

EADC Resident and Research Fellow Section (RRFS)

Exchange through internship programs

Name and location EADC hosting center

Danish Dementia Research Centre

Rigshospitalet

Copenhagen

Denmark

Link to center's website

<https://videnscenterfordemens.dk/en>

PI of the EADC hosting center

Professor Gunhild Waldemar

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Description of the center

Give a full description of main clinical and research activities

The centre was founded with support from the Danish Health Foundation and the Ministry of the Interior and Health. It was established in connection with the existing memory clinic at Rigshospitalet, and the centre opened on World Alzheimer's Day September 21st, 2007.

CLINICAL SERVICES

Located at Rigshospitalet and based in the Department of Neurology, the Danish Dementia Research Centre (DDRC) comprises the following sections: Copenhagen Memory Clinic (with a Clinical Trial Unit), a research unit, the national information and education centre, and an administrative secretariat. The Copenhagen Memory Clinic is a secondary and tertiary

referral based multidisciplinary out-patient clinic offering diagnostic evaluation, treatment, and counselling for patients with cognitive disorders and dementia.

From its establishment in 1995, the clinic has offered diagnostic evaluation and treatment of patients with cognitive disorders and dementia. We receive referrals from general practitioners, private practice neurologists, psychiatrists, and other hospitals in the Capital Region of Denmark. Patients are also referred from other memory clinics in Denmark for second opinion evaluations. A satellite memory clinic is located on the island of Bornholm. For both locations, new patients may be referred for diagnostic evaluation of cognitive, behavioural, or other symptoms suggestive of dementia or cognitive disorders. Our dedicated multidisciplinary team comprise consultant neurologists, psychiatrists, geriatricians, neuropsychologists, specialist nurses, a clinical geneticist, a social counsellor, and medical secretaries.

Diagnostic evaluation and plan for treatment and care

Most patients undergo a standard minimum set of examinations and procedures, beginning with a detailed medical history. Cognitive functions are then assessed with the Mini-Mental State Examination and Addenbrooke's Cognitive Examination. In addition, 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 in subsamples of referred patients, for example: fludeoxyglucose positron emission tomography (18FDG-PET), PET-PE2i and amyloid PET, routine(?) and biomarker examination of cerebrospinal fluid (CSF), EEG, neuropsychological assessment, and psychiatric evaluation. After completion of the initial examinations and procedures, the multidisciplinary team (MDT) prepares a standardized consensus report containing a classification of the cognitive profile, the primary underlying cause, concomitant conditions, and a treatment plan. Following the weekly MDT meetings, the patient and caregivers are invited to meet with the specialist physician and specialist nurse, where information and counselling is given on diagnosis, treatment, and care plan. A short summary is subsequently sent to the patient's general practitioner and community nurse if relevant. Some patients may be offered a follow-up programme in the memory clinic.

Specialised medical services

Patients with rare, complex, or familial disorders may be referred from all parts of Denmark (mainly Eastern Denmark) for treatment and follow-up at our clinic. In accordance with guidelines for local, regional, and highly specialised medical services from the Danish Health Authority, Copenhagen Memory Clinic has been approved as a regional and highly specialised centre in the field of dementia and neurogenetics for the following services:

- 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, e.g. : Alzheimer’s disease (AD), frontotemporal dementia (FTD), spinocerebellar ataxias (SCA), and Huntington’s disease (HD)
- Clinical evaluation, lumbar perfusion and tap tests for patients with suspected normal pressure hydrocephalus (NPH)

The 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). 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 dilation of the ventricular system. 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.

Follow-up programme for patients and families

All patients with mild cognitive impairment (MCI), selected groups of patients with dementia, and specific neurodegenerative disorders from the local catchment area, 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. Most patients are accompanied by their family caregivers when visiting the clinic, and we offer counselling for the caregivers as an integral part of the follow-up programme. For fragile patients with severe dementia home visits are offered.

RESEARCH

The DDRC research programs are focused on epidemiological, clinical, and translational research in cognitive impairment and neurodegenerative disorders. Most of our research is

funded by grants and donations from public and private foundations. Our clinical research is based on important infrastructure, which we have developed to have easy access to well-structured clinical data, biosamples, and national registries which may be linked and combined. Our laboratory facilities offer opportunities for cell and molecular translational research. In addition, our research could not be done without collaboration with expertise and access to infrastructure from our national and international collaborators.

Translational Neurogenetics Laboratory

DDRC has an in-house fully equipped laboratory to perform all aspects of cellular and molecular research. We have labs classified for working with genetically modified organisms (class I and class II conditions) which provides permission to work with molecular cloning, adeno-associated and lenti-viral vectors, and infectious disease models.

Furthermore, we have equipment to perform various standard protein and molecular biological techniques e.g. PCR, quantitative PCR, Western blotting, flow cytometry, and fluorescence microscopy.

We have set up standard routines for reprogramming fibroblasts into induced pluripotent stem cells (iPSC), for gene editing using the CRISPR/Cas9 technique, and differentiating iPSC into e.g. neurons, microglia, astrocytes and 3D brain organoids.

Patient cohorts

Patients with a wide range of diagnostic entities and cohorts of healthy controls and gene mutation carriers serve as the foundation of many DDRC research programs:

The memory clinic receives approximately 2.000 new referrals each year. With informed consent from participants, who are willing to participate, results from diagnostic investigations are stored in a research database, and they form an important basis for research with the aim of improving diagnostic evaluation, treatment, and care for patients in our memory clinic. Several large-scale multicentre intervention studies (e.g. ADEX, BASIC and DAISY) have been coordinated by DDRC leading to large nationwide patient cohorts with follow-up data. Collaboration on dementia research in selected Danish memory clinics has been established in the ADEX consortium (coordinated by DDRC) – a Danish research multicentre net-work comprising of eight different memory clinics across the country. The international multicentre study PredictND, which successfully terminated in 2018, acquired a cohort of 800 patients and continues to produce research results by collaborating partners.

DDRC is a member of several international networks on familial de-mentia disorders, such as the European Huntington Disease Network (EHDN), Enroll-HD which is a clinical research platform and the world's largest observational study for Huntington's disease families, and the Frontotemporal dementia Research in Jutland Association (FReJA) consortium, which provide platforms for professionals to facilitate collaboration through-out Europe. Such networks also have been instrumental in the recruitment of DDRC patients to pharmacological intervention studies.

Danish national registries

All Danish in- and out-patients, who have had contact with a Danish hospital are registered in the Danish national health registries with basic information, such as diagnostic codes and procedures. Access to the nationwide health care registries with the possibility of linking to other national registries makes it possible to carry out large population-based studies. These unique national registries have served as the foundation for our studies in dementia including, quality of health care, validity of dementia diagnosis, pharmacoepidemiology, co-morbidity, prevalence, incidence, and mortality.

Danish Dementia BioBank and clinical cohort research data

The Danish Dementia BioBank (DDBB) contains samples from more than 13,000 patients referred to the Copenhagen Memory Clinic at Rigshospitalet and the Zealand University Hospital Memory Clinic in Roskilde, all of whom provided informed consent for their samples to be used for future research. Whole blood, buffy coat, EDTA plasma and serum are stored for all patients, as well as CSF from approximately 25 % of the patients. Additionally, our biobank contains patient fibroblast and iPSC cultures generated from skin biopsies. All samples are handled and stored according to international biobank recommendations. Furthermore, we collect clinical and paraclinical data to accompany the biofluids, and our database now holds more than 200,000 datapoints associated with the biological specimens. The DDBB provides support and infrastructure for a wide range of internal and external collaborative projects.

Internship program

Give a description of the contents of an internship program at the hosting center. If desirable, give separate descriptions for clinicians and for researchers. Indicate the optimal duration of an internship program (preferably max 4 weeks)

Clinician internship

Clinicians visiting the centre will follow physicians or neuropsychologists seeing a diverse array of patients covering the full spectrum of types of patients seen at the centre. This includes newly referred patients with cognitive complaints, second opinion patients, patients with rare disorders, and patients for genetic counselling. There are several patient conferences each week and participation in this type of activity will also be included. There are weekly journal clubs for young researchers, which are also relevant for a clinician to join. All physicians and most other staff are competent in communicating in English, but all patient visits are conducted in Danish (except for non-Danish speaking patients). Optimal duration is approximately 2 weeks.

Research internship

Research internships will be planned according to the areas of interest of the researcher and may be focused on one of the areas of research that the centre is engaged in. This includes epidemiological and health services research (e.g. pharmaco-epidemiology, risk factors, early symptoms), clinical research (e.g., biomarkers, digital biomarkers, prodromal Lewy body dementia, cognitive symptoms and assessment, hearing loss), and basic research (e.g. within iPSC generated models, autophagy, or anti-viral immune responses). The internship may be focused on a specific area or research project as well as a more broadly based approach, where the visitor will be exposed to multiple areas of research. If possible, the visitor may be involved in a research project (e.g. doing data analysis, writing paper) of interest. The centre usually has a group of around 15-25 young researchers (master students, PhDs, Postdocs) from different countries with different educational backgrounds at any given time, thus offering a vibrant scientific environment with discussions and journal clubs. Young researchers are supervised by a group of senior researchers, associate professors, and full professors. Optimal duration is approximately 2-4 weeks.