The year 2014 was busy, not only with clinical activities as always, but also with several important scientific and social events. Rigmor Jensen was main organizer of the 4th European Headache and Migraine Trust International Congress in Copenhagen in September. The congress was a great success with over 1,000 participants and nominated among the top 3 congresses in Copenhagen in 2014. We thank the staff from DHC for excellent help before and during the congress.

In September, Messoud Ashina was appointed professor at the University of Copenhagen as a result of his very productive research and his visions for future high quality research. This will without doubt further strengthen the research profile of the DHC. Congratulations to Messoud Ashina and DHC.

The work on the new building for the centre has been delayed, but it is now back on track. We expect the building to be ready in the spring 2017. We are looking much forward to be able to greet our patients welcome in modern facilities. On the sad side we had to say goodbye to senior consultant Peer Tfelt-Hansen. Peer has decided that it is time cut down on the clinical work load. We thank Peer for his tremendous efforts during many years of excellent clinical service and look forward to continue the scientific collaboration. On the happy side we welcome Vlasta Vukovic Cvetkovic as a senior consultant in DHC. Vlasta is an experienced senior consultant from Croatia with special interest in headaches. Vlasta is doing great progress in learning the difficult Danish language. We look forward to many years of collaboration.

Rigmor Jensen turned 60 years young in November, which was celebrated on several occasions. Rigmor thanks for the many warm greetings.

Research continued to flourish with one doctoral thesis and three defended PhD theses. Congratulations to Christina Kruuse, Hanne Yri, Anders Hougaard and Dorthe Kjeldgaard Nielsen. Jakob Møller Hansen received the prestigious Woolf Award in Boston for his work on human migraine models. Congratulations to Jakob.

We hope that these small pieces of information may interest our readers so much that they feel stimulated to read in more detail about DHC on the following pages.
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1. Research

1.1 Organization

The Danish Headache Centre has 8 vigorous research groups run by 8 senior researchers, 5 post docs and 23 Ph.D. students. The research groups are shown in Figure 1.

Figure 1. Organization of Research.
1.2 Research Staff

**Senior scientists:**
Jes Olesen
Rigmor H. Jensen
Peer Tfelt-Hansen
Inger Jansen Olesen
Messoud Ashina
Lars Bendtsen
Aydin Gozalov
Vlasta Vukovic Cvetkovic

**Post docs.**
Henrik Winther Schytz
Jakob Møller Hansen
Signe Bruun Munksgaard
Dipak Vasantrao Amrutkar
Deepak Kumar Bhatt

**Technologists:**
Hanne Andresen
Lene Elkjær
Zainab Ahtosh
Winnie Grønning
Mari Salan

**Administrative assistants:**
Kirsten Hjelm
Maria Luisa Jimenez Pranov
Karin Aagaard
Line Nørgaard

**Medical students**
Trine Nielsen
Morten Togo Sørensen
Ninett Louise Find
Benjamin Janjoa
Amina Aharaz
Dana Li
Samaira Younis

**Ph.D.students:**
Anders Hougaard
Faisal Amin
Song Guo
Nanna Bjørkhom Arngrim
Sabrina Khan
Marie Deen Christensen
Stine Maarbjerg
Tone Heinskou
Mads Christian Johannes Barløse
Hanne Marie Yri
Lotte Skytte Krøll
Bjarne Kjeldgaard Madsen
Maria Schmidt Uldall
Maria Lurenda Westergaard
Ann-Louise Esserlind
Anne Francke Christensen
Mona Ameri
Sara Hougaard Pedersen
Sarah Louise Tanggaard Christensen
Katrine Hansen
Rikke Elgård Christensen
Dorte Phillip
Julie Carøe Kristensen

**Other researchers**
Sait Ashina
Steffen Petersen
Vibeke Møllegaard Kristensen
1.3 Research Areas

**Human migraine models**

**Members of the Human Migraine Research Unit (HMRU)**
Messoud Ashina (director), Jes Olesen, Faisal Amin, Anders Hougaard, Song Guo, Nanna Arngrim, Jakob Møller Hansen, Henrik Schytz, Sabrina Khan, Marie Deen Christensen.

**Background**
The HMRU is an integral part of the Danish Headache Center and Department of Neurology, Glostrup Hospital. At the HMRU, we seek to understand molecular mechanisms of migraine and to identify disease specific biomarkers (fingerprints of migraine). The core expertise of our members is human provocation models of migraine and ultrasound-based diagnostic imaging techniques used for visualizing vascular responses during experimentally induced migraine attacks. Over recent years, we have added additional expertise in functional and structural magnetic resonance imaging (incl. MR-angiography & functional MRI). These advanced imaging techniques constitute an important supplement to our provocation models and provide new and exciting insights into migraine pathophysiology. Furthermore, the HMRU has extended its field of interest by utilizing migraine genetic discoveries in human models of migraine to investigate functional consequences of genetic mutations. These achievements would not have been possible without strong collaborative work between the HMRU, the Functional Imaging Unit, Glostrup Hospital and other research groups.

In the future we intend to broaden our research program with novel human models of migraine and new imaging techniques (incl. PET) with the ultimate goal of defining predictive animal models of migraine, and discovery of targets for more specific and more effective mechanism-based anti-migraine drugs.

**Current projects**

**Hypotheses:**
- Hypoxia provokes headache and migraine attacks with aura
- Carbon monoxide provokes headache and migraine attacks
- CGRP provokes more migraine attacks in patients with high genetic load than in patients with a low genetic load
- PACAP38 provokes more migraine attacks in patients with PACAP-associated gene variant
- Migraine attacks are associated with increased in blood-brain barrier permeability
- Natriuretic peptides dilates cerebral arteries and induces headache
- Patients undergoing endovascular procedures develop chronic headache
- Migraine attacks are associated with levels of serotonin in the brain
- Prevalence of migraine is higher in persons with the 3243A>G mutation in mitochondrial DNA
- Low frequency neuro-stimulation of SPG provokes migraine attacks in migraine patients
- Pre-treatment with antihistamine blocks PACAP38 induced migraine attacks
- The migraine brain is characterized by low levels of serotonin

**Collaboration**
Henrik Larsson (Functional and Diagnostic MR Unit, Glo-
Epidemiology

Members
Rigmor Jensen, Lars Bendtsen, Sait Ashina, Maria Westergaard.

Background
Epidemiology is the study of the distribution and determinants of health-related states or events in specified populations. The Glostrup Research for Health and Prevention is the unique Danish facility for epidemiological studies in all chronic diseases including headache and several PhD theses have been conducted from this institution.

Current projects
The Danish National Health Survey (DNHS) was a cross-sectional survey involving 130,000 individuals and that used a self-administered questionnaire with 52 core questions on chronic illness, health behaviour, perceived stress, and quality of life. The survey was implemented in 2010 and headache related questions are now under evaluation. Supplementary data analysis with specific focus on chronification, medication overuse, use of prescription medication and socioeconomic impact are ongoing and will be supplemented with data from the extensive national registers. The prevalence of medication overuse headache in Denmark is 1.8%, equivalent to 80,000 adults and such large figures call for further attention as Medication Overuse Headache is a unique type of disabling pain that in principle both can be prevented and treated. Several new projects focusing on specific treatment results and neurobiological mechanisms underlying medication overuse headache are ongoing. Data from the epidemiological studies are related to newer population studies and predictors for chronification are identified.

Genetics and environment

Members
Jes Olesen, Anne Francke Christensen, Ann-Louise Esserlind, Benjamin Janjoa, Amina Aharaz, Mona Ameri.

Background
Family studies and twin studies show that the risk of migraine is 50% inheritance and 50% environment. The identification of genes involved in migraine may give clues to underlying pathophysiological mechanisms. It is equally important to identify the environmental factors, which so far are largely unknown.
Current projects
One aim of our studies is to identify the genes involved in migraine with aura, familial hemiplegic migraine, and migraine without aura. To date we have collected blood from 3000 migraine patients. Genome wide association typing (GWAS) and exome chipping have been performed. The results are now being utilized in collaboration with the gene finding company DeCode in Iceland and as members of the International Headache Genetics Consortium. We also participate in the STEMBANCC consortium funded under the Innovative Medicines program of the EU taking skin biopsies for fibroblast culture and reprogramming to pluripotent stem cells and further differentiation.

Medication-overuse headache

Members
Rigmor Jensen, Ninett Louise Find, Lars Bendtsen, Signe Bruun Munksgaard, Maria Westergaard, Rossana Terlizzi.

Background
Medication-overuse headache (MOH) is a daily or almost-daily type of headache that usually results from the chronification of primary forms, such as migraine or tension-type headache, as a consequence of the progressive increase in the intake of symptomatic drugs. Limited amount of data exists on the burden of MOH, even in developed countries, but there is general agreement that the disease represents one of the most disabling disorders, which markedly deteriorates the quality of life of patients, exposing them to the risks of side-effects and co-morbid conditions.

Our knowledge on the mechanisms leading to MOH is limited, and there are virtually no data on how these severely patients are treated optimally. Thus, there is an urgent need for studies investigating the pathophysiology and treatment possibilities of MOH.

Current projects
An EU-founded multi-centre study (COMO-ESTAS) investigating the benefit of electronic headache diaries during detoxification of MOH has been finalized and results are underway for publication. The first reports demonstrate a highly significant reduction in headache frequency, more than 2 thirds reverse from chronic to episodic headache. The depression and anxiety-scores are markedly reduced by mere detoxification and indicate that these comorbidities are a function of severe headache and not causative to the pain. A new project testing the efficacy of 2 different detoxification programmes and the potential biomarkers for relapse in close collaboration with University of Bologna is drafted.

Collaboration
C. Tassorelli, Fondazione Istituto Neurologico Casimiro Mondino, Italy. M. Lainez, Fundación de la Comunidad Valenciana para la Investigación Biomédica del Hospital Clínico Universitario De Valencia, Spain. Z. Katsarava, Universitätsklinikum Essen, Germany. R. Fadic, Pontificia Universidad Catolica de Chile, Santiago, Chile. A. Stoppini, Fundacion para la Lucha contra las Enfermedades Neurologicas de la Infancia, Buenos Aires, Argentina. Lars Thorbjørn, Klinik Biokemisk afdeling, Glostrup Hospital. Dr Csaba Ertsey, Department of Neurology, Semmelweis University, Budapest, Hungary; Pietro Cortelli, Department of Neurology, University of Bologna.
Cluster headache

Members
Rigmor Jensen, Mads Barløse, Nunu Lund, Anja Petersen, Lars Bendtsen.

Background
Cluster headache is one of the most severe and disabling type of headaches. The pathophysiology of this disorder is largely unknown and it may be very difficult to treat, in particular the chronic form of cluster headache. There is a peculiar but yet unclarified relation between cluster headache and sleep as most of these severe headache attacks occur during the night, believed to be caused by a hypothalamic disturbance in the chronobiology.

Current projects
Extensive sleep analysis in cluster headache patients as an inpatient study during the active bouts of cluster headache has been finalized and results indicate that cluster headache has a clear diurnal and circannual pattern but are not linked to specific sleep stages. We are continuing a large scale survey on the eventual relation between sleep and cluster headache based on questionnaires. Neurostimulation has been used in selected cases of chronic neuropathic pain and evidence is now accumulating for their use in headache disorders. As chronic cluster headache is one of the most disabling pain disorders known by mankind there is a constant search for new and better strategies, especially for those patients that are refractive to medical treatment strategies. Since 2011 the Danish Headache Center has participated in an international multicentre study of the effect of neurostimulation of the sphenopalatine ganglion in patients with cluster headache, and we have now demonstrated a successful outcome in two-thirds of severely affected patients, and also with a long-lasting effect in 61% after 2 years observation. The significant cost-savings of medication lead to a general approval of this new promising treatment for cluster headache. We have continued to offer this treatment strategy to selected patients in an open labelled register study and in total 62 cluster patients are implanted now in Denmark. Further neuromodulation studies on other strategies are also emerging and DHC is now one of the leading centres for neuromodulation in Europe. DHC is also chairing a new European multicentre study of the effect of SPG stimulation in disabling migraine and results are promising.

Collaboration
Søren Hillerup, professor, DDS, and Jørgen Rostgaard, CMT surgeon, DDS, Department of Oromaxillofacial Surgery, National Hospital, Copenhagen, Denmark. Anthony Carparso, Principal Clinical Scientist, Autonomic Technologies, Inc., CA, USA, Poul Jennum, Danish Center for Sleep Medicine, Glostrup Hospital, ElectroCore LLC, 51 Gibraltar Drive, Suite 3C, Morris Plains, NJ, USA.

Clinical trials

Members
Messoud Ashina (director), Rigmor Jensen and Jes Olesen.

Background
The Centre participates in number of clinical trials designed to test new therapies, or new ways of using known treatments to improve the treatment of headache disorders.
Current trials

- Register study of Sphenopalatine Ganglion Stimulation for the Acute Treatment of Cluster Headache
- Sphenopalatine Ganglion Stimulation for the Acute treatment of severe/chronic disabling migraine
- GC-003: Treatment of acute episodic and chronic attacks of cluster headache with GammaCore®, a non-invasive transcutaneous vagal neurostimulation
- Picotamide for the prophylaxis of migraine with aura
- A Phase 2 Study to Evaluate the Efficacy and Safety of AMG 334 in Migraine Prevention
- A Study to Evaluate the Efficacy and Safety of AMG 334 in Chronic Migraine Prevention
- A Study to Assess the Long-term Safety and Efficacy of AMG 334 in Chronic Migraine Prevention

Trigeminal neuralgia

Members
Lars Bendtsen, Stine Maarbjerg, Tone Heinskou, Samaira Younis, Aydin Gozalov, Morten Togo Sørensen, Jes Olesen.

Background
Trigeminal neuralgia is an extremely painful disease, which may be difficult to treat. Management consists of prophylactic pharmacotherapy and surgery in selected cases. There is a huge lack of high quality research in this field and essential aspects such as epidemiology, pathophysiology, diagnosis and optimal treatment are far from understood.

Current projects
Evaluation of efficacy and side-effects of surgery. Evaluation of a structured management programme. Genetic factors. Investigations on how findings from imaging, e.g. the presence or absence of neurovascular contact on high resolution MR-scans, are correlated to clinical findings and to efficacy of pharmacological treatment and neurosurgery. Quantitative sensory testing in trigeminal neuralgia.

Collaboration
Professor Ralf Baron (Division of Neurological Pain Research and Therapy, Universitätsklinikum Schleswig-Holstein, Kiel). Frauke Wolfram, Department of Diagnostics, Glostrup University Hospital, Denmark. Dr. Per Rochat, Department of Neurosurgery, The National Hospital, Copenhagen, Denmark. Dr. Jannick Brennum, Department of Neurosurgery, The National Hospital, Copenhagen, Denmark. Professor, Dr Med Sci, C.G. Faber, neurologist, Department of Neurology, Maastricht University Medical Center (MUMC), Maastricht; the Netherlands.

Receptor characterization and mechanisms activated after infusion of migraine provoking substances

Members
Inger Jansen Olesen, Maja Myren, Dipak Vasantrao Amrutkar, Deepak Kumar Bhatt, Roshni Ramachandran, Sara Hougaard Pedersen, Jes Olesen.

Background
Using the human migraine models mentioned above, we receive knowledge about the headache provoking properties of endogenous signalling substances in man. We believe that a drug or substance that can block the effect of a headache/migraine provoking substance will be effective in the treatment of migraine and thus be a novel target for future development of medicine for migraine. Moving the
studies of migraine triggering substances from man to animal we have the possibility to characterize the receptors or ion-channels for these substances in the migraine relevant tissues; cerebral arteries, dural arteries, dura mater, trigeminal ganglion and trigeminal nucleus caudalis. The characterization is performed by combining several different molecular and in vitro and in vivo functional studies.

- RT-PCR and in situ hybridization for investigating the presence of mRNA for different subtypes of receptors
- Western blotting and immunohistochemistry to investigate the presence and localization of protein for the different subtypes of the receptors and/or ion channels
- In vitro studies of the calcitonin gene-related peptide (CGRP) (a sensory peptide with a role in migraine pathophysiology) releasing properties of the migraine triggering substances in dura mater, trigeminal ganglion and trigeminal nucleus caudalis
- In vivo pharmacological characterization of the receptors activated in dural and pial arteries after intra carotid infusion of the migraine provoking substances

During infusion of a headache/migraine triggering substance the migraine sufferers experience more pain than non-migraineurs. This immediate headache is 4-5 hrs after the infusion followed by a delayed headache sometimes fulfilling the criteria for migraine. We have recently developed an animal model, where the migraine triggering substances are infused to un-anaesthetized rats and the molecular changes in the migraine relevant tissues mentioned above are investigated. By these studies we expect to unravel the cascade of molecular changes taking place in the time period between infusion of a migraine triggering substance and the development of a migraine attack.

**Current projects**

At present we characterize the receptors for prostanoids and the neuropeptides vasoactive intestinal peptide (VIP) and pituitary adenylate cyclase activating peptide (PA-CAP) in migraine relevant tissues.

We are in addition studying the effect of these substances on CGRP release and nitric oxide synthase (NOS) activity. In the conscious rat migraine model, we further examine what markers are up-regulated after infusion and the possible pathway for this up-regulation after infusion of migraine triggering substances. These studies will give us an understanding of which subtype of receptors that are present in these tissues. In addition, they will give us information to further understand the pathophysiology of migraine and to define new targets for the pharmacological treatment of migraine.

**Collaboration**

Professor Dan Klærke (Faculty of Life Sciences, Copenhagen University), Associate Professor Majid Sheykhzade (Faculty of Pharmaceutical Sciences, Copenhagen University), Professor Karl Messlinger (Institute of Physiology and Experimental Pathophysiology, University of Erlangen-Nürnberg, D-91054 Erlangen, Germany), Professor Frank Porreca (Department of Pharmacology, College of Medicine, University of Arizona, Tucson, Arizona, USA), Professor Sue Duckles and Professor Diana Krause, Department of Pharmacology, University of California Irvine, Irvine, California, USA).
Behavioral animal migraine models

Members
Inger Jansen Olesen, Sarah Louise T Christensen, Steffen Pedersen, Jes Olesen.

Background
Despite advances in migraine treatment, there are still huge unmet needs in terms of both prophylactic and acute therapy. At present the lack of suitable, predictive and valid animal models holds up the development of new drugs for migraine. Using the rat model described above, we study a wide range of different behavioural models before and after administration of migraine provoking substances.

Current projects
We study the effect of i.v. glyceryltrinitrate (GTN) infusion on behaviour in running wheel, burrowing and preference for darkness or light. Also the behavioural effect after administration of the orally available long acting NO donor 5-isosorbidemononitrate is studied. We will establish more behavioural models in 2013.

Collaboration
Associate Professor Dorthe Bratbo Sørensen, the Laboratory Animal Science group at Department of Veterinary Disease Biology, Copenhagen University and Staff Scientist, PhD Johnny Roughan, Laboratory Animal Welfare Group, University of Newcastle upon Tyne, United Kingdom.

Tension-type headache

Members
Lars Bendtsen, Rigmor Jensen, Sait Ashina, Bjarne Kjeldgaard Madsen, Lotte Skytte Krøll.

Background
Increased understanding of the relative importance of peripheral factors (mainly muscular) and central factors (mainly central pain processing) in the pathophysiology of tension-type headache are crucial for the development of more effective treatment options for this disorder. Experimental models studying muscular factors, e.g. muscle pain sensitivity, and central factors, e.g. degree of wind-up, and the interaction between these factors are needed to explore the cause/effect relationship between the various peripheral and central abnormalities reported in tension-type headache. Previous studies from our group have, e.g., demonstrated abnormal tenderness and pain perception indicating central sensitization. Headache patients are often physically inactive because of their headache and a linear relationship between low level of physical activity and increased headache frequency has been demonstrated. The clinical experience and some studies have suggested that physical activity may prevent migraine attacks. However the effect of physical activity in patients suffering from migraine and co-existing tension-type headache and neck pain has not yet been investigated.

Current projects
Epidemiology of neck pain and headache. The effect of specific strength training and the role of muscle strength in neck pain in tension-type headache and migraine. The effect of an exercise program in patients with migraine and co-existing tension-type headache and neck pain.
Collaboration
Professor Tim Steiner, Division of Neuroscience and Mental Health, Imperial College London, London W6 8RP, UK. Professor Karen Søgaard, Institute of sports science and clinical biomechanics, University of southern Denmark. Catharina Sjödahl Hammarlund. University Lecturer, Gunvor Gard, professor, Department of Health Sciences, Lund University, Lund, Sweden.

Idiopathic intracranial hypertension

Members
Rigmor Jensen, Hanne Yri, Maria Schmidt Uldall, Inger Jansen Olesen.

Background
Idiopathic intracranial hypertension (IIH) is an intriguing, clinical condition of increased intracranial pressure without pathological, laboratory or radiological evidence of intracranial pathology in young, obese individuals. The clinical symptoms are severe headache, pulsatile tinnitus, transitory visual obscurations and diplopia. Demographic studies report a rapidly increasing incidence of IIH in obese young females and with the global epidemic increase of obesity a significant increase in the number of IIH patients in Denmark can be predicted. Severe obesity is closely related to a number of neuroendocrinological changes which have still not been evaluated in IIH.

Untreated IIH may lead to severe visual loss and blindness resulting from damage to the optic nerve and chronic disabling headache. The mechanism whereby IIH leads to optic nerve dysfunction is poorly understood but it seems to be closely linked to oedema of the optic nerve head and the associated elevation of hydrostatic pressure inside the optic nerve.

A PhD study from this group has analysed the clinical presentation in more than 40 patients detail and their headache characteristics, provided new suggestions for diagnostic criteria and tested their cognitive function before and after treatment. Our new study of IIH thus comprise neurobiological and ophthalmological aspects is a unique study of still unsolved aspects in IIH.

A new experimental PhD study of the mechanisms of IIH has also been initiated in the research park. A reliable animal model for measuring the intracranial pressure over time has been developed and we continue the search for a better understanding of the CSF dynamics and regulation as well as for the understanding of the molecular basis for IIH.

Current projects

Collaboration
Steffen Hamann and Marianne Wegener, Department of Ophthalmology, Glostrup Hospital. Marianne Juhler and Anders Skjolding, Department of Neurosurgery, National Hospital, Denmark and the Copenhagen CSF study Group. Alexandra Sinclair and her CSF-research group, University of Birmingham, UK.
**Chronic post-traumatic headache**

**Members**
Rigmor Jensen, Dorte Kjeldgaard and Hysse Forchhammer.

**Background**
Chronic post-traumatic headache (CPTH) attributed to mild head injury is still a significant mystery for patients as well as for headache experts and very costly for the society. Clear correlation between severity of injury and the persistence of symptoms over time is lacking and has led to a hypothesis of psychological aetiology to CPTH. Both pharmacological treatments as well as a psychological intervention have not yet shown promising results.

**Current projects**
Describe a large CPTH population in detail in terms of demographics, headache characteristics and personality profile and compare them to a group of patients with chronic primary headache.

A group intervention based on cognitive behavioural therapy, in order to provide the patients with knowledge and strategies to manage their CPTH has been conducted. The results were rather disappointing as very little progress were achieved compared to the waiting list group. Further analysis is ongoing and the treatment strategy will be adjusted accordingly.

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**Headache in cerebrovascular disorders**

**Members**
Elena Lebedeva, Jes Olesen, Nathalia Gourary, Nathalia Kobzeva, Tatiana Tsypushkina, Anton Ushenin and Anastasia Busygina.

JO has directed a major collaborative project with associate professor Elena lebedeva, Ural State University, Jekaterinburg, Russia. He is co-supervisor of 5 PhD students, all neurologists. The first project is completed and in the publishing phase. It is an interview study of more than 3000 Russians from 3 different social Groups. It focuses on prevalence, risk factors and previous diagnosis and treatment. The NeXT is a large study where more than 600 stroke patients have been interviewed in the acute phase of stroke and at least 3 months later. It contains a wealth of data and will result in 3 PhD theses. Lastly more than 300 patients with saccular intracranial aneurysm have been interviewed and have donated blood for genetic analysis. Collection is still ongoing. It will result in one, maybe two PhD theses.
1.4 Sponsors

**Major sponsors:**
- Faculty of health and medical science, University of Copenhagen (Ph.D. grants)
- Lundbeck Foundation (independent grant for genetics)
- Lundbeck Foundation (independent grant for trigeminal neuralgia)
- Lundbeck foundation (independent grant for studying mechanisms of migraine provoking substances)
- Candys Foundation
- The Capital Region of Denmark, Foundation for Health Research
- The Danish Agency for Science, Technology and Innovation, and the Danish Council for Independent Research-Medical Sciences
- European Commission, STEMBANCC project
- European Commission, EUROHEAD project
- IMK Foundation

**Sponsors:**
- Danish Headache Society
- The Danish Headache Foundation
- Augustinus Foundation
- Foundation of Lægevidenskabens Fremme
- Kong Christian IX og Dronning Louises Jubilæumslegat
- The Foundation for Neurological Research
- Trigeminus Foreningen
- Novo Nordisk Foundation
- Spar Nord Foundation
- Gangsted Foundation
- Lykfeldts legat
- The Migraine- and Headache Association (Patient Organization)
- The Cluster Headache Association (Patient Organization)
Figure 2. The research group of Messoud Ashina, who was appointed as a professor in 2014.
2. Collaborations

Departments within Glostrup Hospital
- Department of Ophthalmology
- Danish Center for Sleep Medicine
- Department of Clinical Neurophysiology
- Department of Clinical Experimental Research
- Department of Clinical Physiology
- Department of Clinical Biochemistry
- Department of Diagnostics
- Department of Anaesthesiology
- Functional Imaging Unit, Department of Clinical Physiology and Nuclear Medicine
- Stroke Unit, Department of Neurology

External collaborators

Clinical research
- Department of Oral and Maxillo-Facial Surgery, National Hospital, Copenhagen
- Centre for Health and Preventive Medicine, Copenhagen County, Denmark
- Department of Neurosurgery, National Hospital, Copenhagen, Denmark
- Danish twin registry, University of Odense, Denmark
- Department of Neurology, Høllerød Hospital, Denmark
- Associate Professor Elena Lebedeva, Department of emergency neurology, University of Ural Region, Yekaterinburg, Russia
- Professor John-Anker Zwart, Department of Neurology, Ullevaal University Hospital, University of Oslo, Oslo, Norway
- Professor Knut Hagen, Department of Neuroscience, Faculty of medicine, Norwegian University of Science and Technology, Trondheim, Norway
- Professor Timothy Steiner, Department of Neuroscience, Faculty of medicine, Norwegian University of Science and Technology, Trondheim, Norway
- Professor Hartmut Goebel, The Headache Clinic, Kiel University, Germany
- Mondino Institute of Neurology Foundation, Pavia, Italy
- Department of Physical Therapy, Department of Health Sciences, University of Lund, Sweden
- Department of Neurology, Semmelweis University, Budapest, Hungary
- PAIN Group, Mclean Hospital, Harvard University Boston USA
- Optical Imaging Core & Lab at Martinos Centre Department of Radiology, Boston USA
- Leiden University Medical Centre, Holland
- Division of Neurological Pain Research and Therapy, Universitätsklinikum Schleswig-Holstein, Kiel
- Visual Processing Laboratory, Universitätsaugenklinik, Otto-von-Guericke-Universität, Magdeburg
- Department of Neurology and Division of Neuroradiology, University Hospital Basel, Switzerland
- Centre for Sensory-Motor Interaction, University of Ålborg

Basic Pain Mechanisms
- Department of Pharmacology, University of Washington, Seattle, USA
- Department of Medical Physiology, Faculty of Life Sciences, Copenhagen University, Denmark
- Institute of Pharmacology, Faculty of Pharmaceutical Sciences, Copenhagen University, Denmark
- Department of Biology, Bioinformatics Copenhagen University, Denmark
- Institute of Experimental Research, University of Lund, Sweden
• Professor Karl Messlinger, Institute of Physiology and Experimental Pathophysiology, University of Erlangen-Nürnberg, D-91054 Erlangen, Germany
• Institute of Anatomy, Panum Institute, University of Copenhagen, Denmark
• The Laboratory Animal Science group at Department of Veterinary Disease Biology, Copenhagen University
• Laboratory Animal Welfare Group, University of Newcastle upon Tyne, United Kingdom.

Genetics and environment
• DeCode, Reykjavik, Iceland
• Danish twin registry
• Innovative Medicing Initiative EU
• International Headache Genetics Consortium
• Oluf Petersen and Torben Hansen, Marie Krog Centre for Metabolic research, The Novo Nordisk Foundation Center for Basic Metabolic Research

Headache Epidemiology
• Professor Lars-Jacob Stovner, Kompetencecenter for epidemiology, University of Trondheim, Norway
• Professor Tim Steiner, Lifting The Burden, WHO

Headache diagnosis
• Professor Guiseppe Nappi, Institute Mondino, University of Pavia, Italy (EU-project)

Idiopathic Intracranial Hypertension
• PhD Steffen Hamann, Dr Sci Birgit Sander and Consultant Marianne Wegener, Department of Ophthalmology, Glostrup Hospital
• Copenhagen CSF-study group, Professor Marianne Juhler, Department of neurosurgery, National Hospital
• University of Birmingham, UK

Cluster headache
• Søren Hillerup, professor and Jørgen Rostgaard, DDS, Department of Oromaxillofacial Surgery, National Hospital, Copenhagen, Denmark
• Anthony Carparso, Principal Clinical Scientist, Autonomic Technologies, Inc., CA, USA
• Poul Jernum, Danish Center for Sleep Medicine, Glostrup Hospital

Medication-overuse headache
• Dr. C. Tassorelli, Fondazione Istituto Neurologico Casimiro Mondino, Italy
• Dr. M. Lainez, Fundación de la Comunidad Valenciana para la Investigación Biomédica del Hospital Clínico Universitario De Valencia, Spain
• Dr. Z. Katsarava, Universitaetsklinikum Essen, Germany
• Dr. R. Fadic, Pontificia Universidad Catolica de Chile, Santiago, Chile
• Dr. A. Stoppini, Fundacion para la Lucha contra las Enfermedades Neurologicas de la Infancia, Buenos Aires, Argentina
• Dr. Csaba Ertsey, Department of Neurology, Semmelweis University, Budapest, Hungary

Trigeminal neuralgia
• Professor Ralf Baron, Division of Neurological Pain Research and Therapy, Universitätsklinikum Schleswig-Holstein, Kiel
• Frauke Wolfram, Department of Diagnostics, Glostrup University Hospital, Denmark
• Dr. Per Rochat, Department of Neurosurgery, The National Hospital, Copenhagen, Denmark
• Dr. Jannick Brennum, Department of Neurosurgery, The National Hospital, Copenhagen, Denmark
• Professor, Dr Med Sci, C.G. Faber, neurologist, Department of Neurology, Maastricht University Medical Center (MUMC), Maastricht; the Netherlands
Figure 3. The trigeminal neuralgia group (Stine Maarbjerg, Hanne Andresen, Samaira Younis and Lars Bendtsen) during their visit at Professor Ralf Baron, Division of Neurological Pain Research and Therapy, Universitätsklinikum Schleswig-Holstein, Kiel.
3. Publications in 2014

Papers in peer-reviewed scientific journals


50. Tfelt-Hansen, P.C. & Diener, H.C. (2014) Use of dihydroergotamine (DHE) should be restricted to no more than twice a week. Headache., 54, 1523-1525.


**Doctoral Thesis**

1. Kruuse, C. Role of phosphodiesterase 5 and cGMP signalling in cerebral arteries, cerebral blood flow, and headache - contributions to understanding migraine pathophysiology. Faculty of Health Sciences, University of Copenhagen, 2014.

**PhD Theses**

1. Yri, HM. Idiopathic intracranial hypertension - Exploring headache and cognitive function. Faculty of Health Sciences, University of Copenhagen, 2014.
2. Hougaard, A. Investigations of functional and structural changes in migraine with aura by magnetic resonance imaging. Faculty of Health Sciences, University of Copenhagen, 2014.
3. Kjeldgaard, DN. Personality profile and psychological treatment of patients with chronic post-traumatic headache. Faculty of Health Sciences, University of Copenhagen, 2014.
The clinical activities in DHC consist of a multidisciplinary out-patient service and an in-patient service. At the end of 2014 the staff consisted of 3 psychologists (one on maternity leave), 4 physical therapists (hereof 2 PhD students), 4 nurses, 1 team leader, 1 laboratory technician, 9 secretaries, 7 neurologists specialized in headache (all part time), 1 dentist (one day per month) and a variable number of younger physicians on rotation (all part time). In addition, the nursing staff at the Department of Neurology N 38 take care of the in-patients in close collaboration with DHC.

The out-patient activities continued on a high level in 2014. A total of 3,185 patients were treated in the centre during 2014. Approximately 120 patients have been treated at the in-patient department N 38.

A total of 65% of patients were referred from The Capital Region, while the rest of patients were referred from other parts of Denmark and Scandinavia.

Migraine is the most common disorder seen in out centre followed by cluster headache, tension-type headache and medication-overuse headache (Figure 4). Almost all these patients have previously been seen by several physicians including neurologists and have been referred to DHC, because they are highly disabled and considered treatment resistant. Because of the tertiary nature of our centre, we manage a relatively high number of patients suffering from the excruciating painful disorders cluster headache and trigeminal neuralgia.

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**Figure 4.** Migraine, medication-overuse headache, tension-type headache, cluster headache and combinations hereof are the most common types of headache seen in the centre. Figures add up to more than 100%, because several of our patients suffer from more than disorder.
The in-patient headache service
Six beds at the Department of Neurology N 38 are allocated to the in-patient programme. The majority of patients are suffering from medication-overuse and are admitted for detoxification. In addition, patients suffering from other types of headache can be admitted for observation, certain specialized diagnostic procedures or treatment that requires hospitalization. The medication-overuse patients are all primarily seen on an out-patient basis in the Centre and then admitted for a fixed in-patient period of 14 days where they follow a structured regime. After discharge they are closely followed as out-patients in DHC for at least one year.
5. Teaching and public activities

Teaching activities
Medical students, Faculty of Health Sciences, University of Copenhagen.
Neurology trainees, Faculty of Health Sciences, University of Copenhagen.
Trainees from General Practise, an essential part of their educational programme.
PhD students, Faculty of Health Sciences, University of Copenhagen.
General practitioners at Læge Dage, the annual national congress for general practitioners.
In addition, numerous teaching activities at international and national congresses.

Public activities
Over the years the Danish Headache Center has organized the annual public meeting at Glostrup Hospital for patients, relatives and other with an interest in headache and facial pain. In 2014 the event was held in Bellacentret during the EHMTIC 2014 and organized in close collaboration with the Patient organization Hovedpinesagen. More than 120 participants attended and the event was very successful with lively discussion. The event was chaired by Peter Quortrup Geisling, the TV-doctor from DR who entertained the audience successfully along with a lively discussion and multiple questions to the scientific panel with updates from the scientific congress. The patient day was introduced by Audrey Craven the president for The European Headache Alliance and Director Wendy Thomas from the Migraine Trust in UK exchanged valuable experience about their patient organisation and activities in UK. Staff from the Danish Headache Center has been interviewed on national television and radio more than 10 times in 2014 and contributed to several public meetings arranged by the Danish patient organizations. The staff has contributed to numerous articles in Danish newspapers and other media during the year.
Figure 5. Rigmor Jensen together with Helle Jensby, Jane Sandby-Møller, Karin Aagaard, Ane Lundgaard Dahl and Dianna Bartolin from DHC during the 4th European Headache and Migraine Trust International Congress in Copenhagen in September.
6. Organization and Staff in DHC

**Management**
Rigmor Jensen - Professor, MD, DMSci.
Director of The Danish Headache Centre.
Jes Olesen - Professor, MD, DMSci.
Founder and co-director of The Danish Headache Centre.
Lars Bendtsen - MD, Ph.D., DMSci, associate professor.
Co-director of The Danish Headache Centre.

**Staff Neurologists**
Peer Tfelt-Hansen - MD, DMSc.
Messoud Ashina - MD, Ph.D., DMSc, associate professor.
Director of Human Migraine Research Unit.
Thue Hjortkær Nielsen – MD, senior consultant.
Leader of the department of inpatient treatment of headache patients.
Aydin Gozalov - MD, PhD, senior consultant.
Co-leader of trigeminal neuralgia research.
Vlasta Vukovic Cvetkovic - MD, PhD, senior consultant.

**Medical secretaries**
Karin Aagaard
Katrine Kristensen
Tina Würgler Kaergaard
Jane Sandby-Møller
Dorte Helmundt
Lis Jønsson
Dianna Bartolin
Ane Lundgaard Dahl
Gitte Ellesgaard Sørensen
Malou Sandvær Harrild

**Physiotherapists**
Bjarne Kjeldgaard Madsen
Nina Caspersen
Jeanne René Hirsvang
Lotte Skytte Krøll

**Laboratory technician**
Hanne Andresen

**Psychologists**
Dorthe Kjeldgaard Nielsen
Trine Zimmer
Camilla Bjørbaek Møller (maternity leave)
Kirsten Larsen

**Nurses**
Annette Vangaa Rasmussen
Annette Fjeldborg Jonasson
Hjordis Rasmussen (nurse assistent)
Malene Kjærgaard Danø

**Psychiatrist**
Andreas Tang Varnild-Jørgensen, Centre of Psychiatry, Glostrup

**Dental expertise**
Dr. odont. Merete Bakke, University of Copenhagen
7. Future

Traditionally there is quite limited collaboration between pain specialists and headache specialists. This should not be so. From January 1st, 2015 our centre is part of Rigshospitalet due to the fusion of Rigshospitalet Blegdamsvej and Glostrup Hospital. This will provide new possibilities for collaboration between pain specialists from Rigshospitalet Blegdamsvej, Rigshospitalet Glostrup and DHC. We have much to learn from each other regarding both clinical and research activities. We are planning a closer collaboration between the two specialities along with other excellent opportunities for collaboration between highly specialized departments. We expect that this will further improve the treatment possibilities we can offer to our patients.

The demand for qualified management of headache and facial pain continues to increase. At the same time we lack senior doctors with special knowledge on headache and we are facing increased demands for documentation and implementation of computer programs which are often not functioning optimally. Together this results in unacceptably long waiting lists for our patients. We will work hard to solve this by increasing our efforts for recruiting talented doctors from Denmark or abroad into our field and to handle the registration and computer issues in the most efficient way. At the same time we will consider how the development in registration requirements and digitalization of our clinical work can improve our possibilities for clinical research.

We will continue to focus on our most important task – the management that we can offer to every single patient. Our wonderful staff is the key here – only by offering the highest standards from every member of our multidisciplinary team can we achieve our ultimate goal – to provide the best care for patients with headache and facial pain in the world.