

ANNUAL REPORT 2019

REGION

Rigshospitalet • University of Copenhagen

DANISH DEMENTIA RESEARCH CENTRE

Copenhagen Memory Clinic and
National Info & Education Centre for Dementia



DANISH DEMENTIA
RESEARCH CENTRE



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The seahorse in the DDRC's logo resembles an area of the brain shaped like a seahorse, which is why it is called the hippocampus (Latin for seahorse). This area of the brain plays an important role in memory.



PREFACE

It is a pleasure to present the 2019 Danish Dementia Research Centre (DDRC) annual report, which provides an overview of our clinical services, research and national educational activities over the past year.

In 2019 our two memory clinics at Rigshospitalet Glostrup and Rigshospitalet Blegdamsvej merged and are now located at one physical site on Blegdamsvej, while still maintaining a small satellite clinic on the island of Bornholm. Covering basic multidisciplinary diagnostic evaluation and follow-up for the southern part of the Capital Region of Denmark and advanced specialised services (second opinion evaluations, normal pressure hydrocephalus and familial neurodegenerative disorders) for patients from across Denmark, Copenhagen Memory Clinic is the nation's largest.

In 2019 we celebrated the 20th anniversary of Dementia Days, an annual national conference for professional carers, clinicians and scientists. With 1,200 participants this conference continues to be the most important networking event in the field of dementia in Denmark.

Four PhD students completed their research programmes and defended their theses in 2019 – with promising results in the fields of biomarkers, pharmacoepidemiology and technology in dementia. During the year, DDRC researchers contributed to 65 scientific publications.

Our comprehensive ABC Dementia programmes are available on our website free of charge. In 2019 we launched a new programme, ABC Dementia-Friendly Hospitals, aimed at hospital staff from all professions requiring a brief introduction to dementia. Our app, About Dementia, was also released in an updated version. We are also highly pleased that the authorities in Iceland and the Faroe Islands have made an agreement with us to launch the app in their respective languages.

In 2017-2019, DDRC was responsible for managing three of the 23 initiatives in Denmark's National Dementia Strategy

2025: 1) development of new case-finding tool for use in primary care; 2) development of toolbox for psychosocial support, counselling and teaching patients and caregivers; and 3) development and evaluation of concepts for dementia-friendly hospitals. Towards the end of 2019 we received follow-up grants from the Danish Ministry of Health to ensure further validation and implementation of the new case-finding instrument, called BASIC, and of the toolbox for psychosocial support, both of which have been highly successful already.

A new webshop, available on our main website, was launched in 2019, allowing users to order the psychosocial support toolbox and other printed materials.

Our achievements in patient care, research and education would not be possible without support from the many invaluable organisations and people we collaborate with. We would especially like to thank the Danish Ministry of Health, the Danish Health Authority and the Danish Alzheimer Association for their excellent collaboration and support, and our national and international collaborators and external scientific and educational advisors for their contribution to our work. Finally, we would also like to thank the private and public foundations that support our work financially.



A handwritten signature in black ink, appearing to read 'G. Waldemar'.

Gunhild Waldemar
Professor, Chair of DDRC



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ABOUT THE DANISH DEMENTIA RESEARCH CENTRE

A grey tote bag is held in the foreground, featuring a stylized face graphic in shades of blue and grey. The text on the bag reads "DEMENS DAGENE" in large white letters, with "1999-2019" written vertically in orange to the right. Below this, the Danish phrase "To årtier med stærke visioner" is printed in a smaller font.

**DEMENS
DAGENE** 1999-2019
To årtier med stærke visioner

ORGANISATION

Located at Rigshospitalet and based in the Department of Neurology, the Danish Dementia Research Centre (DDRC) comprises three sections:

- Copenhagen Memory Clinic
- Dementia and Neurogenetics Research Unit
- National Info & Education Centre for Dementia

The Copenhagen Memory Clinic is a secondary and tertiary referral-based multidisciplinary out-patient clinic offering diagnostic evaluation and treatment of patients with cognitive disorders and dementia.

The Research Unit comprises clinical research groups, a neurogenetic research laboratory and the Danish Dementia BioBank.

Initiated and funded by the Danish Ministry of Health, the National Info & Education Centre for Dementia has a steering committee and a scientific advisory board.

With representatives from the Ministry of Health, Danish Regions, Local Government Denmark and Rigshospitalet, the steering committee monitors the strategic development and performance of the National Info & Education Centre according to predefined objectives and milestones, as outlined in our strategy for 2016-2020.

The scientific advisory board reviews and contributes with advice on major educational and scientific activities. The members of the advisory board represent the Danish Health Authority (SST), municipalities in Local Government Denmark, Danish Regions, Danish College of General Practitioners, the Danish Alzheimer's Association, the Danish Huntington's Disease Association and the DaneAge Association.

For an updated list of members of the steering committee and advisory board, see videnscenterfordemens.dk.

VISION

Our vision, "A longer life without dementia – a better life with dementia," provides us with the focus needed to accomplish our goals in finding solutions for prevention of cognitive decline and for improving health care for the benefit of people with dementia.

VALUES

Our four key values serve to guide our priorities and organisational decisions.

Professionalism: Highly ambitious, we constantly strive to reach the highest professional standards, professionalism and innovation with regard to the development of our services.

Commitment: Our commitment is reflected in our work and our dedication to the goal of preventing dementia and improving the quality of life for patients with dementia and their caregivers.

Respect: We show respect for patients, caregivers, professionals and groups. We show respect for the ethical challenges related to caring for people with dementia. We are dedicated to understanding, including and meeting their needs.

Transparency: We assure transparency with regard to our activities and in our professional relationships.

SPECIAL EVENTS 2019



Dementia Days

DDRC's annual Dementia Days conference, which celebrated its 20th anniversary, was held in May. This year's theme was "Two decades with strong visions", and more than 1,200 people from across Denmark were in attendance. Among the keynote speakers were Professor Dawn Brooker, leader of the Association for Dementia Studies, University of Worcester, United Kingdom, Professor Jakob Kjellberg from the Danish Center for Social Science Research (VIVE) and Michael Brautsch, who is a minister at Frederiksberg Church. The conference was opened by Sophie Hæstorp Andersen, chair of the Regional Council in the Capital Region of Denmark.





Study visit from Japan

In March a group of 20 Japanese researchers and health care professionals headed by neurology Professor Katsuya Urakami, Tottori University visited DDRC. The Japanese delegation was introduced to the organisation and activities at Copenhagen Memory Clinic and DDRC, including DDRC's current research projects and e-learning programmes.

Research conference on technology and dementia: "Technology for people with dementia"

The annual DDRC research conference was held at Rigshospitalet in November and the overall theme was technology used by people with dementia. The invited speakers were Dr Franka J. M. Meiland, VU University Medical Center, the Netherlands (right); Dr Marcello Ienca, Health Ethics & Policy Lab, Department of Health Sciences and Technology, ETH Zurich, Schweiz (below); and Dr Sarah Smith, Salford Institute for Dementia, University of Salford, Manchester, England.



Visit from Taiwan

In September DDRC hosted a study visit arranged by Silver Linings Global from 25 leaders from the Taiwanese government, health care and social care organisations and corporations. Their key focus areas were reablement, development of dementia care and support, user-centred service design, application of welfare technology and support for active ageing and intergenerational communities.

Masterclass with Professor Jonathan Schott

In April neurologists, psychiatrists and neuropsychologists from across the country benefitted from the knowledge and experience of Professor Jonathan Schott's at DDRC's masterclass on diagnostic evaluation of dementia. Schott, who is a neuroscientist and an active consultant neurologist at Dementia Research Centre, UCL Institute of Neurology, London, opened the masterclass with the lecture: "Using genetics to understand and diagnose Alzheimer's disease – from autosomal dominant to preclinical sporadic disease".

Launch of the toolbox

At the end of January, the "Toolbox – Supporting life with dementia" was launched at a series of free seminars in Copenhagen, Odense and Aalborg. A National Dementia Strategy initiative, the toolbox includes manuals and materials to be used in psycho-education sessions and consultations with people with dementia and family caregivers. The materials in the toolbox are tailored to various phases of living with dementia, with focus on life with early, middle and late stage dementia. Users were involved in developing the toolbox, including people with dementia, family caregivers and experts from municipalities, regions and NGOs.



PhD defense by Marie Bruun

In May Marie Bruun, MD, was awarded her PhD after defending her thesis: "Data-driven differential diagnosis and prediction of progression in dementia".

Group photo (from left): Kristian Steen Frederiksen (co-supervisor), Oskar Hansson (assessment committee member), Steen Gregers Hasselbalch (principal supervisor), Marie Bruun, Peter Høgh (assessment committee chair), Jørgen Erik Nielsen (primary co-supervisor) and Knut Engedal (assessment committee member)



PhD defense by Ane Nørgaard

In June Ane Nørgaard, MD was awarded her PhD after defending her thesis: "Use of Psychotropic Drugs in Patients with Dementia: A Nationwide Pharmacoepidemiologic Study".

Group photo (from left): Gunhild Waldemar (principal supervisor), Christina Jensen-Dahm (co-supervisor), Merete Nordentoft (assessment committee chair), Christiane Gasse (primary co-supervisor), Ane Nørgaard, Jesper Hallas (assessment committee member) and Paul Newhouse (assessment committee member)



PhD defense by Camilla Steen Jensen

In July Camilla Steen Jensen, MSc was awarded her PhD after defending her thesis: "Fluid based biomarkers to assess the effect of exercise in Alzheimer's disease".

Group photo (from left): Anja Hviid Simonsen (primary co-supervisor), Steen Gregers Haselbalch (principal supervisor), Camilla Steen Jensen, David Brooks (assessment committee member), Charlotte Teunissen (assessment committee member) and Rigmor Højland Jensen (assessment committee chair). Not in photo: Bente Finsen (co-supervisor)



PhD defense by Laila Øksnebjerg

In October Laila Øksnebjerg, MSc was awarded her PhD after defending her thesis: "Assistive technology to support self-management of people with dementia. The ReACT project".

Group photo (from left): Bob Woods (primary co-supervisor), Lars Vedel Kessing (assessment committee chair), Laila Øksnebjerg, Gunhild Waldemar (principal supervisor), Franka Meiland (assessment committee member), Anja Maier (assessment committee member)



COPENHAGEN MEMORY CLINIC



Established in 1995, Copenhagen Memory Clinic at Rigshospitalet is a combined secondary and tertiary referral-based multidisciplinary out-patient clinic. It offers diagnostic evaluation and treatment of patients with cognitive disorders and dementia and also receives referrals from general practitioners, private practice neurologists, psychiatrists and other hospitals in the Capitol Region of Denmark. Patients may also be referred from other memory clinics for second opinion evaluations.

In 2019 the Copenhagen Memory Clinic on Blegdamsvej and the one in Glostrup officially merged and now share renovated facilities at the Blegdamsvej site, which will house a new clinical section offering diagnostic evaluation and follow-up of patients with dementia from the City of Copenhagen and the southern part of the Capital Region. In September 2018 a new outpatient satellite clinic was established on the island of Bornholm. For both sites, general practitioners, hospital departments and private practice specialists from local catchment areas can refer new patients for diagnostic evaluation of cog-

nitive, behavioural or other symptoms suggestive of dementia or cognitive disorders. A dedicated multidisciplinary team of consultant neurologists, psychiatrists, geriatricians, neuropsychologists, specialist nurses, a social counsellor and medical secretaries manage diagnostic evaluation and treatment.

DIAGNOSTIC EVALUATION

The majority of patients undergo a standard set of examinations and procedures, beginning with a detailed medical history. Cognitive functions are then assessed with the Mini-Mental State Examination and the Danish version of Addenbrooke's Cognitive Examination. Physical and neurological/geriatric assessments, routine laboratory tests, ECG and structural CT or MRI of the brain are also performed. Other supplemental investigations are performed when clinically relevant, for example: fludeoxyglucose positron emission tomography (18FDG-PET and PET – PIB), neuropsychological assessment, routine and biomarker examination of cerebrospinal fluid (CSF), EEGs and psychiatric evaluations. After completion of the initial examina-

Table 1. Classification of new patients who completed a diagnostic evaluation programme in 2019

SYNDROME	DIAGNOSIS	BLEGDAMSVEJ	GLOSTRUP	BORNHOLM	TOTAL
Dementia		692	198	71	961
	Alzheimer's disease	288	86	37	411
	Vascular or mixed dementia	160	66	18	244
	Dementia with Lewy bodies, Parkinson's disease with dementia, Parkinson-plus syndromes	51	11	4	66
	Frontotemporal dementia	34	4	3	41
	Other specific conditions, including Huntington's disease and normal pressure hydrocephalus	49	3	4	56
	Dementia of uncertain aetiology and alcohol-related dementia	110	28	5	143
Mild cognitive impairment and other cognitive profiles	Patients with specific neurodegenerative disorders without dementia; patients with depression and other psychiatric conditions and sequelae after traumatic brain injury	317	77	12	406
No cognitive impairment	Patients with subjective symptoms and no significant pathology	197	59	2	258
Genetic counselling	Family members of patients with familial neurodegenerative conditions referred for genetic counselling	165	-	-	165
All completed evaluations (excluding genetic counselling)		1206	334	85	1625



The majority of patients undergo a standard set of examinations and procedures, beginning with a detailed medical history and test of cognitive functions.

tions and procedures, the multidisciplinary team prepares a standardised consensus report containing a classification of the cognitive profile, the primary underlying cause, concomitant conditions and a treatment plan. Following the consensus meeting, the patient and caregivers are invited to meet with the specialist physician and specialist nurse, where information is given on diagnosis and on the treatment and care plan. A short summary is subsequently sent to the patient's general practitioner.

SPECIALISED MEDICAL SERVICES

Patients with rare, complex or familial disorders may be referred from other parts of Denmark (mainly Eastern Denmark) for treatment and follow-up, and genetic counselling is also offered for healthy at-risk family members.

In accordance with guidelines for local, regional and highly specialised medical services from the Danish Health and Medicines Authority, Copenhagen Memory Clinic has been approved as a highly specialised centre in the fields of dementia and neurogenetics in that it offers:

- Second opinion evaluations of patients with possible dementia and dementia with uncertain aetiology
- Diagnosis and treatment of developmental disorders with dementia
- Diagnosis and treatment of frontotemporal dementia

- Diagnosis and treatment of rare and late-onset hereditary neurodegenerative diseases, for instance: Alzheimer's disease (AD), frontotemporal dementia (FTD), spinocerebellar ataxias (SCA) and Huntington's disease (HD)
- Clinical evaluation and lumbar perfusion and tap tests for patients with suspected normal pressure hydrocephalus (NPH)

Accordingly, specialist neurologists in the above areas, a clinical geneticist, a laboratory technician and a social counsellor are also affiliated with Copenhagen Memory Clinic. The highly specialised services are performed in collaboration with several other specialist departments at Rigshospitalet, for example: the Department of Clinical Genetics; the Department of Neurosurgery; the Department of Neuropathology; the Department of Clinical Neurophysiology; the Department of Neuroradiology; and the Department of Clinical Physiology and Nuclear Medicine (the PET and Cyclotron Unit, Rigshospitalet). A monthly clinical conference is held with specialists from the imaging (MR and PET) departments and four annual conferences are held with the Movement Disorders Clinic at Bispebjerg Hospital.

Normal pressure hydrocephalus (NPH)

Diagnostic evaluation of NPH is a complex task. The patients often have multimorbidity and characteristic symptoms such as: gait disturbance, urinary incontinence and cognitive decline, which are also common to various other diseases. Most patients are referred for possible NPH because their CT or MRI

demonstrated a dilated ventricular system. In 2019 there were 297 patients referred for a clinical evaluation of NPH, 107 of whom had a lumbar perfusion test and/or Tap Test after the clinical examination. All patients are discussed at a weekly conference with the NPH team at the Department of Neurosurgery, Rigshospitalet. The treatment, which can involve insertion of a shunt to drain excess CSF from the brain, may reverse some of the symptoms and restore functioning.

Genetic counselling

The Copenhagen Memory Clinic offers a programme for healthy at-risk family members from families with confirmed or suspected late-onset familial neurodegenerative diseases referred for clinical genetic evaluation and counselling. This service is executed in collaboration with the Department of Clinical Genetics at Rigshospitalet and includes an evaluation by our specialist in clinical genetics, as well as a consultation with a trained psychologist before genetic testing is considered. In 2019 there were 109 at-risk family members referred. The clinic also offers post-genetic test counselling when needed.

FOLLOW-UP PROGRAMME FOR PATIENTS AND FAMILIES

All patients with mild cognitive impairment (MCI), and selected groups of patients with dementia or specific neurodegenerative disorders are offered counselling and follow-up in collaboration with primary health care. Patients with conditions of uncertain aetiology and healthy mutation carriers may also be offered follow-up in the memory clinic. The majority of patients in the follow-up programme have MCI, AD, dementia with Lewy bodies (DLB), FTD, HD, SCA, NPH, Down's syndrome with dementia or other neurodegenerative/neurogenetic conditions. Most patients are accompanied by their family caregivers when visiting the clinic, and the social counsellor, specialist nurses, psychologists and medical doctors also offer counselling for the caregivers as an integral part of the follow-up programme. For fragile patients with severe dementia home visits are offered.

For patients from the City of Copenhagen, Copenhagen Memory Clinic has specific collaboration programmes with the Departments of Geriatrics and Palliation at Bispebjerg Hospital, the Mental Health Centre Copenhagen, general practitioners, and the care institutions and home care in the City of Copenhagen and the City of Frederiksberg. After the two memory clinics merged, Copenhagen Memory Clinic continues to work with general practitioners and the 10 local authorities in the southern part of the Capital Region at half-yearly meetings with key dementia coordinators.

As part of its services the clinic offers courses for patients and caregivers:

- Early-phase AD patients are offered a course run by a neuropsychologist focusing on the maintenance of cognitive functions that contains an introduction to compensatory techniques related to cognitive deficits
- A two-session course run by multi-disciplinary staff with weekly meetings is offered four times a year for family caregivers and includes information on symptoms and treatment; legal issues and social services; and treatment, care, communication and practical daily-life issues
- Patients with posterior cortical atrophy are also offered a tailor-made course

BORNHOLM MEMORY CLINIC

In September 2018 a new outpatient clinic was established at the Medical department on Bornholms Hospital led by Copenhagen Memory Clinic management. A team of one consultant neurologist and one neuropsychologist from the Copenhagen Memory Clinic, together with a nurse, secretary and senior consultant in geriatrics from Bornholms Hospital offers consultations twice a week for patients on Bornholm. Consultants from Copenhagen Memory Clinic have also contributed to educational services for health care professionals on Bornholm.

REGIONAL AND NATIONAL COLLABORATION

In 2011 the Capital Region established guidelines for coordinating patient care pathways between hospital-based memory clinics, mental health centres, other hospital departments, general practitioners and primary health care in its 29 municipalities. The guidelines are still under revision. In 2016 the national quality registry for dementia was launched, based partly on a previous regional version from the Capital Region established in 2006. The registry, which includes data from approximately 40 memory clinics in Denmark, is monitored by a national steering committee. Apart from contributing to the national dementia registry, the Copenhagen Memory Clinic is also an active member of the Network of Danish Memory Clinics.

Copenhagen Memory Clinic in 2019

- 1,750 new patients
- 8,952 patient visits

Bornholm Memory Clinic in 2019

- 96 new patients

5,041 patients are in a follow-up programme.

RESEARCH AT DDRC



RESEARCH PROGRAMME AT DDRC

DDRC research programmes cover a wide spectrum of clinical and translational research, including studies on epidemiology, biofluid markers, brain imaging, neurogenetics, genotype-phenotype correlations, patient-specific stem cells, disease course, neuropsychology, drug trials, non-pharmacological interventions and health service research. Our research is funded by external grants and donations from public and private foundations (see Acknowledgements). The health service and intervention research programmes with direct relevance to improving the quality of dementia care in Denmark as an integral part of the National Info & Education Centre for Dementia are funded in part by the Danish Ministry of Health.

The DDRC research team covers many different academic disciplines and comprises professors and clinical trial directors (with shared clinical and research positions), postdocs, senior researchers, PhD students, associated researchers and student research fellows (see Who is who?). In addition, consultant neurologists and neuropsychologists on the clinical team contribute significantly to our research. Three research nurses (study coordinators) and three research administrators are responsible for the coordination and financial aspects of our many research programmes.

In 2019 DDRC published 49 papers in peer-reviewed journals and three book chapters (see Publications). Four PhD theses were completed.

The next sections of the annual report describe:

- Thematic areas of research
- Research resources
- International research consortia and networks
- DDRC researchers – Who is who?

THEMATIC AREAS OF RESEARCH

Early diagnosis: Neuropsychology and biomarkers

Discovery and validation of disease markers for AD and other neurodegenerative disorders are key DDRC research areas, which include new biofluid markers, brain imaging and neuropsychology. The biomarker research aims to discover and validate new biofluid markers for the early diagnosis of AD and for the prediction of disease progression, including the use of proteomics and genomics technologies. DDRC conducts and

participates in several brain imaging studies on early diagnosis of dementia that contain both structural and functional brain imaging, including studies with amyloid-specific PET tracers. In recent years several studies on comorbidity in early diagnosis have been initiated, including multicentre studies on the role of epilepsy in early dementia and MCI, and new studies analysing the use of ear-EEG to examine epilepsy in AD.

Neuropsychological research mainly focuses on characterisation of cognitive deficits in the early phase of dementia diseases and MCI. In recent years DDRC has conducted various studies on cognitive processes in aging, as well as longitudinal studies on cognitive deficits and personality traits in gene-expansion carriers. In 2019, studies on possible changes in self-perception and identity in the earliest phases of neurodegenerative diseases were initiated. Many biomarker studies are carried out in collaboration with other Danish centres and a wide range of European centres.

Rare causes of dementia and inherited neurodegenerative disorders

Neurogenetic research focuses on clinical characteristics, ancillary investigations and basic research on gene function and therapy. Many neurodegenerative disorders, including AD, FTD, HD and ataxias manifest with progressive loss of specific subsets of neurons in the brain. In some diseases genetic mechanisms are involved. Different diseases have different genetic backgrounds, but evidence shows that common neurodegeneration mechanisms may exist. Some of our research focuses on the identification of common molecular mechanisms in neurodegeneration, e.g. in FTD linked to chromosome 3 (FTD3) and spinocerebellar ataxia type 2 (SCA2). We are also exploring the cellular environment in patient-derived cell cultures to pinpoint therapeutic targets. The FReJA Consortium investigates FTD linked to FTD3, which occurs in a large FTD family in western Jutland. Research in this disease focuses on the molecular disease mechanism, with neuronal cell lines now derived using stem cell technology to further explore the potential of gene therapy. The DDRC neurogenetics section is a significant international contributor to research in HD, and our large cohorts of patients are assessed with detailed clinical evaluations, genetic markers and CSF profiles. DDRC conducts highly specialised diagnostic examination and treatment of many rare disorders, including normal pressure hydrocephalus (NPH). The DDRC NPH team is currently studying the effect of treatment and diagnostic procedures.

Public health in dementia

Using nationwide registry data, we analyse the quality of diagnostic evaluation, access to health services and the use of medication in patients with dementia compared to the general Danish population. The research is being carried out in collaboration with the National Centre for Register-based Research at Aarhus University and the Section of Social Medicine, University of Copenhagen. Recently, the partnership conducted projects investigating patterns of use of opioids, other analgesics, psychotropics and anti-dementia medication. The results of ongoing studies aimed at identifying and defining the consequences and background for the high level of use are incorporated into the national dementia plan, where reduction of antipsychotic use is one of several goals. We also conduct studies on the incidence of dementia in Denmark, mortality in dementia and on the role of infections in dementia. Finally, we are taking part in studies on the relationship between stress and dementia. Our research will help provide evidence for creating new guidelines and for DDRC teaching materials.

Rehabilitation and psychosocial support

We have extensive experience in carrying out large-scale multi-centre intervention studies investigating non-pharmacological treatment in neurodegenerative diseases, some of which examine the effects of psychosocial interventions. In the ongoing ReACT study we examine how assistive technology can be designed to support self-management and rehabilitation of people with dementia. As part of the study an app was designed and tested that incorporated user involvement in an innovative process. The study also explores methods for implementation and adoption of assistive technology.

Cross-cultural aspects of dementia

DDRC is conducting several studies on the cross-cultural aspects of dementia. To improve diagnostic evaluation and care of ethnic minorities with dementia, the centre has studied the assessment of dementia in various ethnic groups in Denmark and in other European countries, as well as barriers to accessing dementia care. A special interest is the development and validation of cross-cultural cognitive tests and screening instruments for use in minority ethnic groups in high-income countries, and low and middle-income populations. In the ongoing CLEAR study, we focus on developing culturally sensitive programmes for increasing awareness and help-seeking for dementia in minority ethnic groups, as well as programmes for the provision of post-diagnostic care.

Pharmacological treatments: From first-in-man to proof-of-concept and large-scale clinical trials

DDRC has extensive experience conducting phase 1-3 clinical pharmacological trials in patients with AD, MCI and HD and as advisors for trial design and safety monitoring. The collaboration between Danish memory clinics (ADEX network) represents a platform for Denmark's contribution to international trials. On average DDRC's track record shows that the inclusion of patients is more than 30% above the requested number. Clinical trials are conducted with state-of-the-art imaging techniques in collaboration with the Danish Research Centre for Magnetic Resonance, Hvidovre Hospital and the PET and Cyclotron Unit, Rigshospitalet. In pharmacological trials for dementia DDRC is the national coordinator of the dementia centre in Trial Nation, which is a public-private clinical research partnership involving the regions of Denmark, universities, twelve pharmaceutical companies and one GTS institute, a government-approved, non-profit technological service. NEXT, which works to optimise clinical trials from start to finish, has established centres in various medical areas.

RESEARCH RESOURCES

Clinical cohorts and intervention studies

To study how different neurodegenerative processes arise and become manifest, specific patient cohorts representing a wide range of diagnostic entities and cohorts of healthy controls and gene mutation carriers are the foundation of many DDRC research programmes. These patient cohorts make up an essential basis for most of our clinical studies, with the aim of improving diagnostic evaluation, treatment and care for patients with dementia and neurodegenerative disorders. Often, intervention studies require a large number of patients, demanding multi-centre collaboration with national and international partners/memory clinics. DDRC coordinated two large-scale multicentre intervention studies, DAISY and ADEX, with more than 200 AD patients in each, resulting in two cohorts for future studies. A formalised platform for future collaboration on dementia research in Danish memory clinics has been established in the ADEX network, a multicentre Danish network comprising eight different memory clinics from across the country.

Translational Neurogenetics Laboratory

To investigate the molecular mechanisms underlying neurodegenerative disorders, we work with a variety of molecular



and cellular biology techniques. Our facility is fully equipped to perform all aspects of cellular biological research and has biosafety class I and II laboratories. Using skin biopsies from patients in our memory clinic we establish patient-specific cell cultures to dissect the molecular mechanisms of disease. The patient cells have also been used to induce pluripotent stem cells. These cell models form the basis of our work, in combination with additional advanced techniques such as image cytometry, fluorescence microscopy, viral vector generation and RNA interference.

Danish Dementia BioBank (DDBB)

DDBB was established in 2008 with the aim of collecting biological fluids for biomarker research in neurodegenerative diseases. DDBB contains more than 8,000 samples from patients referred to the Copenhagen Memory Clinic at Rigshospitalet and the Zealand University Hospital Memory Clinic. Whole blood, buffy coat, EDTA plasma and serum are stored for all patients, as well as CSF from approximately 25% of the patients. The samples, handled and stored according to international biobank guidelines, have contributed to multiple international biomarker and stability studies. Furthermore, skin biopsies are taken from selected patients and processed into live fibroblast cultures and stored for future research projects. These cultures have served as the basis for projects studying the molecular mechanisms underlying development of neurodegenerative disorders and have been used in the development of new model systems for neurodegenerative disorders, e.g. induced pluripotent stem cells.

Danish national registries

Access to nationwide health care registries makes it possible to carry out large population-based studies on the health service, risk factors, medication and outcome in neurodegenerative disorders. All Danish in and out-patients who have had contact with a Danish hospital are registered in national registries with basic information on clinical diagnoses and procedures. In some

DDRC research programmes cover a wide spectrum of clinical and translational research, e.g. studies on epidemiology, biofluid markers, neurogenetics and patient-specific stem cells.

of the earliest epidemiological studies, our group examined the validity of dementia diagnoses. Since then, the unique national registries have served as the foundation for various studies on the quality of health care, pharmacoepidemiology, comorbidity and mortality in dementia.

INTERNATIONAL RESEARCH CONSORTIA AND NETWORKS

PredictND

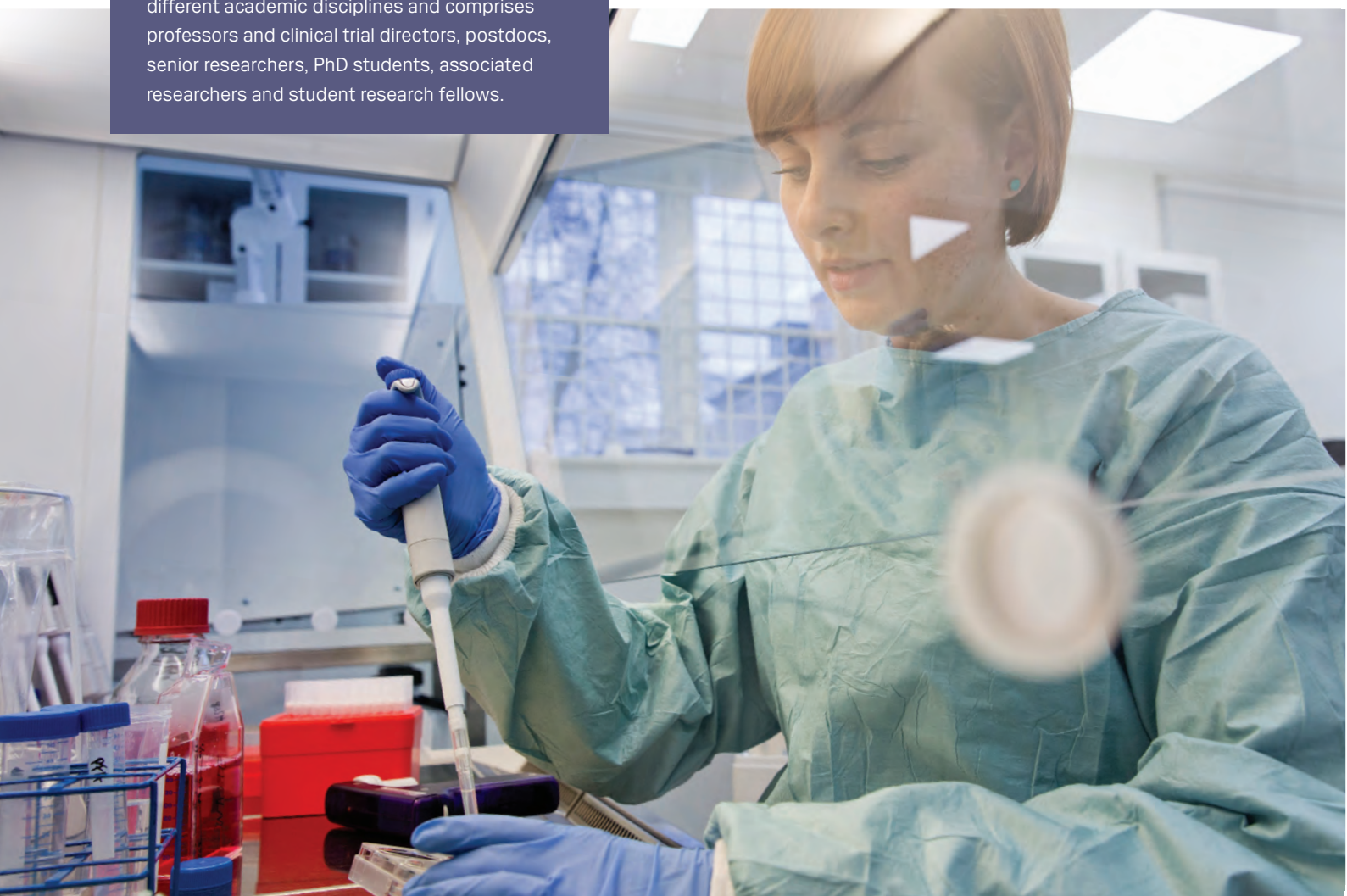
PredictND was a four-year, €4.2m European project funded by the EU's 7th Framework Programme that drew to a close in 2018. It focused on developing tools and means for earlier, evidence-based diagnosis of a range of neurodegenerative diseases. PredictND was coordinated by VTT Technical

Research Centre of Finland Ltd. (Finland), and the consortium members included Alzheimer Europe (Luxembourg), Combinostics Ltd. (Finland), GE Healthcare (UK, Sweden), Imperial College of London (UK), Rigshospitalet (Denmark), Università degli Studi di Perugia (Italy), University of Eastern Finland (Finland) and VU/VUmc (the Netherlands). The collaboration is still very productive and continues to publish data from the project.

European Huntington's Disease Network (EHDN) and Enroll HD

DDRC is part of EHDN, which provides a platform for professionals and people with HD and their relatives to facilitate collaboration throughout Europe. DDRC's staff and families affected by HD have contributed significantly to clinical cohort studies and intervention studies. Enroll HD, initiated in 2012, is the world's largest observational study for HD families. Designed as a clinical research platform, it enables health care professionals, scientists and families affected by HD to work together towards an improved understanding of HD and better care and treatments. At the end of 2019, DDRC's Enroll HD cohort comprised 272 participants.

The research at DDRC is funded by external grants and donations from public and private foundations and the DDRC research team covers many different academic disciplines and comprises professors and clinical trial directors, postdocs, senior researchers, PhD students, associated researchers and student research fellows.



Frontotemporal Dementia Research in Jutland Association (FReJA)

FReJA is an international multidisciplinary consortium established more than two decades ago to investigate a unique, large FTD-3 family in western Jutland. Basic and clinical scientists in Denmark, Sweden and the UK have made major progress over the years in identifying the disease gene and in understanding the disease mechanisms and their wider relevance for neurodegeneration in general.

European Alzheimer's Disease Consortium (EADC)

EADC is a network of more than 50 European academic centres of excellence working in the field of AD and other dementias. It provides a forum for expanding scientific understanding and developing ways to prevent, delay, slow or ameliorate the primary and secondary symptoms of AD. The European Commission provided initial funding for EADC and supports working towards standardisation of diagnostic criteria, assessment tools and data collection methods, with a view to a subsequent trial period involving the testing and practical application of the tools agreed upon. DDRC, the only Danish EADC member, has contributed to or directed studies on assessment tools, health economics, biomarkers and cross-cultural aspects of dementia care. In 2019 we took the lead in launching a new project to develop a position paper on MCI.

BrainStem – Stem Cell Center of Excellence in Neurology

BrainStem – Stem Cell Center of Excellence in Neurology is supported by Innovation Fund Denmark. The project coordinator is Professor Poul Hyttel, University of Copenhagen, and its primary partners are the University of Copenhagen, DDRC at Rigshospitalet, University of Southern Denmark, Aarhus University, Bioneer, Lundbeck A/S (Denmark), Lund University (Sweden) and Innovative Concepts in Drug Development (France). Advanced stem cell technologies are used to re-programme skin cells from patients with AD and Parkinson's disease to diseased neurons to study the underlying molecular mechanisms in order to develop better diagnostics and to test new drugs.

Interdem

DDRC takes part in Interdem, a pan-European network of researchers collaborating on research and dissemination of early, timely and quality psychosocial interventions aimed at improving the quality of life across Europe for people with dementia and their caregivers. Members of the network include academic and clinical researchers from 23 nations.

Nordic Network in Dementia Diagnostics (NIDD)

NIDD, funded by the Nordic Council, comprises eight academic memory clinics in the Nordic countries and Lithuania. The main objective of the network is to examine various aspects of diagnostic procedures in dementia. One ongoing project involves evaluating quantitative EEG in Dementia diagnostics. DDRC and the Zealand University Hospital Memory Clinic are the network's Danish partners.

Nordic Research Network on Dementia and Ethnicity

The Nordic Research Network on Dementia and Ethnicity, established in 2014, comprises researchers with backgrounds in medicine, psychology, occupational therapy, nursing, speech therapy and linguistics who conduct research in dementia and minority ethnic groups. Members collaborate and meet twice annually to plan and share research. The network currently receives support from the Nordic Welfare Centre..

National dementia research and education centres in Scandinavia

Norway, Sweden and Denmark have national non-profit dementia research and education centres commissioned and funded by the national boards or ministries of health. DDRC, the Norwegian Centre for Dementia Research and the Swedish Dementia Centre collaborate and meet annually to share ideas and have exchange programmes for the benefit of professional care staff, people with dementia, and family caregivers throughout Scandinavia.

Joint Programming on Neurodegenerative Diseases (JPND)

JPNE, funded by Horizon 2020 and EU member states, is an innovative, collaborative research initiative established to tackle neurodegenerative diseases. DDRC has taken part in three JPND-funded research consortia on biomarkers in AD and Parkinson's disease (BIOMARKAPD), on the definition of outcome measures in dementia and on the harmonisation of assessment methods.

RESEARCH – WHO IS WHO?



PROFESSORS AND ASSOCIATE PROFESSORS



STEEN G. HASSELBALCH – EARLY DIAGNOSIS, NEUROIMAGING AND BIOMARKERS

Consultant neurologist, clinical professor and research director. Main research interests include diagnosis and pathophysiology of dementia disorders. He has a leading role in several international research collaborations and was the principal investigator (PI) in a recent Danish multicentre trial on physical exercise in AD.



JØRGEN E. NIELSEN – FAMILIAL NEURODEGENERATIVE DISORDERS

Consultant neurologist, clinical professor and research director. Main research areas are genotype-phenotype correlations of inherited neurodegenerative disorders, especially SCA, HD, dystonia, spastic paraplegias and hereditary forms of Parkinson's disease, AD and FTDs.



ASMUS VOGEL – COGNITION AND NEUROPSYCHOLOGICAL DEFICITS

Neuropsychologist and associate professor in clinical neuropsychology. Major research focus is cognitive deficits in dementia diseases and neuropsychological functions, e.g. memory, executive functions and attention. He is initiating and coordinating studies on development and validation of cognitive tests applied in memory clinics.



GUNHILD WALDEMAR – INTERVENTION STUDIES, EPIDEMIOLOGY, GLOBAL HEALTH

Consultant neurologist, clinical professor and chair of DDRC. Main research areas include dementia epidemiology, global health, diagnostic markers, clinical cohort studies and pharmacological and complex interventions.

TRIAL DIRECTORS



LENA ELISABETH HJERMIND – CLINICAL TRIALS – HD

Consultant neurologist, PhD. Directs DDRC's participation in the Enroll-HD cohort study and clinical trials in HD. She also contributes to other studies in familial neurodegenerative diseases.



PETER JOHANNSEN – CLINICAL TRIALS – AD

Consultant neurologist, PhD. Directs DDRC's clinical AD trials, including prodromal-Alzheimer and phase 1-3 trials. He is also involved in studies on familial FTD.

SENIOR RESEARCHERS AND POSTDOCS



KRISTIAN STEEN FREDERIKSEN – PHYSICAL EXERCISE AND CLINICAL APPLICATION OF AD BIOMARKERS

MD, PhD. Main research areas are physical exercise in neurodegenerative dementias with regard to treatment and primary prevention. A second area of interest is the application of biomarkers of AD and other neurodegenerative diseases in the clinic, with a special focus on brain imaging techniques.



KASPER JØRGENSEN – NORMING, VALIDATION AND DEVELOPMENT OF NEUROPSYCHOLOGICAL TESTS AND CASE-FINDING INSTRUMENTS

MSc Neuropsychologist. Main research focus is norming, validation and development of neuropsychological tests and brief case-finding instruments for dementia and mild cognitive impairment.



ADELE MARTHALER – MODELING SCA2 USING PATIENT-DERIVED INDUCED PLURIPOTENT STEM CELLS (IPSCS)

Postdoctoral fellow, MSc. Has generated patient-derived iPSCs that were subsequently gene corrected using CRISPR/Cas9 gene technology. Patient iPSCs and gene-corrected controls will be differentiated into neurons to study the disease phenotype and the role of ATXN2 in the cell type predominantly affected by SCA2. Studies will include electrophysiological assays, global RNA sequencing and functional assays related to autophagy and apoptosis.



T. RUNE NIELSEN – CROSS-CULTURAL ASSESSMENT AND DEMENTIA IN ETHNIC MINORITIES

Postdoctoral fellow, neuropsychologist. Main research focus is cross-cultural assessment of cognitive deficits and ethnic differences in dementia diagnostics, treatment and care. He is initiating and coordinating national and international studies on the development and validation of cross-cultural cognitive tests, and on development of models for culturally sensitive pre- and post-diagnostic support.



TROELS TOLSTRUP NIELSEN – MOLECULAR MECHANISMS IN NEURODEGENERATION

Senior researcher, MSc and DDRC centre manager. Research focus is on neurodegenerative disorders such as AD, FTD and ataxias. His research centres on finding molecular mechanisms in the inherited neurodegenerative disorder spinocerebellar ataxia type 2 (SCA2).



PETER ROOS – INHERITED NEURODEGENERATIVE DISEASES

MD. Clinical research in inherited neurodegenerative diseases and in behavioral features of frontotemporal dementia, mainly FTD3.



ANJA HVIID SIMONSEN – BIOMARKERS AND BIOBANK

Senior researcher, MPharm and director of the Danish Dementia BioBank. Main research focus is molecular and genetic biomarkers for diagnosis and prognosis of neurodegenerative diseases as well as for response to interventions. Coordinator of the Danish Dementia BioBank's participation in international collaborative biomarker projects and projects related to sample quality.



JONATHAN WARDMAN – SCA2 AT THE CELLULAR LEVEL

Postdoctoral fellow, MSc. Is investigating the second-order dysfunction caused by aggregation and interaction of the mutant protein with various aspects of the proteostatic system. Studying the differential responses of SCA2 patient fibroblasts versus controls will make it possible to determine what specific aspects of the proteostatic system are disrupted in SCA2 and to find specific (potentially druggable) cellular targets.

ASSOCIATED RESEARCHERS (CURRENTLY EMPLOYED ELSEWHERE)



CHRISTINA JENSEN-DAHM – EPIDEMIOLOGY AND REGISTER-BASED RESEARCH

MD, PhD. Major research focus is epidemiological studies based on registry data. Current research focuses on medication use (analgesics, anti-dementia drugs, psychotropic medication and polypharmacy) in elderly with dementia, diagnosis of dementia and ethnicity.



KIEU PHUNG – CROSS-CULTURAL DEMENTIA EPIDEMIOLOGY AND PUBLIC HEALTH INTERVENTIONS

MD, PhD and neuroepidemiologist. Main research focus is dementia frequency, risk factors and risk modification across different cultures and ethnic groups.



LEA STEVNSBORG – REGISTER-BASED RESEARCH ON DEMENTIA IN IMMIGRANT POPULATIONS

MD. Her project investigates the use of anti-depressants and anti-psychotics in immigrant populations with dementia to identify possible inequalities in access to treatment in immigrant populations.

PHD STUDENTS



MARIE BRUUN – DIFFERENTIAL DIAGNOSTICS OF NEURODEGENERATIVE DISEASES

MD. Her PhD project explores the potential of and validates the PredictND tool, a data-driven diagnostic decision support system designed to assist clinicians in differential diagnostics of dementia diseases. She is also studying the properties of quantitative measurements of motor signs as diagnostic or prognostic biomarkers.



ANNA ELISE BRUUS – MEMORY IMPAIRMENT IN THE EARLIEST PHASES OF AD

MSc. Her project focuses on memory impairment in the earliest phases of AD. Possible changes in autobiographical memory and identity is studied in persons with Subjective Cognitive Decline, MCI and AD.



ANE NØRGAARD CHRISTENSEN – USE OF PSYCHOTROPIC DRUGS IN PATIENTS WITH DEMENTIA

MD. Using nationwide registry data, her PhD project focuses on the use of antipsychotics and other psychotropic drugs in patients with dementia and investigates the mortality risk associated with the use of psychotropic drugs. The aim is to clarify areas of inappropriate medication use and to help prevent the negative consequences thereof.



CAMILLA STEEN JENSEN – BIOMARKES AND EXERCISE IN PATIENTS WITH ALZHEIMER'S DISEASE

MSc. Her PhD project investigates the beneficial effect of physical exercise on patients with AD measures in CSF. Various aspects of the biochemical parts of AD are being studied, e.g. the diagnostic biomarkers amyloid-beta and tau.



CHRISTIAN SANDØE MUSAEUS – EPILEPTIC SEIZURES IN AD

MD. His PhD assesses subclinical epileptiform activity with continuous EEG monitoring using novel ear EEG registration and correlating findings with MRI hippocampal blood flow assessments. Another area of interest is the use of EEG to assist in the diagnosis of AD and MCI.



JANET JANBEK – ROLE OF INFECTIONS IN DEMENTIA

MSc. Her project will focus on the role of infections in dementia. The project will describe hospital contacts with infections in persons with dementia and compare them to those without dementia and investigate the impact on mortality. Her project will also investigate the role of infections as risk factors, by taking a life-course approach starting from mid-life.



LAILA ØKSNEBJERG – ASSISTIVE TECHNOLOGY AND COGNITIVE REHABILITATION

MSc Neuropsychologist. Her project, ReACT, explores assistive technology for people with dementia. As part of the study a cognitive supportive app was designed and tested through a user-involving innovation process. Methods for implementation and adoption of assistive technology are also investigated, with emphasis on cognitive rehabilitation and self-management of people with dementia.



LÆRKE TAUDORF – DEMENTIA AND MORTALITY: A REGISTER-BASED STUDY

MD. Her PhD project reviews time trends of prevalence, incidence and mortality due to dementia from 1996 to 2015, as well as assesses survival after diagnosis. It will also investigate whether certain comorbidities are associated with higher mortality. Finally, the project will review the registered causes of death in individuals with dementia.



MARIE NATHALIE NICKELSEN HELLEM – HUNTINGTON' S DISEASE

MD. Her PhD project investigates the role of neuroinflammation in the pathogenesis of HD by examining blood and CSF. The aim is also to look for biomarkers and develop HD stem cells.



REBECCA THEA KJÆRGAARD HENDEL – (NEURO)PSYCHOLOGICAL CHANGES IN HUNTINGTON'S DISEASE GENE-MUTATION CARRIERS

MSc. Her PhD project investigates (neuro)psychological changes in Huntington's disease gene-mutation carriers. The project focuses on possible impairments in social cognition, apathy on self-perception in the premanifest and early manifest stages of this neurogenetic disorder.

STUDENT RESEARCH FELLOWS (MASTER'S STUDENTS)



CHUQIAO CHEN – DISEASE MODELING OF FRONTOTEMPORAL DEMENTIA (CHROMOSOME 3)

Her project investigates molecular mechanisms of FTD-3 mutations including in 1) patient-derived fibroblast, 2) induced pluripotent stem cells and 3) a neuroblastoma knock-out model.



HELENA S. GLEERUP – BIOMARKERS IN SALIVA

Her project investigates whether saliva can be a viable biofluid for the detection of biomarkers of neurodegenerative diseases, especially AD.



MATHIAS HOLSEY GRAMKOW – BIOMARKERS OF NEURODEGENERATION

His research focuses on biomarkers of neurodegeneration including MRI, 18F-FDG-PET and tau in cerebrospinal fluid in the diagnosis and prognosis of patients suspected in dementia.



EMIL ELBÆK HENRIKSEN – GENETIC MUTATION

His project investigates how the genetic mutation in spinocerebellar ataxia type 2 (SCA2) affects the mitochondria and the intracellular calcium signaling in stem cell-derived neurons. The outcome of this project will help us understand the disease progression in the early stages.



FREDERIKKE JEPPESEN KRAGH – QUANTITATIVE MEASUREMENTS OF MOTOR SIGNS IN DEMENTIA

Her study investigates whether a quantitative motor assessment provides a more objective, sensitive and standardised measurement of motor dysfunction in AD, FTD and DLB. A second area of interest is different aspects of physical activity and its impact on daily living functions in AD.



RACHEL UNDERLIEN KRISTENSEN – REGISTER-BASED RESEARCH ON POLYPHARMACY IN DEMENTIA

Her project uses nationwide data to investigate the frequency and time trends of polypharmacy among people with and without dementia to examine potential disparities.



CHRISTINA STRAND-HOLM MANNICHE – CSF BIOMARKERS IN NPH, VASCULAR DEMENTIA AND AD

Her project investigates the ability of specific biomarkers in CSF to distinguish idiopathic N from subcortical ischemic vascular dementia and AD.



JOHANNE KØBSTRUP ZAKARIAS – EPIDEMIOLOGY AND QUALITY OF DEMENTIA DIAGNOSES

Using nationwide registry data, this project investigated potential geographical variation in diagnostic rate and quality of dementia diagnoses to examine possible inequality in the access to appropriate diagnostic evaluation and care for patients with dementia.



**NATIONAL INFO &
EDUCATION CENTRE
FOR DEMENTIA**

Established in 2007 and funded by the Danish Ministry of Health, the National Info & Education Centre for Dementia provides research, nationwide education and the dissemination of information about dementia, primarily to health care professionals and care staff in Denmark. DDRC communicates with a variety of professionals and societies on a range of platforms via, for example the DDRC website, training courses, networks, e-learning, public media, apps, publications and conferences.

NATIONAL DEMENTIA STRATEGY 2025

In 2017 the Danish Ministry of Health launched National Dementia Strategy 2025 and an action plan with 23 initiatives for 2017-2019. DDRC is responsible for managing the following three initiatives:

- A new case-finding tool for use in primary care
- A toolbox for psycho-social support, counselling and teaching patients and caregivers
- Concepts for dementia-friendly hospitals

DDRC also contributed to the completion of Denmark's first national research strategy, an initiative headed by the Danish Health Authority and published in December 2018.

COURSES AND CONFERENCES

The National Info & Education Centre for Dementia offers a wide range of courses throughout the country, in addition to two annual conferences.

Course Catalogue 2019

In 2019 the Course Catalogue contained 16 activities lasting one to four days. The various themes included, for example: "rehabilitation for people with dementia", "challenging behaviour", "dementia diagnosis masterclass", "physical training", "early intervention", "pain and delirium", "the physically and mentally disabled", "becoming an ABC Dementia instructor" and "management for dementia professionals".

Dementia Days – A national conference

Every year DDRC organises Dementia Days, a national two-day conference for dementia specialists and practitioners. As Denmark's largest conference on dementia, it provides a valuable educational opportunity for management and staff working in the social services and health care sectors. Held from 23-24 May in 2019, with the theme "Two decades of powerful visions", Dementia Days celebrated its 20th anniversary.

At a joint symposium during Dementia Days, Professor Dawn Brooker, University of Worcester, Professor Jakob Kjellberg, VIVE and Gunhild Waldemar, head of DDRC, gave presentations.

Key topics during symposium sessions included:

- Dementia-friendly hospitals
- Everyday life in nursing homes
- An active life with dementia
- For those inexperienced with dementia
- Support for living with dementia
- End-of-life care
- Detection and timely investigation
- Huntington's disease
- Ethical dilemmas
- Frontotemporal dementia
- Psychosocial research

Once again this year, with 1,131 participants (including exhibitors and speakers), Dementia Days had a large number of attendees.

During the conference there were nine sessions, with speakers from across the nation presenting their views and data on an extensive range of topics. Participants also had the opportunity to present results from their own projects at open lectures.

Scandinavian conference for leaders in dementia care

Every other year DDRC organises a two-day conference for leaders in dementia care in collaboration with Norwegian and Swedish national research and education centres. In 2019 time was spent planning the 2020 programme and conference, which will be held 19-20 October 2020 in Stockholm under the theme: Person-centred culture in dementia care – The responsibility of the manager.

Annual research conference 2019 – Technology and dementia

Every year a full-day national conference primarily devoted to the latest scientific news within a specific topic of interest related to dementia takes place in November at Rigshospitalet, attracting scientists and practitioners from across Denmark. In 2019 the theme was technology and dementia and 57 people attended the conference. Franka J.M. Meiland, VU University Medical Centre, the Netherlands, Marcello Lenca, Department of Health and Technology at ETH Zürich, Switzerland, Sarah Smith, Salford Institute for Dementia in UK and Laila Øksnebjerg, DDRC, gave presentations.

ABC DEMENTIA – FREE ONLINE COURSES

Offering free e-learning is one way of providing easy-access knowledge about dementia to various target groups across the nation. The practice-oriented nature of the topics and the variety of educational approaches used make the courses especially user friendly. DDRRC has now developed four different programmes.

ABC Dementia – Care involves e-learning for professional caregivers, with each module designed to cover a specific topic, such as dementia disorders, behavioural symptoms or communication. In 2019 the programme was updated with a new version. On average, about 800 new users are registered each month.

ABC Dementia for Physicians targets physicians in training, primarily within geriatrics, neurology, psychiatry and general

practice. Launched in October 2016 it targets physicians in training but is also relevant for doctors and other professionals who work with dementia assessments. On average, about 40 new users are registered each month.

ABC Dementia for Hospitals, launched in September 2018, targets care staff at hospitals with knowledge about dementia, care and communication. On average, about 75 new users are registered each month.

ABC Dementia-Friendly Hospitals, which is aimed at all hospital staff, is a short programme that provides an introduction to dementia and the challenges that arise with admissions of people with dementia. Staff also learn how to customise their communication and care. On average, about 125 new users are registered each month.

National Info & Education Centre for Dementia provides nationwide education, research and the dissemination of information about dementia, primarily to health care professionals and care staff in Denmark.



ABC DEMENTIA – FREE ONLINE COURSES

ABC Dementia – Care

E-learning course targeting staff working with care in municipalities and regions. On average, about 800 new users are registered each month.

ABC Dementia for Physicians

E-learning course targeting physicians in training but is also relevant for doctors and other professionals who work with dementia assessments. On average, about 40 new users are registered each month.

ABC Dementia for Hospitals

E-learning course targeting hospital care staff. On average, about 75 new users are registered each month.

ABC Dementia-Friendly Hospitals

E-learning targeting all staff working at hospitals. On average, about 125 new users are registered each month.

The annual meeting of the Network of Danish Memory Clinics was held on 9 October 2019 in Vejle and had 133 participants from among the five regions of Denmark. The themes covered organisation of memory clinics in Denmark, cross-sectoral and interdisciplinary cooperation in the five regions, and the nationwide Clinical Dementia Registry.

The annual meeting included workshops for various professional groups, including discussions on dementia and depression for doctors and psychologists and on rehabilitation, end-of-life care and support for living with dementia for nurses and other care staff.

National network of municipality-based dementia ambassadors

Each of the 98 Danish municipalities has appointed a dementia ambassador to disseminate information about DDRC activities and news from other municipalities to local professionals and to monitor local needs for educational activities. To ensure contact between DDRC and the ambassadors special newsletters are published six times a year and an annual meeting is held with the ambassadors.

DDRC'S NATIONAL NETWORKS

To foster an exchange of knowledge, education and quality programmes, DDRC and its National Info & Education Centre for Dementia coordinate national networks across regional, municipal and professional boundaries.

Network of Danish Memory Clinics

Set up by DDRC in 2008, the Network of Danish Memory Clinics serves as a platform for dissemination and exchange of information, for harmonising and standardising assessment and treatment methods, and for strengthening local and national collaboration. Its members, which comprise multi-disciplinary staff such as nurses, medical doctors and neuropsychologists, are mainly based in hospital psychiatric, geriatric or neurological departments and receive referrals from local general practitioners for diagnostic evaluation of dementia. Network members meet once a year to maintain and further develop national cooperation.



Network of Danish Memory Clinics:

● Memory clinics ● ADEX Memory clinics ● ADEX affiliates

On 14 March 2019 the network met for the tenth time in Odense, where 67 municipalities were represented, in addition to the Danish Health Authority and Local Government Denmark.

DaneDem – network for psycho-social research

For multidisciplinary researchers interested in psychosocial interventions, such as cognitive rehabilitation, music therapy and personalised care, DaneDem, or the Danish Research Network on Psychosocial Methods in Dementia, is the Danish counterpart of the pan-European network Interdem. The network's aim is to provide mutual inspiration and idea development, in addition to members being a sounding board for one another. DaneDem, which meets at least once a year with the aim of improving psychosocial dementia research in Denmark, met in Copenhagen for the seventh time on 8 November 2019. The network continues to grow and currently has 28 members.

COMMUNICATIONS AND PRESS – INTERACTING WITH SOCIETY

All of our platforms show a high level of activity. We have a growing number of newsletter subscribers, media mentions, followers on social media and website users. This is due to an ongoing strategic approach to public relations and a focused effort in reaching out to our stakeholders and the press in general.

DDRC in the press

DDRC takes pride in offering commentary, articles and statements on dementia-related issues to the general media. With more than 500 media mentions in 2019, DDRC was present in the press on an almost daily basis. For example, a documentary team from the Danish Broadcasting Corporation followed Memory Clinic patients who suffer from Huntington's, filming them at home, during exams and while being treated at the clinic.

Website

In 2019 more than 400,000 users visited the DDRC website, viewing a combined 1.4 million pages with information on dementia diseases, risk factors and statistics for people who work with assessment, treatment and care. Materials and tools useful in clinical practice can be downloaded or ordered on the site. The press, patients and caregivers are also frequent users of our website.

As part of the Toolbox: Support for living with dementia, initiative 11 of National Dementia Strategy 2025, DDRC developed the subsite "demensværktøjskassen.dk" in 2019.

In August 2019 a webshop accessible from the main website, was also launched, making materials from the Toolbox and other information on dementia (e.g. a handbook, diagnostic criteria and a screening battery) available for order.

Newsletter

Published 6-8 times per year, the DDRC newsletter contains information about the latest research and current courses and conferences. At the close of 2019 we had 7,490 subscribers.

About Dementia app

The About Dementia app is an observation tool for professional caregivers that was released in an updated version optimised for mobile phones and tablets in January 2019. An agreement was entered into with the Icelandic Alzheimer Association in 2019 for an Icelandic version of the About Dementia app, just as a similar agreement was made with the Faroese Alzheimer Association in late December 2019.

Social media

All of our social media platforms have a growing number of followers, engaging users and generating traffic on the DDRC website. Facebook is a useful way to create and maintain a relationship with the public and to disseminate knowledge about dementia and DDRC, e.g. its activities, courses and conferences, while Twitter is valuable for spreading news about research and building relationships with relevant journalists. On LinkedIn we share updates of interest with dementia stakeholders and professionals.

DDRC conference booth

The DDRC conference booth was present at various events in 2019, e.g. Dementia Days. The booth is instrumental in promoting direct contact with our target groups, allowing us to generate new contacts and disseminate information about our materials to professionals and stakeholders, as well as general knowledge about dementia to the public.

RESEARCH AWARDS, DONATIONS AND GRANTS

DDRC researchers awarded Alzheimer's Research Fund grants

On 20 September 2019 the Danish Alzheimer Association presented awards and grants to researchers and professionals for outstanding contributions to the field of dementia, its Alzheimer's Research Fund awarding DKK 3.5 m to nine specific research projects. These three DDRC researchers were among the recipients.



Senior researcher and director of the Danish Dementia Biobank, **Anja Hviid Simonsen**, MSc, PhD was awarded DKK 447,000 for the project "Serum Neurofilament light chain as an early marker for neurodegeneration". The objective of the project is to investigate the clinical usefulness of serum neurofilament light chain levels for the differentiation between neurodegeneration and non-neurodegenerative diseases in patients referred to a memory clinic.



PhD student **Le Gjerum**, MD was awarded DKK 385,400 for the project "Rational use of cerebrospinal fluid-based biomarkers and FDG-Pet in the diagnostic evaluation of memory clinic patients". The aim of the project is to investigate the optimal use of CSF-based biomarkers and FDG-PET in clinical practice when evaluating patients with memory complaints.



Neurologist **Kristian Steen Frederiksen**, MD, PhD was awarded DKK 246,800 for the project "Neurodegeneration as a target for exercise: effects of exercise on neurofilament light in Alzheimer's disease". The aim of the project is to investigate the effects of physical exercise on neurodegeneration through measurement of neurofilament light chain levels in patients with AD who participated in an aerobic exercise intervention.



Danish Huntington Association

Professor **Jørgen E. Nielsen** and neuropsychologist and Associate Professor **Asmus Vogel** were awarded DKK 500,000 from the Danish Huntington Association for the project "Huntington's disease. Endo-phenotypes and biomarkers: new investigations and prognostic markers in a longitudinal perspective". The aim of the project is to longitudinally characterise the phenotypical spectrum of gene mutation carriers and relate the findings to biomarkers in CSF and blood to identify potentials for more personalised treatment.



Novo Nordisk Foundation

Professor **Jørgen E. Nielsen** was awarded DKK 2,891,218 from the Novo Nordisk Foundation for the project “CHMP2B associated frontotemporal dementia: exploring new therapeutic avenues”. The project addresses a rare type of familial FTD as a model of more common dementias and ALS. FTD runs in a unique, large family from Jutland that has a disease-causing mutation in the CHMP2B gene. The way this mutation leads to dementia is not known in detail; however, the pathway involved is a shared feature of many common dementias and ALS. The project will include a clinical follow-up of the family and use of blood, cerebrospinal fluid and stem cell-derived brain cells to longitudinally clarify the role of neuroinflammation with the aim to uncover a potential immune-modulating treatment option. The project will also apply a new gene editing technique to pursue a treatment targeting the root of the disease, namely the mutation.



2019 Marie and August Krogh Prize

Professor **Gunhild Waldemar**, chair of the Danish Dementia Research Centre, received this award for her contributions to research and education on dementia. The Novo Nordisk Foundation and the Organization of Danish Medical Societies presented the prize at the annual meeting of the Danish Medical Societies on 24

January 2019. Established in 1969, the prize, awarded annually to an outstanding health researcher in Denmark, included a personal award of DKK 250,000 and a DKK 1.25 m research grant.

Grant awarded by Righospitalet's Research Board

Anders Toft, MD, received DKK 1.8 m from Righospitalet's Research Board for the project “CHMP2B-mediated frontotemporal dementia: markers, models and mechanisms”. The project addresses a rare type of FTD as a model of more common dementias and ALS. This PhD project will include clinical and neuropsychological examinations; assessment of inflammatory biomarkers in serum and CSF; and generation of patient-specific neuronal and glial cell models derived from induced pluripotent stem cells to investigate neuroinflammation on a cellular level. The overall objective is to uncover a potential treatment option.

NATIONAL AND INTERNATIONAL POSTS

Birgitte Bo Andersen, inspector, Danish Health and Medicines Authority (appointed by the Danish Neurological Society); appointed member, Dementia Council of the Capital Region of Denmark; appointed member (local chair), steering committee for revision of the patient care pathway programme for dementia in the Capital Region of Denmark.

Eva Bjerregaard, appointed member, Dementia Council of the Capital Region of Denmark.

Nadia Falcon Bærnthsen, board member and manager of quarterly meetings and annual assembly, Danish Neuropsychological Society.

Kristian Steen Frederiksen, co-chair, EAN Scientific Panel on Dementia and Cognitive Disorders, member EAN Scientific Panel on Higher Cortical Functions; appointed member EAN Guideline Production Group; chair, EAN Guideline on "Medical management issues in dementia"; representative, Danish Alzheimer Association; board member, Alzheimer Research Committee under the Danish Alzheimer Association; working group member, National Infection Hygiene Guideline on prion diseases, Statens Serum Institut (appointed by the Danish Neurological Society), PI and Danish national coordinator on two studies on AD.

Steen G. Hasselbalch, board member, Danish Alzheimer Association; board member, Danish Alzheimer Research Foundation, chair, Alzheimer Research Committee under the Danish Alzheimer Association; working group member, National Guideline on diagnosis of MCI and Dementia, Danish Health Authority; member, Scientific Panel on Dementia and Cognitive Disorders, EAN.

Lena Hjermind, PI of global observational study on HD, Enroll-HD; Danish national coordinator and PI on three clinical trials (phase I/II and phase III) on HD; member of EHDN working groups "Genetic testing and counselling" and "Symptomatic treatment and research"; board member, European Dystonia Network.

Peter Johannsen, chair, Danish National Dementia Registry; working group member, Danish National Guideline on Dementia Treatment, Danish National Board of Health; Danish national coordinator on six clinical trials on AD.

Kasper Jørgensen, neuropsychology consultant, Danish Patient Safety Authority; board member, Dansk Psykologisk Forlag.

Jørgen E. Nielsen, Danish national coordinator and PI of the global observational study on HD, Enroll-HD; board member, international SPATAX network on cerebellar ataxias and spastic paraplegias; advisor, European Huntington's Disease Network and steering committee member, EHDN REGISTRY; appointed member, research board,

Rigshospitalet; appointed member, European Academy of Neurology, scientific panel in neurogenetics; appointed member, working group for clinical application of WGS, Danish National Genome Center.

T. Rune Nielsen, co-founder and member, Nordic Research Network on Dementia and Ethnicity; member, advisory group on dementia in ethnic minorities in the Nordic Dementia Network coordinated by the Nordic Welfare Centre; appointed member, Alzheimer Europe expert group on the development of intercultural care and support for people with dementia from minority ethnic groups.

Signe Pertou Ringkøbing, board member and secretary, Danish Neuropsychological Society.

Jette Stokholm, neuropsychology consultant, Danish Patient Safety Authority; neuropsychology consultant, National Legal Medicine Council.

Hanne Sørensen, appointed member, Dementia Council of the Capital Region of Denmark; appointed member, steering committee for revision of patient care pathway programme for dementia, Capital Region of Denmark.

Karen Tannebæk, member, Nordic Dementia Network established by Nordic Welfare Centre; member, Danish Network on Psychosocial Methods in Dementia (DaneDem); member, DDRC professional reference group on dignified elderly care; member, follow-up group on national dementia action plan; member, reference group for handbooks on knowledge-based recommendations for dementia social and health care practice; member, implementation group for national dementia action plan, Danish Ministry of Health.

Asmus Vogel, section editor, *Scandinavian Journal of Psychology*.

Gunhild Waldemar, board member (president-elect), Alliance for Biomedical Research in Europe; committee member, European Affairs Subcommittee and member, Management Committee for Scientific Panel of Dementia of EAN; member, Medical and Scientific Advisory Panel of Alzheimer's Disease International; member, Expert Advisory Panel, Alzheimer Europe; member, Board of Trustees and chair, Grants and Prize Committee Lundbeck Foundation; advisor, National Legal Medicine Council, Danish Ministry of Justice; vice-chair, Dementia Council, Capital Region of Denmark; executive committee member, Neurology Council, Capital Region of Denmark; medical lead, Trial Nation Denmark Dementia Centre.

Laila Øksnebjerg, member of the scientific committee of 14th Nordic Meeting in Neuropsychology, Denmark 2021; founder of DaneDem, Danish research network on psychosocial methods in dementia.

STAFF IN 2019

MANAGEMENT GROUP (per 31/12/2019)



Chair
Gunhild Waldemar, MD,
DMSc, professor, senior
neurologist



Head nurse
**Copenhagen Memory
Clinic**
Hanne I. Sørensen, RN



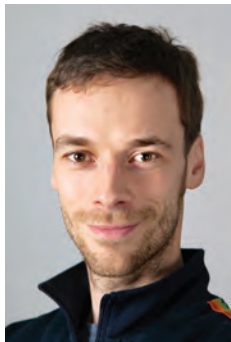
Clinical director
**Copenhagen Memory
Clinic**
Birgitte Bo Andersen,
MD, DMSc, senior
neurologist



Research director
Steen G. Hasselbalch,
MD, DMSc, professor,
senior neurologist



Research director
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neurologist



Centre manager
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PhD, MSc



Educational director
Karen Tannebæk,
occupational therapy
specialist



**Director of communi-
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Marie Ejlersen, MA



Head of administration
Tine Olsen

EMPLOYED AS OF 31/12 2019

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Ditte Majgaard Jensen, accounting staff
Bodil Lykkegaard Kryger, accounting staff
Brit Mouritsen, personal assistant
Tine Olsen, head of administration

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Marie Ejlersen, MA, director of communications and press
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Ann Nielsen, PhD, project manager
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Karen Tannebæk, OT, educational director
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RESEARCH

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Peter Roos, MD, PhD student
Anja Hviid Simonsen, PhD, MSc, senior researcher

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Jette Stokholm Pedersen, MSc, neuro-psychologist
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Gunhild Waldemar, MD, DMSc, professor, senior neurologist
Laila Øksnebjerg, MSc, neuropsychologist, PhD

COPENHAGEN MEMORY CLINIC

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Nela Gorovic, MD
Victoria Gunmalm, MD
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Peter Johannsen, MD, PhD, senior neurologist
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Annette Lauridsen, RN
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Mette Nyboe, RN
Hanne Raaschou, RN
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Social counsellor

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Medical laboratory technologists

Kathrine Bjarnø (maternity leave)
Katrine B. Lauritzen
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External medical consultants

Hanne Elkjær Andersen, MD, geriatrician
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Hanne Pedersen, MD, geriatrician
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PUBLICATIONS IN 2019

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BOOK CHAPTERS AND BOOKS

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EXTERNAL FUNDING FOR RESEARCH AND EDUCATION ACTIVITIES 2019 (DKK M)	
New grants received*	18.3
New grants accumulated 2007-2019*	187.3
External grants spent on specific programmes	20.8
• National Info & Education Centre for Dementia from the Danish Ministry of Health, including projects	13.6
• Other external grants for research*	7.2
Conferences, educational courses and products	5.3
Research contracts	2.8

* excluding the annual main grant from the Danish Ministry of Health

STAFF 2019	
No. of employees/full-time equivalents	104/79
No. of employees funded by	
• Internal sources	54
• External sources	50

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