchers from DRICMR about emerging neurostimulation technology in therapy and recreational use. Through the night, we had several hundred visitors at our demonstrations and the interest from the public was almost overwhelming.



Demonstration of TMS.

Presentation on the history of electric treatments for depression.



COGNITIVE CONTROL OF A HEARING AID

In everyday sound environments, the auditory brain enables us to communicate with a particular person even when other irrelevant sounds reach our ears at the same time. Known as 'The Cocktail Party Effect', this ability to focus attention on one particular talker in a complex sound scene is a remarkable feature of the normal auditory system. Unfortunately, this ability is greatly reduced with hearing impairment. Hearing impaired patients often struggle to communicate in everyday noisy situations, even when they are using a hearing aid. Although the hearing aid restores the acoustic input to the listener, the hearing aid does not know which sounds the impaired listener wants to listen to.

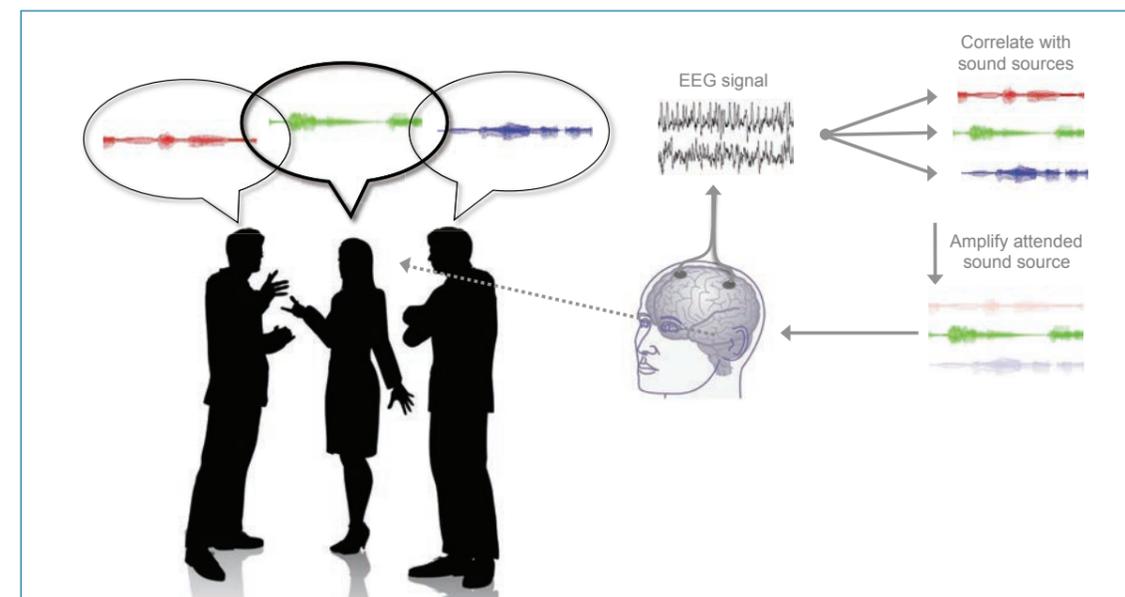
Senior researcher at DRCMR and DTU Electro Jens Hjortkjær is involved in the EU Horizon 2020 project: Cognitive Control of a Hearing Aid (COCOHA) where researchers from the Hearing Systems group at DTU, Danish hearing aid indus-

try and academic partners around Europe collaborate to solve this problem. The idea of the COCOHA project is to use signals from the brain and eyes of a hearing impaired listener to tell the hearing aid which sounds to focus on. Electrodes placed inside or behind the ear pick up brain signals that are analyzed to find out which sound source the listener is attending to. This information is then used to control sound processing in the hearing aid so that irrelevant sounds are filtered out.

The involved researchers demonstrated 'cognitive control' of hearing instruments to HRH Crown Princess Mary and then Minister of Education and Science Sofie Carsten Nielsen – and the story was even released in "Billedbladet".

www.billedbladet.dk/kongelige/danmark/video-nysgerrig-kronprinsesse-mary-ville-gerne-have-haft-boernene-med
The COCOHA project: www.cocoha.org

Jens Hjortkjær (right, above) and Gerard Encina Llamas (right, below) demonstrate 'cognitive control' of hearing instruments to HRH Crown Princess Mary (left) and then Minister of Education and Science Sofie Carsten Nielsen (middle). In this demonstration, eye-tracking technology is used to enhance sounds from the person that the listener is looking towards. After trying the eye-gaze control herself, Crown Princess Mary expressed her fascination with the research. Princess Mary highlighted the beneficial perspectives for the many people who suffer from hearing difficulties. The research demonstration was part of the 2015 opening ceremony of the annual Danish Science Festival organized by the Ministry of Higher Education and Science. The Festival aims to stimulate research interest and to enhance the relationship between researchers and the general public in Denmark. Photo by Alexandre Chabot-Leclerc.



The COCOHA project uses EEG brain signals to determine which talker a listener is attending to in a multi-talker 'Cocktail Party' situation. For a hearing impaired patient, this brain signal can be used to filter out the irrelevant sound sources.



At the Speech-in-Noise (SPiN) 2015 conference, COCOHA researcher Jens Hjortkjær (left) received the Colin Cherry Award for his poster "Single-trial EEG measures of attention to speech in a multi-speaker scenario". The work presented analysis methods that allow the attention of a listener to be decoded from real-time EEG brain signals. The poster award is named after the British cognitive scientist Colin Cherry who first described 'The Cocktail Party effect' in the 1950s. Photo by Alexandre Chabot-Leclerc.

ACADEMIC ACTIVITIES

EDUCATION IS KEY ENHANCING CONFIDENCE, MOTIVATION AND ASPIRATION

All neuroimaging centres are faced with the problem that students come from diverse backgrounds such as mathematics, physics, biology, medicine, economics, psychology, and even further afield. This means that most students are good at some things, yet ill-equipped for others. Typically it's hard to know what it is you need to know, and what it is you don't know. Part of the challenge is that students have to be on the same page to be able to begin to understand one another.

To achieve this we offer a wide-ranging curriculum covering the basic knowledge and skills necessary to follow what is going on at DRCMR and to be able to make an intellectual contribution to whatever their topic. Everyone is expected to be able to ask questions and offer contributions in fields outside of one's own core expertise. The curriculum comprises several modules that most students are expected to take whilst working at DRCMR. Here is a brief overview of the modules:

NEUROIMAGING FOUNDATIONS teaches the most fundamental skills necessary to learn the methods and techniques that are commonly employed at DRCMR. This course assumes almost no prior knowledge and teaches philosophy of science, foundational mathematics, statistics, and programming in Matlab.

NEUROIMAGING BASICS is taught as a peer2peer course where students teach each other with expert help. We cover every major technique used at DRCMR. Our philosophy is that everyone should have a basic grasp of everyone else's research, such that we can critique and think creatively about cross-disciplinary and cross-methodological collaborations. We also have stand-alone workshops in Brain stimulation techniques, Neuroanatomy, Basic Neuroscience, Data quality and much else, on a rolling basis.

MR DRIVER LICENSE gives students the basic training necessary to work in an MR environment, and the scanner license

is the qualification that students need to acquire in order to autonomously operate an MR machine.

MRI ACQUISITION is our course on MR physics. It teaches all of the fundamental physics underlying the magnetic resonance techniques we use at DRCMR. The course introduces MRI starting from a level requiring little or no MR experience. Lectures cover MR understanding, acquisition methods and parameters. The target audience is employees and students at the DRCMR but the course is open for external participants. **PHD COURSES** are held once a year and have a different focus according to actual needs among PhD students and the expertise among DRCMR researchers. The last course, *Tracing brain and behavioral changes across the life span: Influence of intrinsic and extrinsic factors*, was held in January 2016.

WORKSHOPS on Transcranial Magnetic Stimulation (TMS) are held on an annual basis. The course is open to everybody interested in using TMS.

Our classroom during the Neuroimaging Basics course.



THE ANNUAL TRANSCRANIAL MAGNETIC STIMULATION (TMS) WORKSHOP

In November 2016 we organized the 4th annual Workshop on Transcranial Magnetic Stimulation (TMS). The three-day, graduate-level event is meant for international students, scientists and healthcare professionals planning to use TMS as a scientific or therapeutic tool. During the intensive program that interleaves practical and theoretical modules we get a chance to spread our passion for smart, non-invasive brain stimulation applications in research and therapy, and to grow our scientific network beyond Europe's borders: During the last four years more than 80 participants from more than 16 different countries and four continents have participated in the workshop.

WORKSHOP CONTENT

The intensive three-day workshop provides participants with in-depth knowledge on the use of transcranial magnetic stimulation (TMS). The course discusses basic physical and physiological principles of TMS as well as a wide range of cognitive applications. A special focus is put on multimodal combinations of TMS with other neuroimaging techniques (EEG-TMS, fMRI-TMS).

PARTICIPANT FEEDBACK

“All faculty were very professional, helpful and knew a lot about TMS. We've learnt a lot and had a great time.”
Neurologist, Argentina

“Thank you for your hospitality and teaching. I learnt a lot for my TMS studies. The course was great!”
Associate professor, China



Flyer from the TMS workshop 2016.

PHD COURSE 2016

Tracing brain and behavioral changes across the life span: Influence of intrinsic and extrinsic factors

Phd student and medical doctor Katrine Maigaard who took the course had this to say:

The “Lifespan” course kept me on the edge of my seat – from start to finish. The line-up of presenters was impressive and it was a real treat to hear renowned researches from all over the world talking about their work.

The course was structured in a way where one talk naturally led to the next, despite the fact that the topics were widely varied: from genes to environment, from cells to structure, from brain structure to brain function and behavior. The progression between talks was elegant and produced an effective learning environment.

On a very practical level, I came to realize that many of the methodological challenges I thought were specific to my area – the imaging of children – are identical to the concerns of researchers interested in the other end of the spectrum – the ageing brain. That was quite a revelation to me. It was also a great opportunity to meet other students from around the country and the workshop meant that

we had ample opportunity to learn about each other's work, fields and methods.

I walked away with a deeper understanding of typical lifespan changes in brain and behavior and how external factors like diet, stress and exercise affect these, and a new realization of how processes early in life can affect not only childhood development and developmental disorders, but also ageing processes and pathology many decades later.



PhD Student and medical doctor Katrine Maigaard.

NEW ACADEMIC ALLIANCES

It has been a long-standing wish at the DRCMR to strike more academic alliances with the universities in the Greater Copenhagen Area. With an increasing number of researchers affiliated to DRCMR, the need for academic supervision has increased greatly over the years. In 2015–2016, there has been a breakthrough in the establishment of shared academic positions for DRCMR senior researchers.

At the end of 2014, the Capital Region of Denmark initiated a strategic formalized collaboration with DTU that gave a framework for setting up shared positions between the two institutions. This has enabled us to establish three new shared associate professorships with DTU in 2015 and 2016. Within the framework, three senior researchers at DRCMR have received 5-year part-time positions (20%) at DTU as associate professors while maintaining the majority of their work-time at DRCMR. Another long-time collaboration, with the Department of Public Health at the University of Copenhagen, also developed into a half-time associate professorship in 2015, where DRCMR senior researcher Ellen Garde bridges research in healthy ageing between the two institutions.

Finally, a newly established position as senior associate lecturer at the Metropolitan University College was filled by DRCMR senior researcher Kathrine Skak Madsen in 2016. Although not directly a shared position, Kathrine continues her research activities in tight collaboration with the DRCMR. This is both, an important milestone for the DRCMR – as recognition of the research performed at our centre – but even more so for the newly appointed associate professors for whom these appointments represent a significant step forward in their careers. The strengthened academic ties give them much more direct involvement in research and teaching activities at the universities and increasing their interactions with students on a daily level.



KRISTOFFER HAUGAARD MADSEN

Associate professor in statistical machine learning for functional neuroimaging
Technical University of Denmark, Department of Applied Mathematics and Computer Science (DTU-Compute), Section for Cognitive Systems

The Section for Cognitive Systems conducts research and teaching concerning information processing in man and computer, with a particular focus on the signals they exchange – audio, imagery, behaviour – and the oppor-

tunities these signals offer for modelling and engineering of cognitive systems. Functional neuroimaging is a key component of the new position.

TIM BJØRN DYRBY

Associate professor 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

The Section for Image Analysis and Computer Graphics conducts research, teaching and innovation in mathematical modelling of geometry including deformable models, computer vision, multivariate statistics and computer

graphics. Multi-modal medical image analysis in preclinical and diagnostic imaging is a key component of the new position.



ESBEN THADE PETERSEN

Associate professor in ultra-high field MRI
Technical University of Denmark, Department of Electrical Engineering (DTU-Electro), Center for Magnetic Resonance

The Center for Magnetic Resonance at DTU-Electro conducts research related to Magnetic Resonance Imaging and Spectroscopy (MRI, MRS), most notably in the fields of hyperpolarization and its applications, integration of

neuroimaging and neurostimulation, and MRI/MRS methodology. Ultra-high field MRI in preclinical and diagnostic imaging is central in the new position.



ELLEN GARDE

Associate professor in population neuroimaging
University of Copenhagen, Medical Psychology Unit, Department of Public Health and Center for Healthy Aging

Department of Public Health conducts basic research in effect of environmental factors throughout the lifespan using methods that range from experimental models to register-based epidemiology and the Center for Healthy Aging

primarily focuses on multi-disciplinary aging research from molecular biology to the humanities. The position includes managing and conducting larger MR cohort studies.



KATHRINE SKAK MADSEN

Senior associate lecturer in neuroimaging
Metropolitan University College, Department of Technology

The Department of Technology offers four Bachelor programmes, one of which is Radiography. The radiographer program conducts research and teaching within the broader field of radiography. The department has recently scaled

up its research activities in biomedical imaging and radiography. Neuroimaging and research management is central in the new position.



DISSEMINATIONS

10 PhD candidates defended their theses at DRCMR in 2015–16.

The PhD's were done in collaboration with The University of Copenhagen, The Technical University of Denmark and Copenhagen Business School.

MEDICATION-INDUCED IMPULSE CONTROL DISORDERS IN PARKINSON'S DISEASE

Brian Numelin Haagenen



SUMMARY

The project investigated neurobiological correlates of impulse control disorders (ICD) in Parkinson's disease (PD), related to dopamine replacement therapy.

Most common ICD types are pathological gambling, compulsive sexuality, binge eating disorders and compulsive shopping. We scanned 13 PD patients with and 13 PD patients without ICD using functional MRI (fMRI) on two occasions: ON and OFF usual dopamine replacement therapy. Patients performed a dice-gambling task during fMRI that allowed to measure brain activity in relation to accumulating gambling reward, risk and losses of varying sizes. In patients with ICD dopaminergic therapy changed activity in basal ganglia in response to both accumulating rewards/risk and losses. Average activity in key motor inhibitory regions was lower in patients with ICD during both ON and OFF scans. Also, dopaminergic therapy diminished the functional coupling between key nodes of the inhibitory network in patients with ICD. The results indicate that ICD is related to medication-induced changes in monetary risk, reward and loss processing in striatum and at the same time also diminished activity as well as coupling within motor inhibitory networks.

SUPERVISORS

Professor Hartwig R. Siebner, DRCMR

Associate professor Kristoffer H. Madsen, DRCMR

Associate professor Annemette Løkkegaard, Bispebjerg Hospital

UNIVERSITY

University of Copenhagen

DATE OF DEFENCE

September 26th, 2016

WORKING TODAY

Psykiatrisk Center København

DEVELOPMENT AND APPLICATION OF TOOLS FOR MRI ANALYSIS

Christian Thode Larsen



SUMMARY

The thesis presents results from the intervention study "Preserving cognition, quality of life, physical health and functional ability in Alzheimer's disease: the effect of physical exercise" (ADEX). Results were obtained using longitudinal Freesurfer analyses. Exercise load correlated with changes in the hippocampus and in frontal and cingulate cortical thickness. Furthermore, changes in frontal and cingulate cortical thickness were found to correlate with changes in several cognitive performance measures, including mental speed, attention and verbal fluency.

The thesis also explains correction of the bias field artifact using expectation maximization (EM) based methods. It shows how the popular (but heuristic) method N3, in fact, implicitly uses the same generative models and computational strategies, and that purely EM-based methods yield comparable results in less computation time. Finally, a new generative model for longitudinal data, and one that does not require brain masking or probabilistic anatomical atlases to perform well, are presented. All methods are publicly available in the software package "Intensity Inhomogeneity Correction".

SUPERVISORS

Associate professor Koen Van Leemput, DTU Compute

Associate professor Ellen Garde, DRCMR

UNIVERSITY

Technical University of Denmark

DATE OF DEFENCE

December 7th, 2015

WORKING TODAY

Chief Technology Officer at getQueried ApS

MAPPING NEURAL CORRELATES OF VALUE-BASED SEQUENTIAL DECISION-MAKING WITH FMRI

David Meder



SUMMARY

This PhD project addressed the neural mechanisms involved in stay (exploiting ongoing courses of action) vs. switch decisions (choosing a different action) in two different settings. The first setting investigated sequential risky decision-making where subjects had to decide between either continuing foraging (i.e. “stay” choice, involving potentially higher reward but also higher risk of losing) or stopping the forage and harvesting the accumulated rewards (“switch” choice, entailing a lower but safe reward). We found anterior cingulate cortex to be involved in processing different objective and subjective parameters of foraging and we described how the inhibitory control network mediates these risky decisions. The second setting was a task where subjects had to track changing stimulus-outcome probabilities in a 2x2 design, varying outcome valence (reward vs. punishment) and domain (low-salience abstract stimuli vs. highly salient facial expressions). Several regions showed a higher positive scaling of activity with positive surprise (prediction error) in reward-seeking compared to punishment-avoidance conditions, suggesting that the brain is geared towards processing “better-than-expected” rather than “less-bad-than-expected” outcomes.

SUPERVISORS

Professor Hartwig R. Siebner, DRCMR
Senior researcher Oliver Hulme, DRCMR

UNIVERSITY

University of Copenhagen

DATE OF DEFENCE

January 9th, 2015

WORKING TODAY

Postdoc at DRCMR

MODELLING STRUCTURAL BRAIN CONNECTIVITY

Karen Marie Sandø Ambrosen



SUMMARY

Tractography based on diffusion-weighted MRI can be used to estimate the structural brain connections non-invasively and “in vivo”. This estimate is, however, noisy and depends on a great number of parameters that have to be specified by the experimenter. In this PhD project the utility of statistical modelling to aggregate the noisy estimates obtained using tractography and thereby quantifying the underlying structural organization of the brain was explored. Furthermore, the influence of some of the scan acquisition parameters was quantified by comparing the brain connections estimated using tractography to brain connections estimated using invasive tracer injections in monkeys.

SUPERVISORS

Associate professor Morten Mørup, Department of Applied Mathematics and Computer Science, DTU
Associate professor Tim B. Dyrby, DRCMR and Department of Applied Mathematics and Computer Science, DTU
Mikkel Nørgaard Schmidt, Department of Applied Mathematics and Computer Science, DTU

UNIVERSITY

Technical University of Denmark

DATE OF DEFENCE

March 13th, 2017

WORKING TODAY

Postdoc at Department of Applied Mathematics and Computer Science, Technical University of Denmark

INFERRING HUMAN INTENTIONS FROM THE BRAIN DATA

Konrad Stanek



SUMMARY

The human brain is a complex organ composed of approximately a hundred billion interacting neural cells. Complex patterns of dynamic electric discharges across the neural tissue are responsible for emergence of higher cognitive function, conscious perception and voluntary action. This thesis contributes to our understanding of the dynamics of voluntary decision processes about prospective action. We probe different types of decisions, compare them in terms of behavioral and EEG characteristics, and show that decision processes are manifested by complex, broadband modulation of brain oscillatory patterns, primarily in alpha (8–12Hz) and beta (16–30Hz) ranges. Our results suggest that decisions about whether to act or not, what type of action to perform, and about the timing of the action have distinct dynamic representations, and thus are to extent mediated by different neural components. Free action can be partially explained by low level behavioral preferences. We have developed a flexible Virtual Reality Environment (VRE) platform suitable for neuroscientific study of cognition with EEG, fMRI, eye-tracking and behavioral measures, which provides ecologically valid, semi-realistic experience and reinforces the natural decision processes.

SUPERVISORS

Professor Ole Winther, DTU Compute
Professor Hartwig R. Siebner, DRCMR
Professor Lars Kai Hansen, DTU Compute

UNIVERSITY

Technical University of Denmark

DATE OF DEFENCE

October 12th, 2016

WORKING TODAY

DTU Compute, Cognitive Systems

NEUROTICISM AND FUNCTIONAL CONNECTOMICS OF THE RESTING ADOLESCENT BRAIN

Louise Barué Johansen



SUMMARY

The personality trait neuroticism is a well-known risk factor for anxiety and mood disorders with onset in childhood and adolescence. This thesis examines whether associations between neuroticism and characteristics of the functional brain network are already present in children and adolescents. Network analysis was applied to resting-state functional MRI acquired in a cohort of healthy children and adolescents. Cross-sectional analyses revealed that higher neuroticism scores were associated with less efficient information processing in the whole-brain network. On a local level, the orbitofrontal network had a less prominent role within the network the higher individuals scored on the neuroticism scale. Longitudinal analyses confirmed the latter finding, but the association did not change over the age range covered by the cohort. The diminished role of the orbitofrontal network, involved in evaluating action-outcome associations, may underlie the inflexible and negatively biased appraisal of situations that typically is associated with neuroticism. The reliability of the estimated network properties was low and we speculate this to be caused by fluctuations in mental states.

SUPERVISORS

Professor Hartwig R. Siebner, DRCMR
Senior researcher William F.C. Baaré, DRCMR
Senior researcher Kathrine Skak Madsen, DRCMR

UNIVERSITY

University of Copenhagen

DATE OF DEFENCE

April 6th, 2016

WORKING TODAY

Postdoc at DRCMR and at Copenhagen University
Hospital Glostrup

TOWARDS MOTION- INSENSITIVE MAGNETIC RESONANCE IMAGING USING DYNAMIC FIELD MEASUREMENTS

Mads Andersen



SUMMARY

Subject motion during scanning is one of the main challenges in MR imaging and spectroscopy lowering diagnostic image quality in the clinical practice and the data quality in research.

In my thesis three studies are presented that investigate new methods for correcting three different effects of head motion in MR acquisitions of the brain.

In study 1, a technique is developed for monitoring motion of the head and updating the imaging volume in real time to follow the head position (prospective motion correction). This is done based on acquired signals from an electroencephalography (EEG) cap that the subject wears during scanning.

In study 2, the effect of head motion on the transmitted radiofrequency field is studied, focusing on single voxel spectroscopy where this effect is believed to have a significant impact.

Motion of other body parts (e.g. breathing) can give artefacts in brain imaging, through fluctuations in the background field.

In the 3rd study, it was investigated how field sensors placed around the head can help stabilize such fluctuations.

SUPERVISORS

Associate professor Lars G. Hanson, DRMR and DTU Elektro
Associate professor Kristoffer H. Madsen, DRMR and DTU Compute

UNIVERSITY

Technical University of Denmark

DATE OF DEFENCE

February 5th, 2016

WORKING TODAY

Clinical scientist for Philips at the 7T MR facility at Lund University Hospital

NEURAL AND ENDOCRINOLOGICAL CORRELATES OF GLUCOCORTICOID TREATMENT IN CHILDREN

Martin Vestergaard Gøtzsche



SUMMARY

Full Title: Neural and endocrinological correlates of previous glucocorticoid treatment in children.

The aim of the present PhD project was to examine whether treatment with synthetic glucocorticoids during childhood and adolescence might trigger changes in fronto-limbic brain structure and function as well as diurnal cortisol levels. Children and adolescents previously treated with glucocorticoids for rheumatic disease or nephrotic syndrome were included in the study and matched to healthy controls. Findings suggested that glucocorticoid treatment was linked to increases in diurnal cortisol levels as well as differences in fronto-limbic white matter microstructure and brain function during encoding of fear-associated input.

SUPERVISORS

Professor Hartwig R. Siebner, DRMR
Professor Peter Uldall, Department of Paediatrics and Adolescent Medicine, Neuropaediatric Unit, Copenhagen University Hospital Rigshospitalet
Senior researcher William Baaré, DRMR
Senior researcher Kathrine Skak Madsen, DRMR

UNIVERSITY

University of Copenhagen

DATE OF DEFENCE

January 19th, 2015

WORKING TODAY

Psychiatric Research Unit, Psychiatry Region Zealand, Denmark

THE ASSOCIATIVE NATURE OF CREATIVITY

Morten Friis- Olivarius



SUMMARY

Our ability to create is one of the most unique of human traits and the very key to our successful evolution and superiority as a species. Yet, compared to other sciences little is known about the nature of the mechanisms underlying this extraordinary ability. Even though Sigmund Freud already at the birth of psychology postulated that creativity is connected to the unconscious, we still don't know whether and how original ideas emerge automatically in the brain.

Across three studies, the dissertation investigated this knowledge gap and provides first-time evidence that not only does creative individuals differ in how their associative memory system respond to stimuli in the environment, but that more associates are automatically made accessible for ideation, even when no ideation is explicitly called for. This was shown to be automatic, detectable at the neural level, and tied to the stimulus-specific ability to produce ideas. Furthermore, metacognition and manipulation of the associative system was shown to be a most effective instrument in creativity training.

SUPERVISORS

Professor Bo T. Christensen, Copenhagen Business School
Senior Researcher Thomas Z. Ramsøy, DRMR & Center for Decision Neuroscience

UNIVERSITY

Copenhagen Business School

DATE OF DEFENCE

March 26th, 2015

WORKING TODAY

Center for Decision Neuroscience, CBS & Copenhagen Institute of Creativity

BRAIN FUNCTION AND STRUCTURE IN CHILDREN TREATED WITH GLUCOCORTICIDS

Sara Krøis Holm



SUMMARY

Full title: Brain function and structure in children and adolescents treated with glucocorticoids during childhood. Glucocorticoids are used in treatment of several paediatric diseases. The aim of the thesis was to evaluate whether children with either nephrotic syndrome or rheumatic disease previously treated with glucocorticoids during childhood have different brain function and structure in comparison to healthy controls. Firstly, we found lower verbal intellectual abilities in patients relative to controls, while no differences in perceptual intellectual abilities, memory performance, or behavioural problems were identified. Secondly, we used MRI to measure global brain volumes and found smaller white matter and cortical grey matter volumes in patients relative to controls. Finally, we combined morphometric and diffusion-weighted MRI to evaluate volume and microstructure of subcortical limbic and striatal regions-of-interest. The results warrant larger and preferably longitudinal studies of potential impact of glucocorticoid treatment on the developing brain.

SUPERVISORS

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Professor Hartwig R. Siebner, DRMR
Alfred Peter Born, Rigshospitalet
Senior researcher Kathrine Skak Madsen, DRMR

UNIVERSITY

University of Copenhagen

DATE OF DEFENCE

May 5th, 2015

WORKING TODAY

Department of Pediatrics and Adolescent Medicine, Copenhagen University Hospital Rigshospitalet

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Torkil Svendsgaard,
System Administrator

TECHNICIANS

Hanne Schmidt,
Research Radiographer

Sascha Gude, Research Medical
Laboratory Technologist

Sussi Larsen, Research Medical
Laboratory Technologist

COMING TO DRCMR

Ayna Baladi Nejad

I obtained my PhD at the DRCMR carrying out a longitudinal fMRI study of schizophrenia patients. As a PhD student, I was free to focus the study to my specific interests and further pursue those interests at specialized international meetings and lab stays. This brought me into contact with people who would later facilitate my postdoc positions in Paris and Boston. Although my stay abroad was exciting, I was very happy to return in 2015 to an institution that is remarkably friendly but also uncompromising in the high scientific standards it expects from its research teams. Junior DRCMR researchers have autonomy and plentiful resources available to them which are two things that are otherwise hard to find together in other institutions. Furthermore, my priorities have now expanded to include family and there is a very real understanding of the importance of life outside work at DRCMR and in Denmark, generally.



Oula Puonti

I started as a postdoctoral researcher at DRCMR in May 2016 after having finished my PhD studies in Informatics at the Technical University of Denmark. During my PhD project I developed methods for computational analysis of MR brain images in both healthy subjects as well as subjects suffering from pathologies such as lesions and tumors.



My current project focuses on creating accurate, patient-specific head models for electric and magnetic field simulations. These models can be used for precise targeting of brain structures when using TMS or TDCS, or for EEG and MEG source reconstruction. The main focus of my work is to create tools for robust segmentation of the head anatomy from MR scans which is the first step in the construction of the head models.

I applied for a postdoc position at DRCMR to get a chance to pursue my interests in computational brain analysis in one of the leading research centres in the field of biomedical MRI in Europe. The interdisciplinary environment and state-of-the-art imaging facilities at DRCMR are vital for testing and discussing new ideas, and further developing my skills as a researcher.

David Meder

I am a psychologist by training and first joined DRCMR in 2010. After finishing my PhD at the DRCMR, I went to the University of Oxford to join one of the world-leading groups in the field of decision neuroscience led by Prof. Matthew Rushworth. Here, I worked on a project on the neural correlates of learning and decision-making where I developed a new technique for analysing MR-images of brain activity. Even though my time in Oxford was wonderfully inspiring and a great personal and scientific success, I was also very thankful for the opportunity to return to DRCMR. The DRCMR offers a truly unique collaborative and international work environment. The large number of researchers from many different scientific and cultural backgrounds requires more formalized coordination than in smaller laboratories. However, having so many experts in many different areas within the same building also allows us to perform research at the highest possible level, combining many different techniques.



Mitusaki Takemi 武見充晃

I came to work as a post-doctoral researcher at the DRCMR in April 2015 after having finished my PhD study in Neural Engineering at the Graduate School of Science and Technology, Keio University in Japan. My PhD work was focusing on the interaction of EEG-based brain-computer interface on human corticospinal system. Besides that, I studied hand motor control in non-human primates by using invasive brain stimulation and recordings at RIKEN Brain Science Institute. Currently I am involved in the BaSiCs project under the supervision of Prof. Hartwig R. Siebner and funded by a postdoc fellowship from the "Japan Society for the Promotion of Science".



My main motivation to come to the DRCMR was to establish a new transcranial brain stimulation (TBS) method that is suitable for closed-loop application. Closed-loop methods deliver TBS at a time when a specific response is observed in ongoing brain signals, enabling establishment of links between specific brain responses and their function by actively manipulating them. However, the development of closed-loop TBS methods

is highly technically demanding and requires fundamental knowledge on multiple topics. Researchers at the DRCMR have various backgrounds, such as medicine, psychology and engineering. This environment allowed me to get suggestions from different points of view and thus to accelerate my research. I have no doubt that coming to the DRCMR has given me the chance to expand on my expertise, to work with an interdisciplinary group and to contact with international researchers.

Anouk Marsman

I came to work at DRCMR in April 2015 after 2 years in the United States. After obtaining a MSc degree in Biology at the University of Groningen, The Netherlands, I started my PhD studies in 2008 at the University Medical Center Utrecht, also in The Netherlands. A 7T MR system was just installed and my work focused on exploring the possibilities for psychiatric MRS research at 7T and initiating a 7T MRS study on schizophrenia. In 2013 I obtained my PhD degree and started a postdoc at the Johns Hopkins University in Baltimore. I was involved in MRS studies on schizophrenia and first-episode psychosis, and I worked on MR spectroscopic imaging of high-grade glioma. In 2015 I decided to go back to Europe to be together again with my now-husband Vincent Boer. We were very lucky that our former colleague from Utrecht Esben Petersen offered us both a position in his new Ultra-High Field Group at DRCMR as part of the Danish National 7 Tesla MR Project. I am involved in several high-field MRS studies including research on healthy ageing and the development of new MRS techniques. As the 7T scanner is a national initiative, I also work together with external collaborators on 7T MRS studies in the fields of psychiatry, neurology and endocrinology. DRCMR has given me ample opportunity and support to develop my own research ideas, and distinguishes itself as an international and interdisciplinary work place by a personal approach and facilitation of a healthy work-life balance.



Vincent Boer

I am a physicist from the Netherlands, and I have been doing research with high field MRI scanners mainly at the University Medical Center in Utrecht, The Netherlands. Coming to Denmark and joining the DRCMR has been a great experience,



as a new high field MRI magnet has just been installed that will allow us to do new exciting research on imaging the human brain. In the two years that I'm now at the DRCMR, I've integrated into a group of broadly interested and internationally oriented scientists. I moved here together with Anouk Marsman and we both have the chance to work on the strongest MRI scanner in Denmark. It's been great to be involved in the start of the 7T project here at the DRCMR. We've learned a lot about the system in the start-up phase, and I'm convinced we can keep developing new and exciting methods together with everyone using the system, so that we can keep discovering new things in the brain.

Lene Cividanes

I am a political scientist by training and until I joined the DRCMR in September 2015 I knew nothing about the brain or MRI – and I am still far from being an expert, but I am learning every day from all the talented students and researchers at the DRCMR. I was hired by the leadership as a Senior advisor to focus on development of the more strategic aspects of the DRCMR along with a number of other tasks such as communication, relations with the Danish Health Authorities as well as relevant authorities within science, research and innovation, external financing, external collaboration, political and ethical aspects of research and career development. Before I came to the DRCMR I worked eight years in the Danish central administration – mainly as a special advisor on international relations at the Danish Agency for Science, Technology and Innovation. I was responsible for negotiating and developing agreements on international collaboration within political prioritised research fields as well as for advising researchers based in Denmark on how to engage in international collaboration within the framework of the Danish Research Council for Strategic Research.



It has been great joining the DRCMR. I really enjoy working in the ambitious, international environment with researchers from a wide range of disciplines; however it has also been challenging to adapt to a completely different workflow and mind-set.

VISITING PROFESSOR: CARL-JOHAN BORAXBEKK

Thanks to generous support from Lundbeckfonden, I was able to move from Umeå University in the northern parts of Sweden and join the DRCMR as a visiting Professor in October 2016. The central goal of my research is to study life-long brain plasticity and to obtain unique insights into the potential for neuro-enhancement in the ageing population. The objective to come to DRCMR, was to strengthen the profile within life-long brain plasticity by creating synergies between groups of healthy ageing research, motor control, and non-invasive brain stimulation.

step was reached when a motor-cognitive communication task was developed to specifically examine successful brain communication in ageing, and some initial piloting is showing potential. This is an exciting project that could pave the way for future efforts to maintain or restore brain health in ageing and to take care of our growing older population. I have also had many inspiring discussions with the healthy ageing group regarding ways of analyzing multi-modal imaging data. This is an important topic considering that more research sites across the world are collecting a large quantity of brain imaging data,

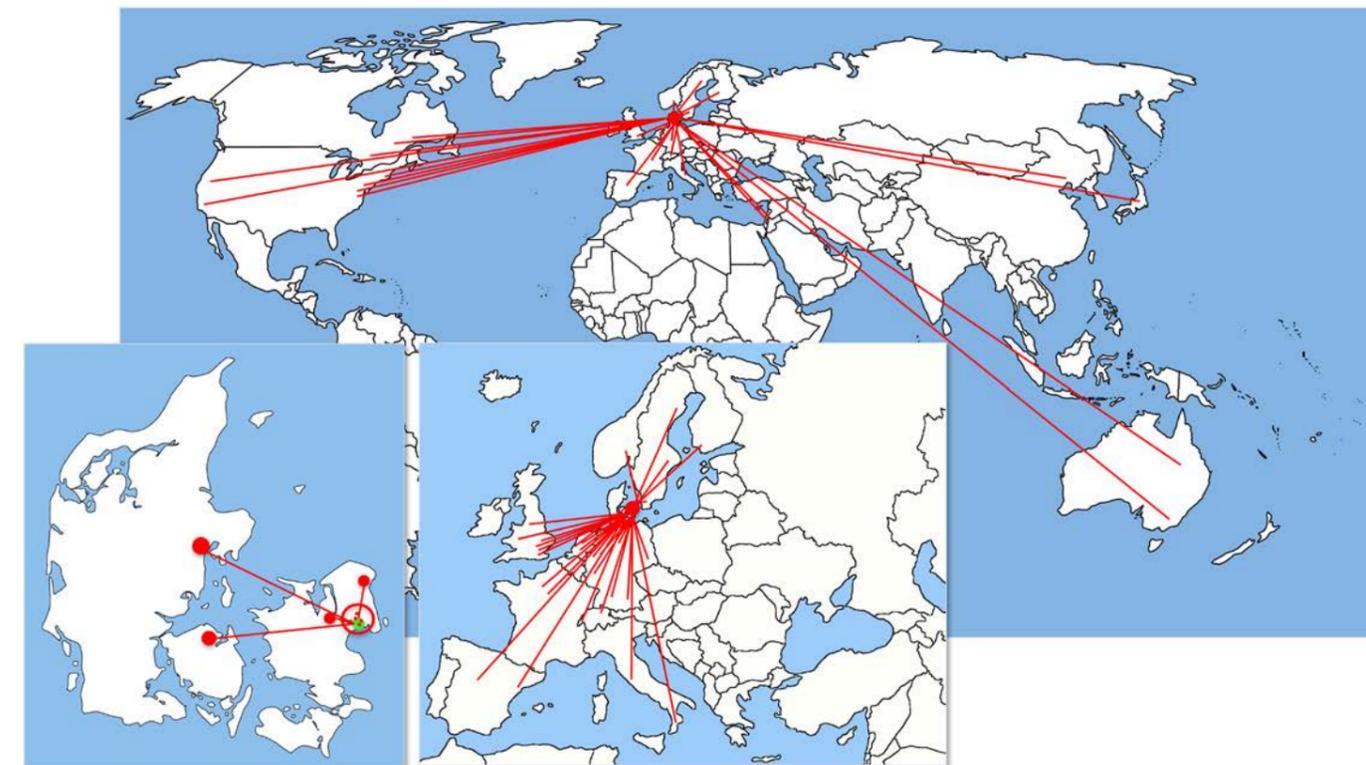


Moving to Denmark from Sweden is of course not a particularly dramatic move. After all, there is a bridge between the two countries. Nevertheless, this isn't without challenges. One is the language...this became obvious to me already the first day, actually even before I came to the centre. DRCMR is located in Hvidovre, if you're not Danish and tries to pronounce this place, you are for sure doing it wrong. I don't know how many times I tried to explain to the bus driver where I wanted to go before he understood; I still don't know how to properly pronounce it. Being at DRCMR is exciting, people from all over the world meets in a working environment full of enthusiasm and talent. So far, great progress in designing a novel interventional study using transcranial alternating current stimulation to improve brain functions in older people has been made. An important

but how to best handle and combine all these data is not a trivial problem. Also, discussions with the brain maturation group about ways of understanding brain development and creating novel cohorts based on some of the unique Danish registers are ongoing. It is an intriguing approach to utilise the strengths of population based register-data in a completely novel way to understand brain development, something that is a rather unique possibility in Scandinavian countries. I am very much looking forward to continue with this work, and, in the future, establish more fruitful collaborations between DRCMR and my other lab Umeå center for Functional Brain Imaging. We share many of the scientific challenges associated with brain imaging, and together I am sure we can deepen our understanding about the human brain.

SUCCESSFUL INTERNATIONALISATION AT THE DRCMR

Internationalisation is highly prioritised at the DRCMR. We have a long tradition of international collaboration with successful research sites from all over the world and in parallel we focus on attracting young talented researchers as well as highly specialised experts from abroad to join the research groups at the DRCMR. In 2015–16, researchers and students from 27 nations were present at the DRCMR and we had bilateral collaborations with a large number of research sites in the world. On top of that comes all the multilateral projects we participate in – mainly within the framework of the EU.



The DRCMR is a very international work environment and we have had students or researchers from all these countries in 2015–16.

COLLABORATIONS

NATIONAL COLLABORATIONS

Aarhus University, Aarhus, Denmark

Center of Functionally Integrative Neuroscience

Assoc. Professor Torben Lund, Assoc. Professor Sune Jespersen, Simon Eskildsen, Professor Leif Østergård

Center for Insoluble Protein Structures (inSPIN)

Professor Niels Christian Nielsen

Danish School of Education

Assoc. Professor Lisser Rye Ejersbo

Department of Chemistry

Professor Niels Christian Nielsen

Interdisciplinary Nanoscience Center (iNANO)

Professor Niels Christian Nielsen

MR Research Centre, Department of Clinical Medicine

Professor Hans Stødkilde Jørgensen

The Danish Research Institute of Translational Neuroscience – DANDRITE

Assoc. Professor Duda Kvitsiani

Albeda Research Aps

Drs. Mathilde Lerche, Magnus Karlsson

Copenhagen Business School, Frederiksberg, Denmark

Department of Marketing, Decision Neuroscience Research Group

Martin Skov

H. Lundbeck A/S, Lundbeck Research, Valby, Denmark

Dr. Michael Didriksen, Lead scientist, Kenneth Vielsted Christensen, Principal Scientist

Metropolitan University College, Radiography

Senior associate lecturer Kathrine Skak Madsen, Anne-Mette Briand de Crevecoeur

Odense University Hospital, Odense, Denmark

Department of Neurology

Professor David Gaist

Department of Neurology

Professor Zsolt Laszlo Illés

Steno Diabetes Center, Copenhagen

Professor Peter Rossing

Technical University of Denmark, Lyngby, Denmark

Department of Electrical Engineering

Assoc. Professors Sadasivan Puthusserypady, Helge B. Sørensen, Vitaliy Zhurbenko, Pernille Rose Jensen, Professors Torsten Dau, Jan Henrik Ardenkjær-Larsen

Department of Applied Mathematics and Computer Science

Assoc. Professor Koen van Leemput, Professor Lars Kai Hansen, Professor Rasmus Larsen, Assoc. Professor Morten Mørup

Department of Physics

Professor Ulrik Lund Andersen

University of Copenhagen, Copenhagen, Denmark

Faculty of Health and Medical Sciences

Cluster for Molecular Imaging, Department of Biomedical Sciences

Professor Andreas Kjær

Department of Biostatistics

Assoc. Professor Klaus Köhler Holst

Department of Food and Resource Economics

Assoc. Professor Toke Reinhold Fosgaard

Department of Neuroscience and Pharmacology

Professor Jens Bo Nielsen, Professor Maurice Plito, Professor Ron Kupers

Department of Nutrition, Exercise and Sport Sciences

Professor Jens Bo Nielsen, Assoc. Professor Nikolai Nordsborg, Assoc. Professor Mark Schram Christensen

Institute of Public Health, Department of Health Psychology

Professor Erik Lykke Mortensen

Wilhelm Johannsen Centre for Functional Genome Research,

Department of Cellular and Molecular Medicine

Professor Niels Tommerup

Center for Healthy Aging

Professor Lene J. Rasmussen

Faculty of Humanities

Department of Economics

Assoc. Professor Alexander Sebald

Department of Scandinavian Studies and Linguistics

Assoc. Professor Kasper Boye

Faculty of Sciences

The Department of Computer Science

Professor Mads Nielsen, Assoc. Professor Sune Darkner

Faculty of Social Sciences

The Unit for Cognitive Neuroscience, Department of Psychology

Professor Jesper Mogensen

University of Southern Denmark, Odense, Denmark

Department of Psychology

Assoc. Professor Christian Gerlach

Institute of Clinical Medicine

Professor David Gaist

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Department of Neurology

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Department of Radiology

Senior Consultant Anders Christensen

Research Laboratory for Stereology and Neuroscience

Professor Bente Pakkenberg

Department of Clinical Medicine

Professor Michael Kjær

Copenhagen University Hospital Hvidovre

Gastro Unit Surgical Division

Chief Consultant Svend Schulze, Professor Thue Bisgaard

Department of Clinical Medicine

Professor Sten Madsbad

Clinical Research Center

Assoc. Professor Thomas Bandholm

Copenhagen University Hospital Rigshospitalet

Centre for Integrated Molecular Brain Imaging, Neurocenter

Professor Gitte Moos Knudsen, Professor Olaf B. Paulson, Dr. Vibe Frøkjær, Dr. Patrick Fisher

Danish Multiple Sclerosis Centre, Neurocenter

Professor Finn Sellebjerg, Professor Per Soelberg Sørensen, Consultant Morten Blinkenberg

Danish Dementia Research Centre, Neurocenter

Professor Gunhild Waldemar

Department of Clinical Physiology, Nuclear Medicine and PET

Professor Andreas Kjær

Department of Paediatrics and Adolescent Medicine

Professor Peter Uldall, Peter Born PhD

Department of Radiology

Professor Carsten Thomsen

Department of Rheumatology

Professor Mikkel Østergaard

Functional Imaging Unit

Assoc. Professor Egill Rostrup

Psychiatric Centres in the Capital Region

Centre for Clinical Intervention and Neuropsychiatric Schizophrenia Research, Glostrup

Professor Birte Glenthøj, Bjørn Ebdrup PhD

Danish Research Institute for Suicide Prevention – DRISP
Professor Merete Nordentoft

Child and Adolescent Psychiatric Centre Bispebjerg
Professor Kerstin Plessen, Consultant Katrine Pagsberg PhD

Psychiatric Centre Nordsjælland Hillerød

Professor Per Beck

Psychiatric Centre Rigshospitalet

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University College London, London, United Kingdom

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Sobell Department of Motor Neuroscience and Movement Disorders

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University Medical Center Utrecht, Utrecht, The Netherlands

Image Sciences Institute

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Department of Radiology

Professor Jeroen Hendrikse, Professor Peter Luijten, Assoc. Professor Dennis Klomp, Assoc. Professor Hans Hoogduin

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Leiden University Medical Center, Leiden, The Netherlands

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Center for Human Development

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University of Leipzig, Leipzig, Germany

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Biomedical Imaging Institute

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University of Medicine and Dentistry of New Jersey, USA

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University of Messina, Messina, Italy

Department of Neurosciences, Psychiatry and Anaesthesiological Sciences

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University of Montreal, Canada

School of Optometry

Professor Maurice Ptito

Department of Physiology/Biomedical Engineering

Claudien Gautier

University of Oslo, Oslo, Norway

Centre for the Study of Human Cognition

Professor Kristine Walhovd, Professor Anders Fjell

University of Queensland, Brisbane St Lucia, Australia

Queensland Brain Institute

Assoc. Professor Martha Garrido

University of Zürich, Zürich, Switzerland

Department of Economics

Dr. Justin Chumbley

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Australia National University, Canberra, Australia

Centre for Research on Ageing, Health and Wellbeing

Professor Kaarin Anstey

Research Centre for the Neurosciences of Ageing, Academic Unit of Psychiatry and Addiction Medicine

Assoc. Professor Jeffrey Looi

Brookhaven Laboratory, New York, USA

Medical Department

Professor Helene Benveniste

Cambridge University, Cambridge, United Kingdom

Department of Clinical Neurosciences; Medical Research Council Cognition and Brain Sciences Unit

Professor James B Rowe

Centre de Recherche de l'Institut du Cerveau et de la Moelle Épinière, Paris, France

CENIR – Centre for Neuroimaging Research

Professor Stéphane Léhericy

Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

Dr. Antoine Lutti

Charité University Medicine Berlin, Germany

Department of Neurology

Professor Andrea Kühn

Chinese Academy of Sciences

Institute of Biophysics

Professor Rong Xue

Institute of Psychology

Professor Raymond Chan, Associate professor Yuan Zhou

Christian-Albrechts-University, Kiel, Germany

Institute for Medical Psychology and Medical Sociology

Professor Michael Siniatchkin

Department of Neurology

Oliver Granert

Institute for Sexual Medicine

Priv.-Doz. Jorge Posenti

Concordia University, Montreal, Canada

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CR Developments AB, Lund, Sweden

Samo Lasic, Karin Bryske

Eberhard Karls Universität Tuebingen, Germany

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Ecole Normale Supérieure, Paris, France,

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École polytechnique fédérale de Lausanne, Lausanne, Switzerland

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Consiglio Nazionale delle Ricerche, Isola Tiberina, Rome, Italy

Istituto di Scienze e Tecnologie della Cognizione

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Lund University Hospital, Lund, Sweden

Department of Medical Radiation Physics

Professor Freddy Ståhlberg, Assoc. Professor Gunther Helms, Lecturer Markus Nilsson, Assoc. Professor Martin Beck

Department of Physical Chemistry

Professor Daniel Topgaard

Massachusetts General Hospital, Harvard Medical School, Charlestown, Massachusetts, USA

A Martinos Center for Biomedical Imaging

Assoc. Professor Koehn van Leemput

Max Planck Institutes, Germany

Biological Cybernetics, Tübingen

Professor Klaus Scheffler

Human Cognitive and Brain Sciences, Leipzig

Dr. Thomas Knösche, Professor Robert Turner, Professor Nikolaus Weiskopf

Neurological Research, Cologne

Assoc. Professor Marc Tittgemeyer

Munich University of Technology, Munich, Germany

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Professor Volker Mall

Neurospin, Gif-sur-Yvette, France

Laboratoire de Neuroimagerie Assistée par Ordinateur

Professor Jean-François Mangin

Oxford University, Oxford, United Kingdom

Department of Physiology, Anatomy and Genetics

Dr. Kristine Krug

Division of Cardiovascular Medicine, Radcliffe Department of Medicine

Professor Jürgen Schneider and Irvin Teh

Decision and Action Laboratory, Dept. of Experimental Psychology

Professor Matthew Rushworth and Junior Research Fellow Nils Kolling

Philips Healthcare

Dr. Mads Andersen

Radboud University Nijmegen, Nijmegen, The Netherlands

Department of Neurology

Professor Bastian Bloom

INTERNATIONAL MULTI-CENTRE RESEARCH COLLABORATIONS

Neuroprotective autologous mesenchymal stem cells for multiple sclerosis – A randomised, placebo controlled, blinded phase II trial (MESEMS):

Danish Multiple Sclerosis Research Center

Department of Clinical Immunology Rigshospitalet

University of Genoa – Department of Neurosciences

Ottawa Hospital Research Institute – MS Research Clinic

University Hospital Basel – MIAC, Queen Square – Queen Square MS Centre

European cooperation in science and technology (COST) framework:

1. COST Action BM1309: European network for innovative uses of EMFs in biomedical applications (EMF-MED)
2. Arterial spin labelling Initiative in Dementia, European cooperation in science and technology (COST) framework.

EU Joint Programme – Neurodegenerative Diseases (JPND) Research 2016 call: “Working Groups for Harmonisation and

Alignment in Brain Imaging Methods for Neurodegeneration”

1. ASAP SynTau: Alignment and Standardization of Neuroimaging Methods in Atypical Parkinsonism, specifically Synucleinopathies and Tauopathies
Coordinator: Thilo van Eimeren, University of Cologne, Germany;
Co-coordinator: Hartwig R. Siebner, University of Copenhagen, Denmark
2. EUFIND: European Ultrahigh-Field Imaging Network for Neurodegenerative Diseases
Coordinators: Emrah Duzel and Oliver Speck, University of Magdeburg, Germany

Neuroimaging Study Group in Movement Disorders

Steering Committee: Nico Bohnen, Stephane Lehericy, Oury Monchi, Hartwig R. Siebner, John Stoessl

<http://www.movementdisorders.org/MDS/About/Committees--Other-Groups/Study-Groups/Neuroimaging-Study-Group-in-Movement-Disorders.htm>

CLINICAL TRIALS

Collaborators in Clinical Trials include:

AC-Immune SA

Biogen Idec Ltd

Danish Dementia Research Center

Danish Multiple Sclerosis Center

Hoffmann-La Roche Ltd, Genzyme Europe B.V.

GlaxoSmithKline Pharma A/S

Merck/MSD

Novartis Healthcare A/S

Sanofi AB.

PUBLICATIONS

PH.D. THESES AND DISSERTATIONS

2015

- 1 Friis-Olivarius, Morten / **The Associative Nature of Creativity**. Copenhagen Business School, 2015.
- 2 Krøis Damsted, Sara / **Brain function and structure in children and adolescents treated with glucocorticoid during childhood**. Faculty of Health and Medical Sciences, University of Copenhagen, 2015.
- 3 Larsen, Christian Thode / **Development and Application of Tools for MRI Analysis : A Study on the Effects of Exercise in Patients with Alzheimer's Disease and Generative Models for Bias Field Correction in MR Brain Imaging**. Institute for Applied Mathematics and Computer Science, Technical University of Denmark, 2015.
- 4 Meder, David / **Mapping neural correlates of value-based sequential decision-making with fMRI**. Faculty of Health and Medical Sciences, University of Copenhagen, 2015.
- 5 Vestergaard, Martin / **Neural and endocrinological correlates of previous glucocorticoid treatment in children and adolescents treated for non-cerebral diseases**. Department of Neuroscience and Pharmacology, Faculty of Health and Medical Sciences, University of Copenhagen., 2015.
- 6 Ambrosen, Karen S.; Mørup, Morten (Ph.d.-vejleder); Dyrby, Tim B (Ph.d.-vejleder); Schmidt, Mikkel Nørgaard (Ph.d.-vejleder) / **Modelling Structural Brain Connectivity**. 2016.
- 7 Andersen, Mads; Hanson, Lars Peter Grüner (Ph.d.-vejleder); Madsen, Kristoffer H (Ph.d.-vejleder) / **Towards Motion-Insensitive Magnetic Resonance Imaging Using Dynamic Field Measurements**. Technical University of Denmark, Electrical Engineering, 2016.
- 8 Baruël Johansen, Louise; Baaré, William Frans Christian (Ph.d.-vejleder); Madsen, Kathrine Skak (Ph.d.-vejleder); Siebner, Hartwig Roman (Ph.d.-vejleder) / **Neuroticism and Functional Connectomics of the Resting Adolescent Brain : Insights from a Danish Child Cohort**. Department of Neuroscience and Pharmacology, Faculty of Health and Medical Sciences, University of Copenhagen., 2016.
- 9 Bianchi, Frederica; Dau, Torsten (Ph.d.-vejleder); Santurette, Sébastien (Ph.d. vejleder); Hjortkjær, Jens (Ph.d.-vejleder); Wendt, Dorothea (Ph.d.-vejleder) / **Complex-tone pitch representations in the human auditory system**. Hearing Systems, Department of Electrical Egnieering, Technical University of Denmark 2016.
- 10 Haagensen, Brian Numelin; Siebner, Hartwig Roman (Ph.d.-vejleder); Løkkegaard, Annemette (Ph.d.-vejleder); Madsen, Kristoffer H / **Medication-induced impulse control disorders in Parkinson's disease**. 2016.
- 11 Stanek, Konrad; Winther, Ole (Ph.d.-vejleder); Siebner, Hartwig Roman (Ph.d.-vejleder); Hansen, Lars Kai (Ph.d.-vejleder) / **Inferring human intentions from the brain data**. 2016.

BOOK CHAPTERS

2015

- 12 Hanson, L.G. / **The Ups and Downs of Classical and Quantum Formulations of Magnetic Resonance**. *Anthropic Awareness: The Human Aspects of Scientific Thinking in NMR Spectroscopy and Mass Spectrometry*; Edited by: C Szantay, Jr.. Elsevier, 2015. s. 141–171 (Part II).
- 13 Innocenti, Giorgio M; Carlén, Marie; Dyrby, Tim B / **The Diameters of Cortical Axons and Their Relevance to Neural Computing**. *Axons and Brain Architecture*. 2015.
- 14 Liu, Thomas T; Glover, Gary H; Mueller, Bryon A; Greve, Douglas N; Rasmussen, Jerod; Voyvodic, James T; Turner, Jessica A; Erp, Theo G. M.; Mathalon, Daniel H.; Andersen, Kasper Winther; Lu, Kun; Brown, Gregory G; Keator, David B.; Calhoun, Vince D.; Lee, Hyo Jong; Ford, Judith M.; Diaz, Michele; O'Leary, Daniel S.; Gadde, Syam; Preda, Adrian; Lim, Kelvin O.; Wible, Cynthia G.; Stern, Hal S.; Belger, Aysenil; McCarthy, Gregory; Ozyurt, Burak; Potkin, Steven G.; , FBIRN / **Quality assurance in functional MRI**. *fMRI: From Nuclear Spins to Brain Functions*. 2015.
- 15 Innocenti, Giorgio M; Carlén, Marie; Dyrby, Tim B / **Axons and Brain Architecture : The Diameters of Cortical Axons and Their Relevance to Neural Computing**. *Axons and Brain Architecture*. Elsevier, 2016. s. 319–337.
- 16 Karabanov, Anke; Lohse, Allan; Siebner, Hartwig Roman / **Hjernestimulation og Den forudsigende hjerne**. *Den forudsigende hjerne*. Hjerneforum, 2016. s. 46–52.

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2015

- 17 Barthélemy, Dorothy; Willerslev-Olsen, Maria; Lundell, Henrik; Biering-Sørensen, Fin; Nielsen, Jens Bo / **Assessment of transmission in specific descending pathways in relation to gait and balance following spinal cord injury**. *Progress in Brain Research*, Vol. 218, 2015, s. 79–101.
- 18 Chao, Chi-Chao; Karabanov, Anke Ninija; Paine, Rainer; Carolina de Campos, Ana; Kukke, Sahana N; Wu, Tianxia; Wang, Han; Hallett, Mark / **Induction of Motor Associative Plasticity in the Posterior Parietal Cortex-Primary Motor Network**. *Cerebral cortex (New York, N.Y.:1991)*, Vol. 25, Nr. 2, 2015, s. 365–373.
- 19 Cogliati Dezza, I; Zito, G; Tomasevic, L; Filippi, M M; Ghazaryan, A; Porcaro, C; Squitti, R; Ventriglia, M; Lupoi, D; Tecchio, F / **Functional and structural balances of homologous sensorimotor regions in multiple sclerosis fatigue**. *Journal of Neurology*, Vol. 262, Nr. 3, 2015, s. 614–622.
- 20 Daducci, Alessandro; Canales-Rodríguez, Erick J; Zhang, Hui; Dyrby, Tim B; Alexander, Daniel C; Thiran, Jean-Philippe / **Accelerated Microstructure Imaging via Convex Optimization (AMICO) from diffusion MRI data**. *NeuroImage*, Vol. 105C, 2015, s. 32–44.
- 21 De Vis, J B; Hendrikse, J; Bhogal, A; Adams, A; Kappelle, L J; Petersen, E T / **Age-related changes in brain hemodynamics; A calibrated MRI study**. *Human brain mapping*, Vol. 36, Nr. 10, 2015, s. 3973–87.
- 22 Fisher, Patrick MacDonald; Haahr, Mette Ewers; Jensen, Christian Gaden; Frokjaer, Vibe G; Siebner, Hartwig Roman; Knudsen, Gitte Moos / **Fluctuations in [(11)C]SB207145 PET Binding Associated with Change in Threat-Related Amygdala Reactivity in Humans**. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology*, Vol. 40, Nr. 6, 2015, s. 1510–18.
- 23 Frokjaer, Vibe Gedsoe; Pinborg, Anja Bisgaard; Holst, Klaus Kähler; Overgaard, Agnete; Henningsson, Susanne; Heede, Maria; Larsen, Elisabeth Clare; Jensen, Peter Steen; Agn, Mikael ; Nielsen, Anna Pors; Stenbæk, Dea Siggaard; da Cunha-Bang, Sofi; Lehel, Szabolcs; Siebner, Hartwig Roman; Mikkelsen, Jens Damsgaard; Svarer, Claus; Knudsen,

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