



Danish Headache Centre

Annual Report 2007





Preface

The most remarkable event for the Danish Headache Center in 2007 was the appointment of the director Rigmor Jensen as a Professor of Headache and Neurological Pain. This achievement was based on an impressive scientific production over the last 2 decades dealing with both pathophysiological and epidemiological aspects of headache as well as with headache treatment. The new position will secure a high scientific standard and production in the Danish Headache Center also in the future. Congratulations to Rigmor Jensen and the Danish Headache Center.

2007 was a year of consolidation in The Danish Headache Center. The many new staff members of the multidisciplinary team who were engaged in 2006 have done a tremendous job in 2007. This has allowed us to reduce the waiting list. The high productivity has put pressure on our secretaries, but we hope to improve this situation in 2008, so that the waiting time can be further reduced.

The commitment of the multidisciplinary team has allowed us to focus not only on quality and productivity but also on further development of our treatment possibilities. By the end of 2007 a new bio-feed back programme was introduced, which will allow bio-feed back treatment on a larger scale than what has previously been possible. Treatment of patients with posttraumatic headache is notoriously difficult. A new treatment programme for this severely affected group of patients has therefore been developed and will be introduced at the beginning of 2008.

The Danish Headache Center for Children and Adolescents within the Department of Pediatrics collaborating closely with the Danish Headache Center, has had its first full year of functioning. It has assembled an excellent multidisciplinary team and already enjoys great popularity.

The research at The Danish Headache Center continues to be very active with a high frequency of publications and a large impact factor. Glostrup Research Park has had its first full year of functioning.

The European Headache Summer School was held in the Danish Headache Center in May and was a great success.

We aim to further develop and improve the quality and documentation of our various treatment modalities to the benefit of our patients.

Glostrup, March 2008

Lars Bendtsen

Rigmor Jensen

Jes Olesen





2007

Organization and Staff



Rigmor Jensen – MD, DrMedSci

The center's director Dr. Rigmor Jensen is Professor of Headache and Neurological Pain at the University of Copenhagen. Dr. Jensen has published more than 170 scientific papers and book chapters. Her main research interests include headache epidemiology and the pathophysiological mechanisms underlying tension-type headache and medication-overuse headache. Dr. Jensen is the president of the Danish Headache Society, President of The Medical Society in Copenhagen, and member of the Executive Board (treasurer) of The European Headache Federation.



Jes Olesen – MD, DrMedSci, Dr hon C/Rome University, FRCP

The center's founder and co-director Jes Olesen is Professor of Neurology at the University of Copenhagen. Professor Olesen has published over 500 scientific papers and more than 20 books on headache. His main research interests include pathophysiological mechanisms underlying migraine, headache epidemiology, classification and genetics. Professor Olesen has held a numerous honorary positions and is the former president of the International Headache Society (IHS) and the European Federation of Neurological Societies (EFNS) as well as current president of the European Brain Council (EBC). He has received numerous national and international prizes. He is an honorary member of the Austrian, British, and French neurological societies.



Lars Bendtsen - MD, Ph.D., DrMedSci

The center's co-director Lars Bendtsen has published more than 80 scientific papers and book chapters. His main research interests include the pathophysiological mechanisms underlying tension-type headache, in particular central sensitization, and the treatment of tension-type headache.



Helle Jensby – BSc Economics and business adm., Med. sec.

Helle Jensby is as the Team leader the head of personnel. She coordinates the daily interdisciplinary resources. She has previously worked as a medical secretary in an intensive care unite and with strategic media planning.





Staff Neurologists:



Peer Tfelt-Hansen - MD, DrMedSci

Dr. Peer Tfelt-Hansen has published more than 250 scientific papers and book chapters. His main research interests include clinical drug trials.



Messoud Ashina - MD, Ph.D., DrMedSci

Messoud Ashina has published more than 60 scientific papers and book chapters. Dr. Ashina is currently a director of Human Migraine Research Group. His main research interest includes experimental headache models and functional neuroimaging.



Peter Thede Schmidt-Hansen - MD, specialist in Neurology and General Medicine

Peter Thede Schmidt-Hansen has research interest in experimental pain, especially in tension-type headache. Leader of department of inpatient treatment of headache patients.



Thue Hjortkær Nielsen - MD

Consultant in Neurology since 1998 with special interests in headache and stroke. Publications about the vascular mechanisms of migraine.



**Secretaries**

Helle Jensby (Team leader)
Katrine Kristensen
Karin Aagaard
Pernille Sellebjerg-Andersen
Jane Sandby
Dorte Helmundt
Birgitte Suhr
Lis Jønsson
Tina Kærgaard

Physio-therapists

Bjarne Madsen
Nina Caspersen
Jeanne Hirsvang

Psychologists

Dorthe Kjeldgaard Nielsen
Bruno Vinter
Trine Zimmer

Nurses

Annette Vangaa Rasmussen
Hjørdis Rasmussen (assistent)
Annette Jonassen

Psychiatrist

Marianne Nilsson
Department of Psychiatry P
Glostrup Hospital

Gynecologist

Birgit Hansen
Department of Gynecology
Glostrup Hospital

Dental expertise

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





Research

Danish Headache Center has a vigorous research group including 7 senior researchers, 15 Ph.D. students mostly MD's and medical students. The organization of research is shown in Figure 1.

Figure 1. Organization of Research





Research Staff

Senior scientists:

Jes Olesen
Rigmor Jensen
Lars Bendtsen
Messoud Ashina
Inger Jansen Olesen
Christina Kruuse
Saraub Gubta

Associate senior researchers:

Lise Lykke Thomsen
Peter Schmidt-Hansen
Malene Kirchmann

Technologists:

Hanne Andresen
Lene Elkjær
Kirsten Brunsgaard

Administrative assistants:

Kirsten Hjelm
Vikki Johansen

Ph.D.students:

Henrik Winther Schytz
Lars Schack Kruuse
Sohail Agshar
Peter Zeeberg
Line Buchgreitz
Kim Lindelof
Louise Susanne Juhl
Kenneth Beri Plough
Jakob Møller Hansen
Troels Wienecke
Anne Werner Hauge
Lena Raffn
Maren Skau
Helle Wulf
Michael Baun





Present research Areas

Human migraine models

Members

Messoud Ashina, Sohail Asghar, Jakob Møller Hansen, Henrik Schytz, Troels Wienecke, Jes Olesen and Dorte Phillip.

Background

Experimental headache models offer unique possibilities to study mechanisms responsible for migraine. Using the nitric oxide (NO) and calcitonin gene-related peptide (CGRP) model of experimental headache, our group demonstrated that NO- or CGRP-induced a biphasic response with an immediate and a delayed headache identical to migraine. These provocation experiments show the importance of NO and CGRP in spontaneous migraine attacks. The efficacy of the NO synthase inhibitor and a CGRP antagonist are final proof of this relation.

Current projects

The aims of current studies are to study human migraine models in patients with genetically explained hemiplegic migraine, to explore the possible role of the parasympathetic nervous system and prostanoids in migraine pathophysiology, and to study activation of trigeminal pain pathways by fMRI during different sequences of a headache attack.

Collaboration

Henrik Larsson and Adam Espe Hansen (Department of Clinical Physiology); Vibeke Andre Larsen (Department of Radiology); EUROHEAD (www.eurohead.org); David Borsook and Lino Becerra, PAIN Group, Mclean Hospital, Harvard University Boston USA; David A Boas, Optical Imaging Core & Lab at Martinos Center Department of Radiology, Boston USA; Professor Hayrunnisa Bolay, Department of Neurology, Gazi University Hospitals, Ankara, Turkey.

Tension-type headache

Members

Lars Bendtsen, Line Buchgreitz, Kim Lindelof, Messoud Ashina, Peter Schmidt-Hansen, 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, processing, and modulation of peripheral nociceptive input in the central nervous system.

Collaboration

Lars Arendt Nielsen, Center for Sensory-Motor Interactions, Department of Health Science and Technology, Aalborg University, Denmark. Professor Jens Elrich; Institute of Physiology, Achen University Hospital, Germany and Center for Sensory-Motor Interactions, Department of Health Science and Technology, Aalborg University, Denmark.





Epidemiology

Members

Line Buchgreitz, Ann Lyngberg, Peter Zeeberg, Rigmor Jensen.

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 in 2001 than in 1989. 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 dataanalysis 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 planned.

Genetics and environment

Members

Malene Kirchmann, Lise Lykke Thomsen, Anne Hauge, Jes Olesen.

Background

Family studies and twin studies show that migraine is an inherited disorder. The genes involved in migraine have not been identified except for some families presenting a rare subtype of migraine with aura, familial hemiplegic migraine. The identification of genes involved in migraine may give clues to underlying pathophysiological mechanisms.

Current projects

The 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 genetic analyses have been initiated.

Intracellular transduction mechanisms in migraine

Members

Christina Kruuse, Carina Jørgensen, Lars Schack Kruse.

Background

Studies in humans help to explore possible migraine and headache provoking factors, in order to understand migraine pathophysiology. It is known that pain signalling in humans involve second messenger signalling through both types of second messengers; cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP). However, the function and interaction of these signalling pathways and the cellular location in either neuronal or vascular cells is not fully understood. The aim is thus to





localize and investigate function of tissue and cells assumed relevant in initiation of the pain process in order to investigate potential treatment targets. In collaboration with Department of Clinical Biochemistry Glostrup and Department of Neuroscience and Pharmacology, we have described the presence of some of the intracellular enzymes involved in the pain process and the possible effect of modulating the signalling cascade in pain and regulation of cerebral artery diameter.

Current projects

We are currently looking at the distribution and function of phosphodiesterases (PDE), which are responsible for controlling the cAMP and cGMP levels in the cells. In particular how they may relate to the pain sensing structures in the brain and play a part in the induction and possible maintenance of headache and migraine.

Pharmacological and molecular studies of the cranial circulation

Members

Inger Jansen Olesen, Saurabh Gupta, Louise Juhl, Kenneth Beri Ploug, Helle Wulf, Michael Baun, Maja Myre, Jes Olesen.

Background

We have during the last 20 years studied the pharmacology of isolated cranial blood vessels from animals and humans in vitro. This work has led to several publications on the characterization of cerebrovascular receptors for 5-hydroxytryptamine and the sensory neuropeptides calcitonin gene-related peptide and substance P. During the last 5-8 years we have introduced new techniques, giving us the ability to study the expression of mRNA and proteins for specific receptors in migraine relevant tissue. In addition, we have established the genuine closed cranial window technique. This method allows us to perform in vivo measurements of the effect of a drug on pial and dural arteries when administered intravenously. We have further developed the method such it is possible to give drugs by intracarotid infusion.

Current projects

The episodic nature of migraine attacks suggests that ion channels are involved in its pathophysiology. This is confirmed by finding the mutation in patients suffering from familial hemiplegic migraine within three different ion channel genes identified to date. Potassium channels have an important role in the regulation of vascular tone and an opener of ATP sensitive potassium (K(ATP)) channels has in clinical trials been found to induce headache. An other channel we find might be important in migraine pathophysiology are the large conductance calcium activated potassium (BK(Ca)) channel. Furthermore, the receptors for vasoactive peptides and prostanoids such as vasoactive intestinal peptide (VIP) and pituitary adenylyl cyclase activating peptide (PACAP), calcitonin gene-related peptide (CGRP), prostaglandin E2 and prostacyclin are of interest. The aim of the current projects is to explore the subunit composition and role of these ion channels and receptors in pial and meningeal arteries and trigeminal ganglion. This will give us an understanding of which channels and subtype compositions that is present in these arteries. Thus, giving us information to further understand the pathophysiology of migraine and to define new targets for the pharmacological treatment of migraine.

Collaboration

Lars Edvinsson (Department of Experimental Clinical Research) Anders Hay-Schmidt (Panum Institute, Copenhagen), Dan Klærke (The Royal Veterinary and Agricultural University, Copenhagen).





Idiopathic intracranial hypertension

Members

Rigmor Jensen, Maren Skau.

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 edema of the optic nerve head and the associated elevation of hydrostatic pressure inside the optic nerve.

The multidisciplinary study of IIH comprising neurobiological and ophthalmological aspects is a unique study of still unsolved aspects in IIH. Read more about IIH on www.danishheadachecenter.com.

Current projects

One cross-sectional study of ophthalmological and neurobiological aspects in Idiopathic intracranial hypertension.

One longitudinal study of ophthalmological and neurobiological aspects in Idiopathic intracranial hypertension, with specific focus on treatment and functional outcome.

Collaboration

Dan Milea, Department of Ophthalmology, Glostrup Hospital, Denmark

Jens Peter Gøtze, Department of Clinical Biochemistry, Danish National Hospital, Copenhagen, Denmark.





Research and clinical 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 Pediatrics
- Department of Radiology
- Department of Gynecology
- Department of Anesthesiology
- Department of Oral and Maxillo-Facial Surgery
- Department of Clinical Neurophysiology

External collaborators

Basic clinical research

- Center for Health and Preventive Medicine, Copenhagen County, Denmark
- The Pain Clinic, Herlev University Hospital, Copenhagen, Denmark
- Department of Ophthalmology, Herlev University Hospital, Copenhagen, Denmark
- The Pain Clinic, The National University Hospital, Rigshospitalet, Copenhagen, Denmark
- Department of Neurology, Frederiksborg Amts Sygehus Hillerød, Denmark
- Professor John-Anker Zwart, Department of Neurology, Rigshospitalet, Oslo, Norway
- Professor Knut Hagen, Department of Neurology, University of Trondheim, Norway
- Institute of Anatomy, Panum Institute, University of Copenhagen, Denmark
- Department of Medical Physiology, Royal School of Veterinary Medicine, Denmark
- Institute of Pharmacology, University of Pharmacology, Copenhagen, Denmark
- NeuroSearch A/S, Denmark
- The Headache Clinic, Kiel University, Germany
- Department of Neurology, Parma University Hospital, Parma, Italy
- The Headache Center, Thomas Jefferson University, Philadelphia, USA
- Department of Physical Therapy, Department of Health Sciences, University of Lund, Sweden

Basic Pain Mechanisms

- Professor Lars Arendt-Nielsen, Center for Sensory-Motor Interaction, University of Ålborg, DK
- Professor Jens Elrich, Center for Sensory-Motor Interactions, Department of Health Science and Technology, Aalborg University, Denmark
- Institute for Physiology, Johannes Gutenberg University in Mainz, Germany
- Department of Pharmacology, University of Washington, Seattle, USA
- Department of Experimental Research, University of Lund, Sweden

Genetics

- DeCode, Reykjavik, Iceland

Headache Epidemiology

- Professor Richard Lipton, Albert Einstein Hospital, NY, USA
- 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, Department of Ophthalmology, Glostrup Hospital
- Copenhagen CSF-study group, Department of neurosurgery, Glostrup and Rigshospitalet
- Professor Jens Rehfeld, Department of Clinical Biochemistry, Rigshospitalet

Sponsors

Major sponsors:

Lundbeck Foundation as part of the Lundbeck Foundation Center for Neuro-vascular Signalling
Mauritzen LaFontaine Foundation
Toyota Foundation
Copenhagen County Foundation
Augustinus Foundation
Faculty of health, University of Copenhagen
Danish Research Council
European Commission
H. Lundbeck A/S

Sponsors:

Cool Sorption Foundation
Danielsens Foundation
The Danish Horton Patient Association





Teaching activities

The European Headache Summer School organized by Rigmor Jensen, DHC and Stefan Evers, Germany.



Participants at the highly successful European Headache School held at the Danish Headache Center May 10-12, 2007.





Guest lectures and visitors

Professor Jens Ellrich, Aachen, Aalborg, Denmark
Professor HC Diener, University Clinic of Essen, Germany
Professor Zaza Katsarava, University Clinic of Essen, Germany
Professor Tim Steiner, London, UK
Professor Dominique Valade, University Hospital salpêtrier?, Paris, France
Professor Peter Kropp, University of Rostock, Germany
Professor Dr. Med. Mathias Keidel, Bayreuth, Germany
Dr Ana Sundic, Institute of Neurology, Belgrade University, Serbia
Dr. Vlasta Vukovic Department of Neurology, University of Zagreb, Croatia
Dr Aleksander, Department of Neurology, University of Vilnius, Latvia.
As well as numerous Danish colleagues

Future Research Areas

In 2008 the scientific focus is directed towards

- Neurovascular signalling in LUCENS center
- Experimental humans models of migraine with implementation of the new imaging techniques
- Pain processing in tension-type headache
- Medication-overuse headache
- Idiopathic intracranial hypertension
- The clinical division 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)





Publications in 2007

In reviewed scientific journals

1. Ashina M. Pathophysiology of tension-type headache: potential drug targets. *CNS Neurol Disord Drug Targets* 2007;6(4):238-9.
2. Bendtsen L, Buchgreitz L, Ashina S, Jensen R. Combination of low-dose mirtazapine and ibuprofen for prophylaxis of chronic tension-type headache. *Eur J Neurol* 2007;14(2):187-93.
3. Birk S, Sitarz JT, Petersen KA, Oturai PS, Kruuse C, Fahrenkrug J, et al. The effect of intravenous PACAP38 on cerebral hemodynamics in healthy volunteers. *Regul Pept* 2007;140(3):185-91.
4. Buchgreitz L, Lyngberg AC, Bendtsen L, Jensen R. Increased pain sensitivity is not a risk factor but a consequence of frequent headache: A population-based follow-up study. *Pain* 2007.
5. Buchgreitz L, Lyngberg AC, Bendtsen L, Jensen R. Increased prevalence of tension-type headache over a 12-year period is related to increased pain sensitivity. A population study. *Cephalalgia* 2007;27(2):145-52.
6. Couppe C, Torelli P, Fuglsang-Frederiksen A, Andersen KV, Jensen R. Myofascial trigger points are very prevalent in patients with chronic tension-type headache: a double-blinded controlled study. *Clin J Pain* 2007;23(1):23-7.
7. DHC. Hovedpine kan afhjælpes med øvelser og hovedpinekalender. *Fysioterapeuten* 2007:16-18.
8. Goadsby PJ, Dodick DW, Almas M, Diener HC, Tfelt-Hansen P, Lipton RB, et al. Treatment emergent CNS symptoms following triptan therapy are part of the attack. *Cephalalgia* 2007;27(3):254-62.
9. Gozalov A, Jansen-Olesen I, Klaerke D, Olesen J. Role of BK(Ca) channels in cephalic vasodilation induced by CGRP, NO and transcranial electrical stimulation in the rat. *Cephalalgia* 2007;27(10):1120-7.
10. Hansen JM, Pedersen D, Larsen VA, Sanchez-del-Rio M, Alvarez Linera JR, Olesen J, et al. Magnetic resonance angiography shows dilatation of the middle cerebral artery after infusion of glyceryl trinitrate in healthy volunteers. *Cephalalgia* 2007;27(2):118-27.
11. Hansen JS, Bendtsen L, Jensen R. Predictors of treatment outcome in headache patients with the Millon Clinical Multiaxial Inventory III (MCMI-III). *J Headache Pain* 2007;8(1):28-34.
12. Jensen RM, Lyngberg A, Jensen RH. Burden of cluster headache. *Cephalalgia* 2007;27(6):535-41.
13. Jensen RA, Gilliam LK, Torn C, Landin-Olsson M, Karlsson FA, Palmer JP, et al. Multiple factors affect the loss of measurable C-peptide over 6 years in newly diagnosed 15- to 35- year-old diabetic subjects. *J Diabetes Complications* 2007;21(4):205-13.
14. Juhl L, Edvinsson L, Olesen J, Jansen-Olesen I. Effect of two novel CGRP-binding compounds in a closed cranial window rat model. *Eur J Pharmacol* 2007;567(1-2):117-24.
15. Katsarava Z, Jensen R. Medication-overuse headache: where are we now? *Curr Opin Neurol* 2007;20(3):326-30.





16. Kukava M, Dzagnidze A, Mirvelashvili E, Djibuti M, Fritsche G, Jensen R, et al. Validation of a Georgian language headache questionnaire in a population-based sample. *J Headache Pain* 2007;8(6):321-4.
17. Magis D, Ambrosini A, Bendtsen L, Ertas M, Kaube H, Schoenen J. Evaluation and proposal for optimization of neurophysiological tests in migraine: part 1--electrophysiological tests. *Cephalalgia* 2007;27(12):1323-38.
18. Olesen J, Lekander I, Sobocki P. Resource allocation to brain research in Denmark: an example for other European countries. *Eur J Neurol* 2007;14(6):667-71.
19. Olesen J. Collaboration to promote neurological research--the European Brain Council experience. *Nat Clin Pract Neurol* 2007;3(6):298-9.
20. Olesen J, Lekander I, Andlin-Sobocki P, Jonsson B. Funding of headache research in Europe. *Cephalalgia* 2007;27(9):995-9.
21. Phillip D, Lyngberg A, Jensen R. Assessment of headache diagnosis. A comparative population study of a clinical interview with a diagnostic headache diary. *Cephalalgia* 2007;27(1):1-8.
22. Schmidt-Hansen PT, Svensson P, Bendtsen L, Graven-Nielsen T, Bach FW. Increased muscle pain sensitivity in patients with tension-type headache. *Pain* 2007;129(1-2):113-21.
23. Obocki P, Olesen J, Jonsson B. Brain research has high returns but Europe is lagging behind. *Eur J Neurol* 2007;14(6):708-10.
24. Steiner TJ, Paemeleire K, Jensen R, Valade D, Savi L, Lainez MJ, et al. European principles of management of common headache disorders in primary care. *J Headache Pain* 2007;8 Suppl 1:S3-47.
25. Stovner L, Hagen K, Jensen R, Katsarava Z, Lipton R, Scher A, et al. The global burden of headache: a documentation of headache prevalence and disability worldwide. *Cephalalgia* 2007;27(3):193-210.
26. Tfelt-Hansen P. Parenteral vs. oral sumatriptan and naratriptan: plasma levels and efficacy in migraine. A comment. *J Headache Pain* 2007;8(5):273-6.
27. Tfelt-Hansen P, Steiner TJ. Over-the-counter triptans for migraine: what are the implications? *CNS Drugs* 2007;21(11):877-83.
28. Tfelt-Hansen P, Edvinsson L. Pharmacokinetic and pharmacodynamic variability as possible causes for different drug responses in migraine. A comment. *Cephalalgia* 2007;27(10):1091-3.
29. Tfelt-Hansen P. Acute pharmacotherapy of migraine, tension-type headache, and cluster headache. *J Headache Pain* 2007;8(2):127-34.
30. Tfelt-Hansen P, Nilsson E, Edvinsson L. Contractile responses to ergotamine and dihydroergotamine in the perfused middle cerebral artery of rat. *J Headache Pain* 2007;8(2):83-9.
31. Thomsen LL, Kirchmann M, Bjornsson A, Stefansson H, Jensen RM, Fasquel AC, et al. The genetic spectrum of a population-based sample of familial hemiplegic migraine. *Brain* 2007;130(Pt 2):346-56.
32. Tibaek S, Gard G, Jensen R. Is there a long-lasting effect of pelvic floor muscle training in women with urinary incontinence after ischemic stroke? A 6-month follow-up study. *Int Urogynecol J Pelvic Floor Dysfunct* 2007;18(3):281-7.





33. Vinding GR, Zeeberg P, Lyngberg A, Nielsen RT, Jensen R. The burden of headache in a patient population from a specialized headache centre. *Cephalalgia* 2007;27(3):263-70.

PhD Thesis University of Copenhagen

1. Kirchmann M. Migraine with aura - New understanding of diagnosis and classification from clinical epidemiological studies [Ph.D.]. Glostrup: University of Copenhagen; 2007.

Textbook

1. Jensen R Diener HC, Olesen J. *Headache Clinics - organizations, patients and treatment*. 1 ed. New York: Oxford University Press; 2007.

Bookchapters in International Textbooks

1. Bendtsen L. Evaluation and quantification of tenderness and sensitization. In: Jensen R DH, Olesen J - eds., editor. *Headache Clinics, organization, patients and treatment*. New York: Oxford University Press; 2007. p. 128-135.

2. Jensen R. Organization of a multidisciplinary headache center in Europe. In: Jensen R DH, Olesen J - eds., editor. *Headache Clinics*. New York: Oxford University Press; 2007. p. 29-34.

3. Jensen R. Discussion Summary - Multidisciplinary Management. In: Jensen R DH, Olesen J -eds., editor. *Headache Clinics*. New York: Oxford University Press; 2007. p. 264-266.

4. Jensen R. Tension-type Headache. In: Lipton R BM, editor. *Migraine and Other Headache Disorders*; 2007.

5. Jensen R, Hansen JM, Rechter L. Physical therapy. In: Jensen R DH, Olesen J - eds., editor. *Headache Clinics*. New York: Oxford University Press; 2007. p. 192-198.

6. Kruuse C. Role of PDE5 in Migraine. In: Joseph A Beavo SHF, Miles d. Houslay, editor. *Phosphodiesterases in health and disease*: CRC; 2007.

7. Nappi G JR, Sances G, Torelli P, Olesen J. Diaries and calendars for migraine. A review. In: Jensen R DH, Olesen J - eds., editor. *Headache Clinics*. New York: Oxford University Press; 2007. p. 152-156.

8. Thomsen OØ GN, Hippe M, Engelmann M, Kruuse CR. *Akutte Medicinske Tilstande*. Copenhagen: FADLs forlag; 2007.

9. Zeeberg P. Cost-effectiveness of headache clinics. In: Jensen R DH, Olesen J - eds., editor. *Headache Clinics*. New York: Oxford University Press; 2007. p. 273-276.

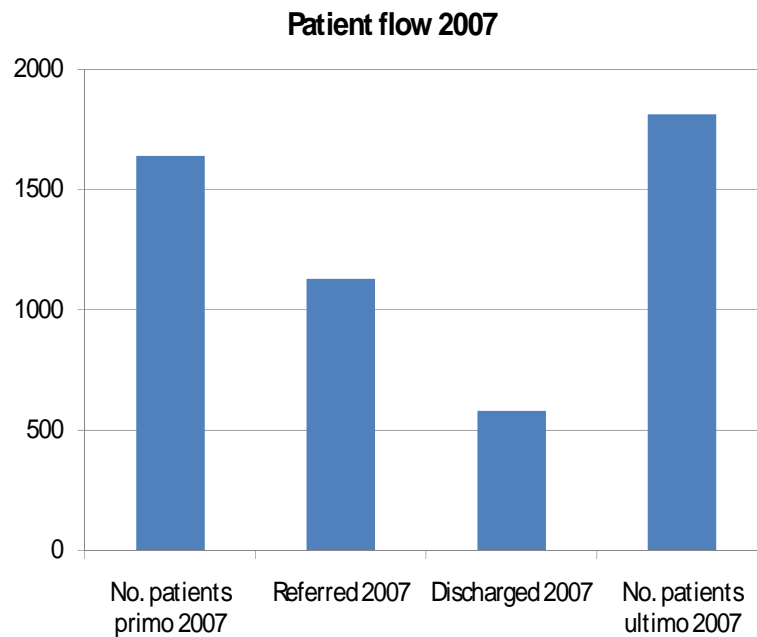




Clinical Activities

The clinical activities in DHC consist of a multidisciplinary out-patient service and an in-patient service. At the end of 2007 the staff consisted of 3 psychologists, 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.

Figure 2. The patient flow in the Danish Headache Center in 2007.



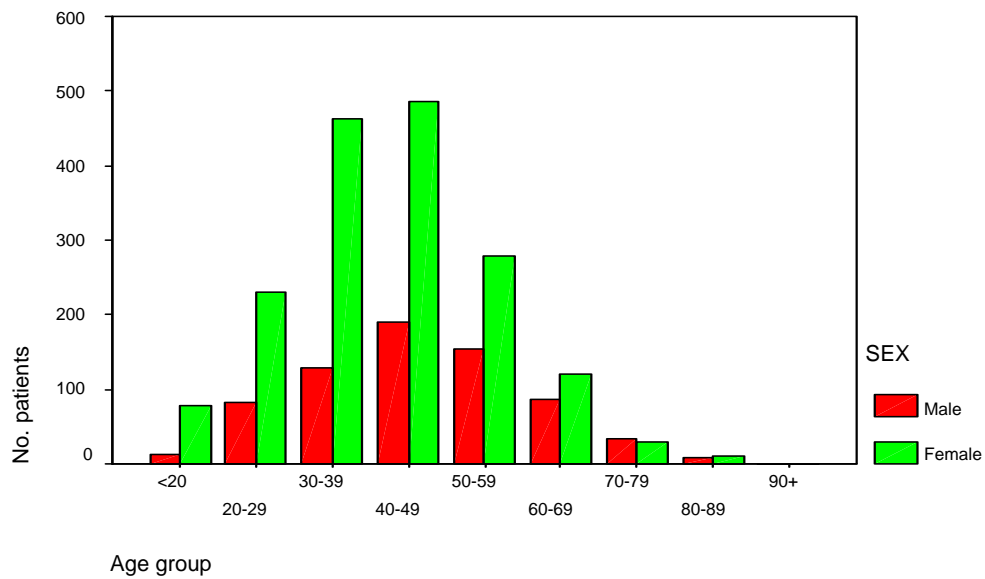
The multidisciplinary out-patient activities in 2007 are shown in figure 2. The intake was 1.127 new patients and 580 patients were discharged. A total of 2.392 patients were treated in the center during 2007. The total number of visits in the out-patient clinic was 7.409. In addition there was a number of telephone contacts. By the end of the year 1.812 patients were in active treatment. Approximately 120 patients have been treated at the in-patient department N 38.

A total of 68% of patients were referred from Region Hovedstaden, i.e., the county of Copenhagen, the City of Copenhagen and Northern Zealand, while the rest of patients were referred from other parts of Denmark (and 6 patients from foreign countries).



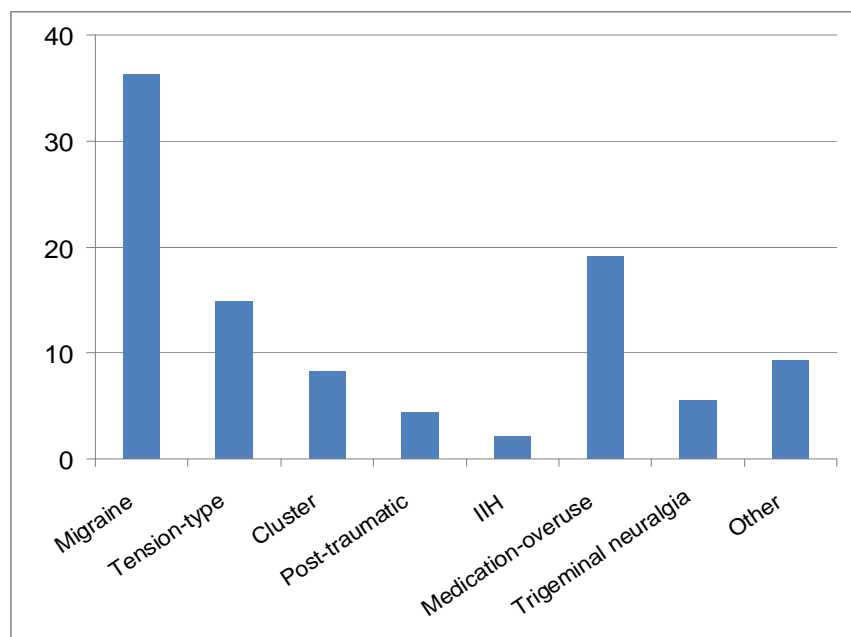


Figure 3. Numbers of patients by gender and age in 2007 (n=2392).



The female/male ratio is 2.4 and the mean age of our patients is 43 years with a range from 12 to 90 years (Figure 3).

Figure 4. Relative frequencies of diagnostic categories in 2007.



Migraine, medication-overuse headache and tension-type headache are the most common types of headache seen in the center (Figure 4).

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 Centre 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.

Perspectives

We aim to continue the high research productivity, and facilitate scientific documentation and development of the treatment strategies in the Danish Headache Center. The primary research focus in 2008 is concentrated on neurovascular signalling, medication overuse headache, idiopathic intracranial hypertension and chronic pain mechanisms. 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 continue to develop the Danish Headache Center and provide optimal external facilities for children and adult patients, the dedicated clinical staff and large research group in order to achieve our goal to be in among the leading international centers for headache and neurological pain.

