Annual Report

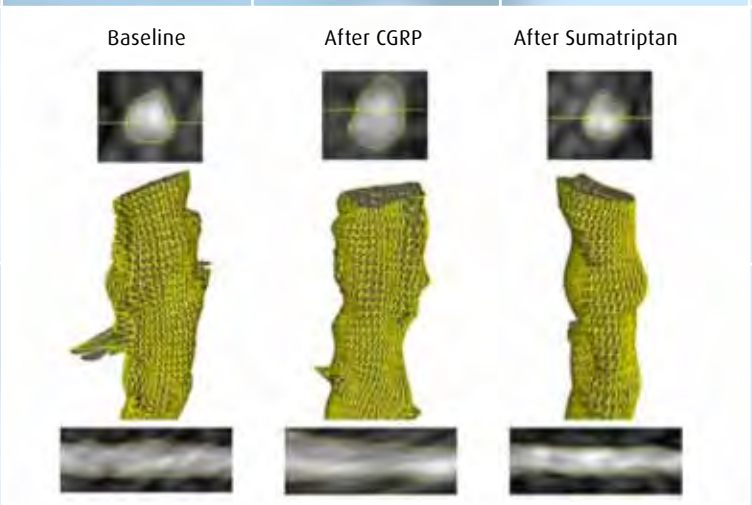
Danish Headache Center

2010

Department of Neurology

Glostrup Hospital, University of Copenhagen

www.danishheadachecenter.dk



Danish Headache Center

Table of contents

Preface

This annual report provides an overview of the clinical and research activities that took place at The Danish Headache Center and the affiliated Glostrup Research Park in 2010. Two extraordinary events have occurred during 2010.

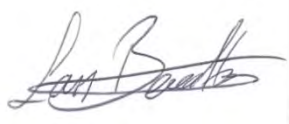
Firstly, Professor Jes Olesen was awarded the highly prestigious Lundbeck Foundation's Nordic Award for Outstanding Research 2010 in recognition of his seminal and comprehensive contributions to clinical headache research. Jes Olesen was celebrated on September 3rd at a symposium with attendance of many leading international and national researchers. The Danish Headache Center is very proud that Jes Olesens leading position among world researchers is acknowledged in this way.

Secondly, The Danish Headache Center was awarded the Global Excellence in Health Prize by the Capital Region (Region Hovedstaden) for being among the leading headache centers in the world with respect to both research, education, dissemination and clinical activities. This official recognition is very important for the center, for our patients and for headache research in general and will undoubtedly help to pave the way for further development of our clinical and research activities.

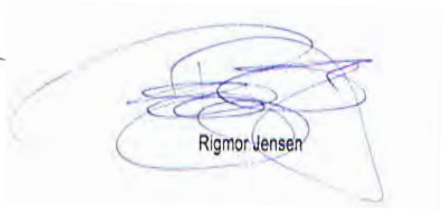
The clinical activities in 2010 have been maintained at a high level and we are grateful to our highly committed staff members for their continuous efforts. Several new treatment programmes have been initiated or carried forward in 2010 in order to continuously improve the quality of the clinical work. A new and highly innovative surgical programme for the treatment of severely affected treatment resistant patients with chronic cluster headache and a new study on neck pain have been implemented. Other innovative treatment programmes regarding difficult to treat headaches, posttraumatic headache, idiopathic intracranial hypertension, headache due to increased contraction of jaw muscles and medication-overuse headache have been carried forward. Likewise a number of interesting new research projects within the multidisciplinary treatment programme have been initiated.

The research at The Danish Headache Center and the affiliated basic research at Glostrup Research Park continue to be very active with a high number of publications and a large impact factor. In 2010, three PhD-theses were successfully defended by our young researchers. Congratulations. Additional information can be found at our homepage: www.danishheadachecenter.dk

Glostrup, April 2011.



Lars Bendtsen



1. Research

1.1 Organization

Danish Headache Center has a vigorous research group including 8 senior researchers, 4 post docs, 17 Ph.D. students mostly MD's and medical students. The organization of research is shown in Figure 1.

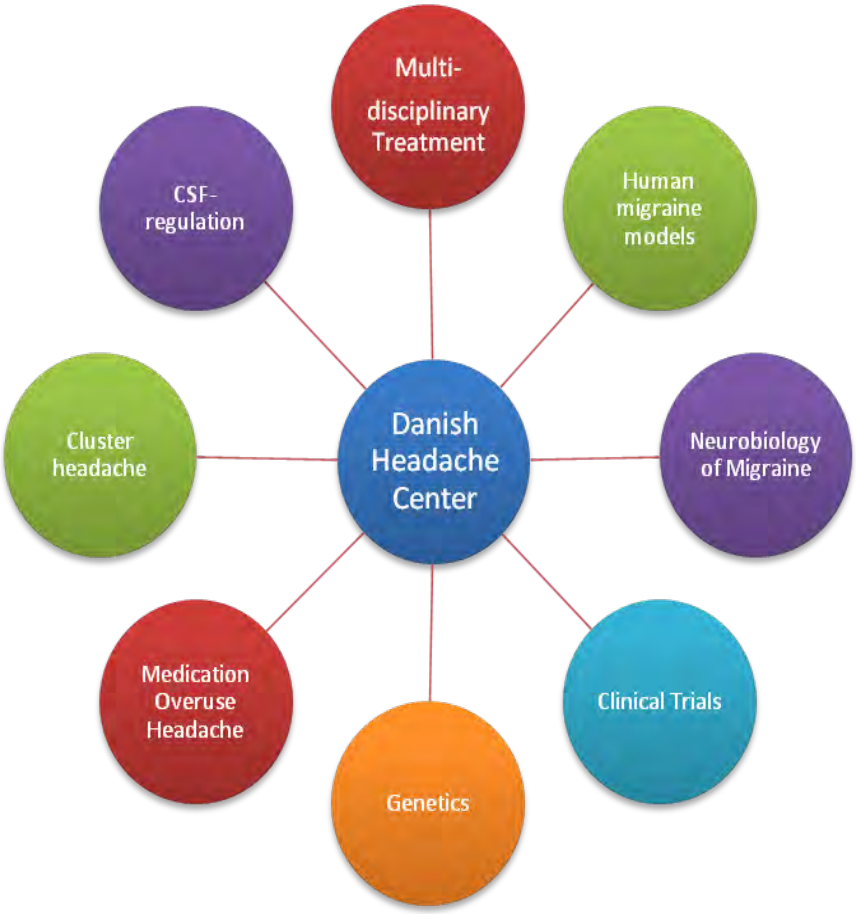


Figure 1. Organization of Research.

1.2 Research Staff

Senior scientists:
Jes Olesen
Rigmor Jensen
Peer Tfelt-Hansen
Inger Jansen Olesen
Messoud Ashina
Saurabh Gupta
Lars Bendtsen
Aydin Gozalov

Associate senior researchers:
Christina Kruuse
Malene Kirchmann

Post docs.
Henrik Winther Schytz
Jakob Møller Hansen
Lars Schack Kruuse
Kenneth Beri Plough

Technologists:
Hanne Andresen
Lene Elkjær
Winnie Grønning

Administrative assistants:
Kirsten Hjelm
Susie Andersen
Karin Aagaard

Ph.D.students:
Sohail Asghar
Anne Werner Hauge
Maren Skau
Helle Wulf
Michael Baun
Han Le
Signe Bruun Munksgaard
Maja Myren
Dipak Vasantrao Amrutkar
Deepak Kumar Bhatt
Roshni Ramachandran
Julie Carøe Kristensen
Anne-Louise Esserlind
Anders Hougaard,
Faisal Amin
Maria Antonova

Other researchers
Hanne Yri
Mads Barløse
Sait Ashina
Asif Munir Shah

1.3 Research Areas

Human migraine models

Members

Messoud Ashina, Sohail Asghar, Jakob Møller Hansen, Henrik Schytz, Troels Wienecke, Anders Hougaard, Faisal Amin, Jes Olesen & Maria Antonova.

Background

Fast tracking of new drugs for migraine have faced the major challenge of poorly-predictive preclinical models. Indeed, novel, migraine-specific preventive drugs have not been developed in decades. Furthermore, the acute therapy armamentarium remains suboptimal, with no new chemical entities since the triptans. On the other hand, human experimental studies are surfacing as a powerful tool in targeted migraine therapy. To this end, human studies have identified three novel targets: inhibitors of cortical spreading depression, antagonists of calcitonin gene-related receptors, and chemicals that prevent the production of nitric oxide. Two of these novel mechanisms are in phase 3 clinical development and one is in phase 2. These encouraging observations, which are based on 20 years of research in human models, have led us to develop a research paradigm for the identification of novel migraine drug targets, which combines human provocation studies and preclinical models.

Current projects

- Role of prostaglandins in migraine pathophysiology: Effect of EP receptor antagonist in PGE2 model of headache
- PGF2lalfa model of headache
- Activation of trigeminal pain pathways during different sequences of CGRP induced migraine attack: fMRI study
- Changes in diameter of extra- and intracranial vessels during CGRP induced migraine attack: MRA study
- Changes in diameter of extra- and intracranial vessels during PACAP induced headache before and after sumatriptan administration: MRA study
- Intrinsic brain connectivity during PACAP induced headache: fMRI study

Collaboration

Henrik Larsson and Adam Espe Hansen (Department of Clinical Physiology); Vibeke Andre Larsen (Department of Radiology); David Borsook and Lino Becerra, PAIN Group, Mclean Hospital, Harvard University Boston USA; David A Boas, Optical Imaging Core & Lab at Martinos Centre Department of Radiology, Boston USA; Professor van der Geest, Leiden University Medical Centre, Holland.

Tension-type headache

Members

Lars Bendtsen, Lotte Skytte Krøll, Sait Ashina, Rigmor Jensen.

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.

Current projects

Investigations of muscular pain sensitivity, epidemiology of neck pain and headache, processing and modulation of peripheral nociceptive input in the central nervous system and the role of neck pain in tension-type headache.

Collaboration

Professor Jens Elrich, Centre for Sensory-Motor Interactions, Department of Health Science and Technology, Aalborg University, Denmark. Professor Lars Arendt Nielsen, Centre for Sensory-Motor Interactions, Department of Health Science and Technology, Aalborg University, Denmark. Professor Tim Steiner, Division of Neuroscience and Mental Health, Imperial College London, London W6 8RP, UK.

Epidemiology

Members

Rigmor Jensen, Sait Ashina, Asif Munir Shah.

Background

Epidemiology is the study of the distribution and determinants of health-related states or events in specified populations. The Glostrup County population study from 1989 was the first prevalence study of specific headache entities in a representative general population, based on a structured interview and examination by a physician. This study demonstrated the huge impact headache has on individuals and society. A follow-up study showed an increase in frequency and health care utilisation and thereby indicated a higher impact of

headache over a 12-year period. Risk factors for migraine were young age, female gender, familial disposition, no vocational education, high work load and frequent tension-type headache. For tension-type headache risk factors were young age, female gender, poor self-rated health, inability to relax after work, and sleeping fewer hours per night. In general migraine and tension-type headache had a favourable prognosis with increasing age and only a minority of subjects had increased headache frequency. Prognostic factors were identified.

Current projects

Supplementary data analysis of the large follow-up study is ongoing with specific focus on chronification, clinical headache characteristics and socioeconomic impact. A large clinical study of patients treated at the Danish Headache Center has already been conducted with main focus on medication overuse headache. It has been demonstrated that detoxification have a very positive outcome, especially in migraineurs and that these patients becomes reactive to migraine prophylactics again. 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 searched.

Genetics and environment

Members

Anne Hauge, Han Le, Ann-Louise Esserling, Jes Olesen.

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 more than 1400 migraine patients and the molecular genetics analyses have been initiated. In twin studies we try to identify the most important environmental risk factors for migraine. We also study the influence of co-morbidity and secular trends.

Intracellular transduction mechanisms in migraine

Members

Christina Kruuse, Carina Jørgensen, Lars Schack Kruse, Julie Carøe Kristensen.

Background

In order to fully understand the cellular signalling behind the effects of headache inducing substances in humans, basic molecular studies are warranted applying the compounds in isolated tissue or cells to supplement the results from modulating specific signalling pathways in human. Pain signalling in humans involve second messenger signalling through second messengers; cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP). We know from human studies that specific modulation of such signalling by inhibiting the breakdown of cyclic nucleotides induce headache, though the tissues in which the processes take place not the possible interaction is not fully understood. We aim to localize and investigate the role of cyclic nucleotide signalling in tissue and cells relevant for the pain process. In collaboration with Department of Clinical Biochemistry Glostrup, Department of Neuroscience and Pharmacology and Functional Imaging Unit and Dept Clinical Physiology and Nuclear medicine we have found unique localisation and function of molecules, phosphodiesterases (PDE), responsible for modulation of cGMP and cAMP signalling in cerebral arteries and the brain.

Current projects

We have described the unique presence of specific PDEs in the cerebral arteries and trigeminovascular system, and is currently investigating the co-localisation of PDEs with other relevant cellular signalling molecules in vascular and neuronal cell systems. Further, by modulation of the cells and tissue with inhibitors of specific PDEs as well as migraine related substances, we try to locate potential new targets for treatment in the pain mechanism of headache and migraine.

Collaboration

Henrik Larsson and Adam Espe Hansen (Functional Imaging Unit, Department of Clinical Physiology); Morten Møller (Department of Neurobiology and Pharmacology, Panum Institute); Andreas Straube (Dept Neurology, Clinicum Grosshardern, Munich, Germany); Joe Beavo and Sergei Rybalkin (Dept Pharmacology, University of Washington, Seattle); Lars Edvinsson (Department of Experimental Clinical Research, Glostrup Hospital); Steen Gammeltoft (Dept. Clinical Biochemistry, Glostrup).

Basic science studies of migraine

Members

Inger Jansen Olesen, Saurabh Gupta, Kenneth Beri Ploug, Helle Wulf, Michael Baun, Maja Myren, Dipak Vasantrao Amrutkar, Deepak Kumar Bhatt, Roshni Ramachandran, 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 the different subtypes of receptors and/or ion channels.
- 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 pharmacological characterization of the vascular receptors activated by the migraine triggering substances.
- 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 two ion channels; ATP sensitive potassium (K(ATP)) channels and large conductance calcium activated potassium (BK(Ca)) channel in

migraine relevant tissues. They are interesting because of the episodic nature of migraine attacks which suggests that ion channels are involved in its pathophysiology. Potassium channels have an important role in the regulation of vascular tone and an opener of the K(ATP) channel has in clinical trials been found to induce headache. Furthermore, the receptors for vasoactive peptides and prostanoids such as vasoactive intestinal peptide (VIP) and pituitaty adenylyl cyclase activating peptide (PACAP), CGRP, prostaglandin E2 and prostacyclin are of interest.
The studies will give us an understanding of which subtype compositions of ion channels and receptors that are present in theses 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 Lars Edvinsson (Department of Experimental Clinical Research, Glostrup Hospital), Lektor Anders Hay-Schmidt (Panum Institute, Copenhagen University), Professor Dan Klærke (Faculty of Life Sciences, Copenhagen University), Lektor 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).

Idiopathic intracranial hypertension

Members

Rigmor Jensen, Maren Skau, Hanne Yri.

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 has still not been evaluated in IIH.
Untreated IIH may lead to severe visual loss and blindness resulting from damage to the optic nerve. 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 described the diagnostic value of new and atraumatic OCT-examinations and a new biomarker was identified. A new multidisciplinary follow-up study of IIH comprising neurobiological and ophthalmological aspects is a unique study of still unsolved aspects in IIH.

Current projects

Long term follow-up of patients with idiopathic intracranial hypertension, ophthalmological and neurobiological aspects. Biomarkers in Idiopathic intracranial hypertension. Experimental models of idiopathic intracranial hypertension.

Collaboration

Dan Milea, Department of Ophthalmology, Glostrup Hospital, Denmark.
Jens Peter Gøtze and Jens Rehfeld, Department of Clinical Biochemistry, National Hospital, Copenhagen, Denmark.
Marianne Juhler, Department of neurosurgery, National Hospital, Denmark.

Medication-overuse headache

Members

Signe Bruun Munksgaard, Rigmor Jensen, Lars Bendtsen.

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. MOH affects a percentage of 1.4-3% of the general population. 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

A prospective study comparing two different treatment options for MOH (abrupt drug withdrawal and a 2 month drug free period compared with restricted intake of analgesics combined with prophylactic headache treatment).

A prospective study investigating pain modulation (peripheral and central pain sensitivity) before and after drug withdrawal.

An EU-founded multi-centre study (COMO-ESTAS) investigating the benefit of electronic headache diaries during detoxification of MOH.

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, Universitaetsklinikum 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, Klinisk Biokemisk afdeling, Glostrup Hospital.

Cluster headache

Members

Rigmor Jensen, Mads Barløse, 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.

Current projects

Neurostimulation has been used in selected cases of chronic neuropathic pain but there is only very llimited evidence of neurostimulation 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. At present, the Danish Headache Center is participating in an international multicenter study of the effect of neurostimulation of the sphenopalatine ganglion in 10 patients with chronic cluster headache. Further neuromodulation studies are emerging and in case of positive outcome this principle can contribute to a significant therapeutic breaktrough for these patients. Likewise, important information on modulation of the pain signaling during cluster headache periods can be provided.

Collaboration

Søren Hillerup, professor, Department of Oromaxillofacial Surgery, National Hospital, Copenhagen, Denmark. Anthony Carparso, Principal Clinical Scientist, Autonomic Technologies, Inc., CA, USA.

Clinical trials

Members

Messoud Ashina, Rigmor Jensen, Jes Olesen and Peer Tfelt-Hansen

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

- Study MK-0974-065: A multicenter, double-blind, placebo-controlled, parallel group study to compare the efficacy and safety of oral MK-0974 with placebo for the preventive treatment of menstrual migraine

- Study NXN-188-202. An investigator initiated, double-blind, placebo-controlled, cross-over study to compare the efficacy and safety of oral NXN-188 with placebo for the acute treatment of migraine with aura. Included 49 patients

1.4 Sponsors

Major sponsors:

Lundbeck Foundation as part of the Lundbeck Foundation Centre for
Lundbeck Foundation (independent grant for genetics)
Neuro-vascular Signalling
Candy´s Foundation
Capital Region Foundation
Faculty of health, University of Copenhagen
Danish Research Council
European Commission
IMK Foundation

Sponsors:

Danish Headache Society
Cool Sorption Foundation
Danish Headache Foundation
Augustinus Foundation
Foundation of Lægevidenskabens Fremme

Familien Hede Nielsens Foundation

The Foundation for Neurological Research

The Illum Foundation

Novo Nordisk Foundation

Torben og Alice Frimodts Foundation

Ulla and Mogens Folmer Andersens Foundation

Grocer Sven Hansen and wife Ina Hansens Foundation

Figure 2. Professor Jes Olesen was awarded the highly prestigious Lundbeck Foundation's Nordic Award for Outstanding Research 2010 in recognition of his seminal and comprehensive contributions to clinical headache research. Jes Olesen was celebrated on September 3rd at a symposium with attendance of many leading international and national researchers.

2. Collaborations

Departments within Glostrup Hospital

- Department of Neurosurgery
- Department of Ophthalmology
- Department of Clinical Experimental Research
- Department of Clinical Physiology
- Department of Clinical Biochemistry
- Department of Paediatrics
- Department of Radiology
- Department of Gynaecology
- Department of Anaesthesiology
- Department of Oral and Maxillo-Facial Surgery
- Department of Clinical Neurophysiology
- Functional Imaging Unit, Dept Clinical Physiology and Nuclear medicine
- Stroke Unit, Department of Neurology

External collaborators

Clinical research

- Centre for Health and Preventive Medicine, Copenhagen County, Denmark
- Danish twin registry, University of Odense, Denmark
- Department of Neurology, Hillerød Hospital, Denmark
- 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
- 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
- Centre for Neuroimaging, Harvard University, Boston, USA
- Centre for Sensory-Motor Interaction, University of Ålborg, DK

Basic Pain Mechanisms

- Professor Jens Elrich, Centre for Sensory-Motor Interactions, Department of Health Science and Technology, Aalborg University, Denmark

- 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
- 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

Genetics and environment

- DeCode, Reykjavik, Iceland
- Danish twin registry

Headache Epidemiology

- Professor Michael Bjørn Russell, University of Oslo, Akershus Hospital, Norway
- Professor Lars-Jacob Stovner, Kompetencecenter for epidemiology, University of Trondheim, Norway

Headache diagnosis

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

Idiopathic Intracranial Hypertension

- Professor Dan Milea, Dr Sci Birgit Sander and Consultant Marianne Wegener, Department of Opthalmology, Glostrup Hospital
- Copenhagen CSF-study group, Professor Marianne Juhler, Department of neurosurgery, National Hospital
- Ass Professor Jens Peter Gøtze and Professor Jens Rehfeld, Department of Clinical Biochemistry, National Hospital

Cluster headache

- Søren Hillerup, professor, Department of Oromaxillofacial Surgery, National Hospital, Copenhagen, Denmark
- Anthony Carparso, Principal Clinical Scientist, Autonomic Technologies, Inc., CA, USA

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

Guest lectures and visitors

Professor Tim Steiner, University of Trondheim and London
Ass professor Cristina Tassorelli, Instituto Mondino, University of Pavia, Italy
As well as numerous Danish colleagues.

3. Global Excellence in Health Prize

In several areas within headache DHC is driving international research, and also a driver of the international implementation of new treatments and diagnostic methods. The research is clinical, clinical experimental and animal experimental and there are excellent facilities for all these 3 types of research, which are mutually supportive and inspiring resulting in a strong emphasis on translational research. Five employees have an H-factor over 25 and annually approximately 3 Ph.D. dissertations are defended and 30-40 original scientific publications in English language journals are published with an average impact factor of 3.8. Collaboration with the pharmaceutical industry includes patents and randomised controlled double blind drug trials. There is a high volume of patients both with common types of headache and with rare types allowing extensive clinical research and high clinical expertise. The center has extensive teaching at both pregraduate and postgraduate level as well as towards allied health professionals. Staff members are responsible for international guidelines on headache classification, the methodology of drug trials and therapeutic guidelines. Several staff members have high positions in professional societies and many honorary memberships and prizes have been received.

On the basis of the above-mentioned activities, the Danish Headache Center was awarded the Global Excellence in Health Prize by the Capital Region (Region Hovedstaden) in 2010. This official recognition is very important for the center, for our patients and for headache research in general and will undoubtedly help to pave the way for further development of our clinical and research activities.

Figure 3. Professors Rigmor Jensen and Jes Olesen at the presentation of the Global Excellence in Health Prize.

4. Teaching activities

Headache disorders. Clinical course for neurologists, general practitioners and younger doctors. Glostrup Hospital, May 12th, 2010.
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.
In addition, numerous teaching activities at international and national congresses.

5. Future Research Areas

In 2011 the scientific focus shall be directed towards

- Neurovascular signalling in the LUCENS centre
- Experimental human models of migraine with implementation of new imaging techniques
- Basic mechanisms of migraine in animal models
- Pain processing in tension-type headache
- Neck pain
- Medication-overuse headache
- Surgical treatment of cluster headache
- Idiopathic intracranial hypertension
- Posttraumatic Headache
- Clinical research in The Headache Center
- Diagnostic procedures in Headache (EU-project)
- Monitoring of Medication Overuse Headache and development of a decision support system in Europe and Latin America (EU-project)

6. Publications in 2010

PhD Theses

1. Schytz, H. W. Investigation of carbachol and PACAP38 in a human model of migraine. 1-130. 15-4-2011. Faculty of Health Sciences, Faculty of Health Sciences, University of Copenhagen, Glostrup Hospital.
2. Skau, M. Idiopathic Intracranial Hypertension - New aspects of diagnosis and handling. 1-112. 17-5-2010. Faculty of Health Sciences, University of Copenhagen, Glostrup Hospital.
3. Wulf-Johansson, H. Expression of BKca channels in the trigeminovascular systemet – relevance for migraine pathophysiology. 1-97. 17-5-2010. Faculty of Health Sciences, University of Copenhagen, Glostrup Hospital.

In peer-reviewed scientific journals

1. Asghar MS, Hansen AE, Kapijimpanga T, et al. Dilation by CGRP of middle meningeal artery and reversal by sumatriptan in normal volunteers. Neurology 2010;75:1520-6.
2. Ashina M, Tvedskov JF, Lipka K, Bilello J, Penkowa M, Olesen J. Matrix metalloproteinases during and outside of migraine attacks without aura. Cephalalgia 2010;30:303-10.
3. Ashina S, Lyngberg A, Jensen R. Headache characteristics and chronification of migraine and tension-type headache: A population-based study. Cephalalgia 2010;30:943-52.
4. Bendtsen L. Pain sensitivity in children with frequent episodic tension type headache. Cephalalgia 2010;30:1029-30.
5. Bendtsen L, Evers S, Linde M, Mitsikostas DD, Sandrini G, Schoenen J. EFNS guideline on the treatment of tension-type headache - Report of an EFNS task force. European Journal of Neurology 2010;17:1318-E102
6. Bendtsen L, Bigal ME, Cerbo R, et al. Guidelines for controlled trials of drugs in tension-type headache: Second edition. Cephalalgia 2010;30:1-16.
7. Bhatt DK, Ploug KB, Ramachandran R, Olesen J, Gupta S. Activation of PAR-2 Elicits NO-Dependent and CGRP-Independent Dilation of the Dural Artery. Headache 2010;50:1017-30.
8. Buchgreitz L, Egsgaard LL, Jensen R, Arendt-Nielsen L, Bendtsen L. Abnormal brain processing of pain in migraine without aura: A high-density EEG brain mapping study. Cephalalgia 2010;30:191-9.

9. Chan KY, Gupta S, de Vries R, et al. Effects of ionotropic glutamate receptor antagonists on rat dural artery diameter in an intravital microscopy model. British Journal of Pharmacology 2010;160:1316-25.
10. Daugaard D, Tfelt-Hansen P, Thomsen LL, Iversen HK, Olesen J. No effect of pure oxygen inhalation on headache induced by glyceryl trinitrate. Journal of Headache and Pain 2010;11:93-5.
11. Gupta S, Villalon CM. The relevance of preclinical research models for the development of antimigraine drugs: Focus on 5-HT1B/1D and CGRP receptors. Pharmacology & Therapeutics 2010;128:170-90.
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7. Organization and Staff

Management

Rigmor Jensen - Professor, MD, DrMedSci. Director of The Danish Headache Center.

Jes Olesen - Professor, MD, DrMedSci. Founder and co-director of The Danish Headache Center.

Lars Bendtsen - MD, Ph.D., DrMedSci, associate professor. Co-director of The Danish Headache Center.

Helle Jensby - BSc Economics and business adm., Med. sec. Team leader in The Danish Headache Center.

Staff Neurologists

Peer Tfelt-Hansen - MD, DrMedSci, associate professor.

Messoud Ashina - MD, Ph.D., DrMedSci, associate professor. Director of Human Migraine Research Group.

Thue Hjortkær Nielsen – MD, senior consultant. Leader of the department of inpatient treatment of headache patients.

Aydin Gozalov - MD, PhD, senior consultant. Leader of trigeminal neuralgia research.

Medical secretaries

Karin Aagaard
Katrine Kristensen
Tina Würgler Kærgaard
Jane Sandby-Møller
Dorte Helmundt
Lis Jønsson
Dianna Bartolin
Ane Lundgaard Dahl

Physiotherapists

Bjarne Madsen
Nina Caspersen
Jeanne Hirsvang (maternity leave)
Lotte Skytte Krøll (maternity cover)

Psychologists

Dorthe Kjeldgaard Nielsen
Bruno Vinter
Trine Zimmer

Nurses

Annette Vangaa Rasmussen
Annette Fjeldborg Jonassen
Hjørdis Rasmussen (assistent)
Lykke Rønberg Bruhn (maternity cover)

Psychiatrist

Marianne Nilsson, Centre of Psychiatry, Glostrup

Gynaecologist

Birgit Hansen, Department of Gynaecology, Herlev Hospital

Dental expertise

Professor, dr. odont Peter Svensson
Department of Oral Physiology, Institute of Odontology, University of Aarhus

Anaesthesiologist

Jonna Fomsgaard, Department of Anaesthesiology, Glostrup Hospital

Figure 4. Annette Vangaa Rasmussen and Hjørdis Rasmussen participated in Nurses forum at The 2nd European Headache and Migraine Trust International Congress. Nice, October 28-31, 2010.

8. Clinical Activities

The clinical activities in DHC consist of a multidisciplinary out-patient service and an in-patient service. At the end of 2010 the staff consisted of 3 psychologists (hereof 1 PhD student), 3 physical therapists, 3 nurses, 1 team leader, 1 laboratory technician, 7 secretaries (several part time jobs), 7 neurologists specialized in headache (all part time), 1 psychiatrist (one day per week), 1 dentist (one day per month) and a variable number of younger physicians (all part time). In addition, nurses at the Department of Neurology N 38 take care of the in-patients.

The out-patient activities continued to be at a very high level in 2010. A total of 2,548 patients were treated in the centre during 2010. The demand for treatment is still increasing leading to longer waiting lists by the end of the year. Approximately 120 patients have been treated at the in-patient department N 38.

A total of 68% of patients were referred from The Capital Region, while the rest of patients were referred from other parts of Denmark and Scandinavia.

Figure 5. Numbers of patients by gender and age in 2010 (n=2,548). The female/male ratio was 2.4 and the mean age of our patients was 44 years with a range from 15 to 90 years.

Relative frequencies of major diagnostic categories in 2010

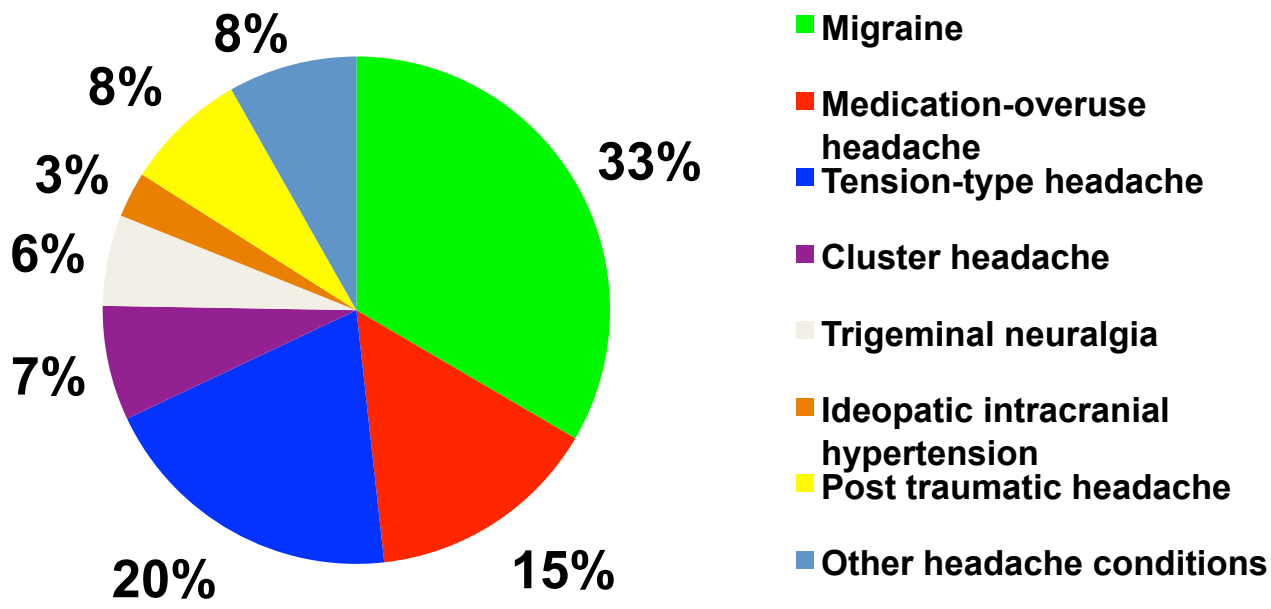

Figure 6. Migraine, medication-overuse headache, tension-type headache and combinations hereof are the most common types of headache seen in the centre.

The in-patient headache service

Six beds at the Department of Neurology N38 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 Center and then admitted for a fixed in-patient period of 14 days and follow a structured regime. After discharge they are closely followed as out-patients in DHC for at least one year.

9. Perspectives

We aim to continue the high research productivity, and facilitate scientific documentation and development of the treatment strategies in the Danish Headache Center. It is of utmost importance to improve the quality of the services offered to our patients, and increasingly try to combine basic experimental research with clinical experience on a daily basis in order to develop new therapeutic avenues. We aim to expand the pain rehabilitation programme for our severely affected patients and continue to develop the Danish Headache Center in order to achieve our goal to be in among the leading international centres for headache and neurological pain. Our significant expansion within clinical and research activities request additional space and facilities and a geographical implementation in the other clinical activities within the hospital plan.

Editors:
Lars Bendtsen
Rigmor Jensen
Jes Olesen

Frontpage:
Middle meningeal artery (MMA) cross section, 3-dimensional reconstruction, and longitudinal section at baseline, 30 minutes after start of calcitonin gene–related peptide (CGRP) infusion and 15 minutes after subcutaneous sumatriptan 6 mg. The images show dilation of MMA after CGRP and contraction of MMA after sumatriptan.

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