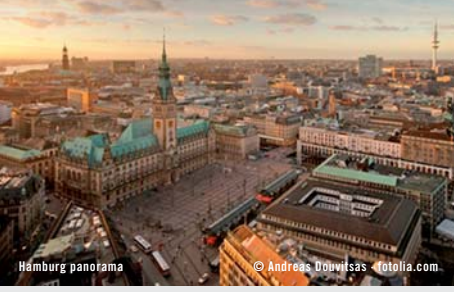
WILEY-BLACKWELL
25 / 2011
MedReport
THE JOURNAL OF MEDICAL CONFERENCES AND EDUCATION
WILEY-BLACKWELL

21–24. 9. 2011

7th Congress of the European Federation of IAASP® Chapters (EFIC®)

Hamburg, Germany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Pain in Europe VII:
A scientific congress on pain – addressing societal impact

Prof. Hans G. Kress, Vienna (Austria)

Starting out as a triennial congress in 1995, the now biennial EFIC® Pain in Europe Congress has become a major event in the calendar of worldwide pain medicine, and today its international scientific reputation reaches far beyond Europe. The current issue of MedReport exclusively focuses on this year's Pain in Europe VII Congress held in the beautiful city of Hamburg. The 7th EFIC® Congress promises to be a huge success building upon its excellent reputation and extending it further.

Besides CME accreditation for each participant, and financial help to enable some 30 young colleagues from economically weak countries to attend the congress, new congress features will include a free two-year online plus an additional free one-year print subscription to the *European Journal of Pain* (Impact Factor: 3.82) for each registered participant, a website-based personalized itinerary planner for all scientific sessions and posters providing access to abstract and author information, and the "Faculty of 1000" full format internet poster repository. In addition Young Scientists' Luncheons will provide the opportunity to informally meet and interact with a select group of well-known senior researchers from all over Europe, to discuss personal career plans and scientific projects while enjoying a buffet lunch provided by EFIC. For details about all these new exciting features please visit the congress website <www.efic.org>.

Without doubt, chronic pain is primarily a challenge to patients and their physicians. Chronic pain is also an underestimated or even neglected true challenge to our national health care systems, to budget holders, strategic decision makers and politicians throughout Europe. Having realized the obvious low-level awareness – not only in the media and the general public, but even among health care professionals – of chronic pain as a disease in its own right and of its considerable societal consequences, the *European Federation of IASP Chapters (EFIC®)* will explicitly address the societal impact of pain at this *Pain in Europe VII Congress,* taking place from 21st to 24th September in Hamburg. Societal impact of pain will be the official theme of this congress, and an *EFIC ® Road Map for Action* will be extensively discussed during a congress symposium particularly dedicated to this important initiative.

Two decades after the decline of communism and the fall of the Berlin Wall, far-reaching influences impacted on pain medicine in many European societies. Central and eastern Europe has been affected by fundamental political and social upheavals. Not only in these regions, but to variable extent also in western, northern and southern Europe, decentralization of health services, freezing or even cutting down public health care budgets have coincided with growing private services for those who can afford it, making patient's access to competent and full-spectrum pain medicine unequal throughout Europe and not always easily available to those, who are in most urgent need. Moreover, pain medicine and research remains chronically underfunded even in the richest countries of Europe.

This *7th EFIC® Congress,* however, is not exclusively about societal aspects of pain. As in the past, the 2011 congress in Hamburg will also cover, above all, the whole wide spectrum of pain medicine, from basic and clinical research results to their translation into practical treatment strategies and options for daily multidisciplinary therapeutic practice. Our Scientific Program Committee (SPC), chaired by Martin Koltzenburg, has prepared an attractive four-day scientific program covering the most recent advances as well as established standards of state-of-the-art pain medicine and latest pain-related research. Internationally renowned experts will provide new insights into relevant basic science, clinical research and practical management of acute and chronic pain. An excellent Refresher Course program, outstanding daily plenary sessions, 34 Topical Seminars, the Ulf-Lindblom Lecture and the David Niv Lecture in honour of two former EFIC® presidents will provide ample opportunity to discuss and learn about the newest developments in the pain field. The current MedReport issue will highlight many of these topics and wet your appetite for dropping in at the congress site.


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More than 1,100 posters will showcase latest work, and as in the past, the congress delegates can exchange their ideas and knowledge, explore the frontiers of pain research, learn about new clinical studies, and envision new invasive or non-invasive treatments and theories. Supplemented by the sponsored Satellite Symposia and the comprehensive Industrial Exhibition, this congress program will be highly innovative and informative for active researchers as well as for practicing physicians and other health professionals working in the pain field.

Last but not least, EFIC® congresses have always been known as an effective opportunity for meeting colleagues and old friends, making new acquaintances and for networking among basic scientists, clinicians and pain practitioners from all over Europe.

EFIC® gratefully acknowledges the members of our Local Organising Committee and the Scientific Program Committee for their continuous efforts, but also our Industrial sponsors and the Kenes Congress Organisers for making this outstanding congress happen.

Do not miss the enjoyment of the inspiring atmosphere of this 7th EFIC® Congress and the exciting city of Hamburg, which is famous for its discreet Hanseatic charm combined with open-minded, young international flair, and its many cultural attractions.

Prof. Hans G. Kress, MD, PhD
President of the European Federation
of IASP Chapters (EFIC)
Medical University of Vienna, Austria


Prof. Hans G. Kress

Classification, Epidemiology and cost of headache disorders

Prof. Jes Olesen, Glostrup (Denmark)

Prof. Jes Olesen

Headache disorders are a subgroup of pain disorders, but the two groups are only partially overlapping because migraine and some other headache disorders have specific mechanisms that can be treated with drugs without any analgesics efficacy. As a scientific field headache has been relatively independent from the activities of IASP and EFIC.

One result of this is that headache disorders have their own classification different from the classification of the IASP. This international classification of headache disorders (ICHD-1) was first published in 1988 and subsequently in a second edition (ICHD-2) in 2004. The third edition (ICHD-3) is scheduled to be published in the beginning of 2014. The ICHD has a number of features that are not a part the IASP pain classification. First of all, it is hierarchical using up to five digits. This means that the classification can be used at different settings from general practice to highly specialized tertiary referral centres and in research. It is simply a question of how many digits or in other words, to how much detail one wants to classify the patients. Secondly, the ICHD provides unambiguous (previously called operational) diagnostic criteria for all kinds of headache. This is different from definitions used formerly which are short written statements about the most important characteristics of the disorders. Unambiguous criteria are specific in their requirement for the diagnosis. Usually they consists of letter headings A, B, C all of which must be fulfilled to get the diagnosis. In some of these letter headings it is enough to fulfil for example two out of four sub criteria.

The existence of a modern disease classification with unambiguous diagnostic criteria has resulted in a wealth of valid epidemiological data. The epidemiology of headache disorders is now fully known, not only in the United States and Europe but throughout the world. The WHO has recognized the importance of headache disorders because of their enormously high prevalence and is now working together with the headache community and headache organizations on the global campaign against headache called "Lifting the Burden". The one year prevalence of migraine is between 10 and 15% in the adult population and approximately half in children and elderly. Tension-type headache is known to more than half of the population and approximately 2% have chronic tension type headache – meaning headache on more than half of all days. Unfortunately, medication overuse headache which is a headache induced by the overuse of acute migraine medications or analgesics is common, estimated at 1-2% of the global population. It is thus the most common iatrogenic problem of any field of medicine and a prime target for preventive efforts.

The existence of an excellent classification has thus resulted in excellent epidemiological data and that has again resulted in the possibility of calculating the societal cost of the headache disorders. In a European wide study of brain disorders, it was also attempted to analyze the cost of headache disorders. Unfortunately there was a lack of good cost data on the non-migraine headaches. In extremely simple terms, the cost of a disorder is calculated by multiplying the number of subjects who have the disorder with the cost per subject per year with the disorder. While the prevalence was known for all types of headache, the lack of cost data made it impossible to calculate the cost of non-migraine headaches. For migraine the cost was 27 billion Euros per year in the European population of 450 million persons. Headache disorders were the most costly neurological disorders after dementia and stroke and more costly than epilepsy, movement disorders and multiple sclerosis.

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On the basis of this experience, how is it possible to better classify pain disorders in general and better described their epidemiology and cost? The latter is certainly no simple task because the great majority of pain disorders are secondary to another disease. Headache disorders have been grouped in two big classes, those at are primary and those that are secondary to another disorder. Migraine, tension type headache, cluster headache and miscellaneous headaches are primary and the rest are secondary. Some of the secondary headaches are of special interest either because headache is an important diagnostic feature of the primary disorder e.g. giant cell arthritis, others are important because the outlast the primary disorder and represent an independent therapeutic problem.

In the WHO Classification of Diseases, ICD-10 and the forthcoming ICD-11, the aim is to classify according to etiology. This means that a post traumatic headache would for example be classified under trauma and a headache caused by a brain tumour under the brain tumours. For pain in general this problem may be even bigger. Neuropathic pain is for example caused by a neuropathy. The neuropathy, however, has its own etiology for example diabetes. In the WHO system, neuropathic pain caused by a diabetic neuropathy will be classified under diabetes, maybe with a crosslink to the neuropathy section. It could perhaps be linked also to a specific pain chapter if such a chapter were to be included in ICD-11. It is not included in ICD-10.

While the classification of pain in ICD and the estimation of cost of pain are problematic for the above reasons, it is perfectly legitimate for a specialist society to try to calculate the cost of pain, but it requires that the component cost that is due to the pain is clearly distinguished from component cost attributed to the primary disorder.

There are huge challenges in the classification, epidemiology and cost attributed to pain. Dividing pain syndromes into primary pain syndromes as distinct from secondary pain syndromes might perhaps make it easier.

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21 . – 24. September 2011
PAIN IN EUROPE VII
7th Congress of the European Federation of IASP® Chapters (EFIC®)

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Effective Management of chronic pain requires a multidisciplinary team approach

Central topic discussed at the 5thCHANGE PAIN® Advisory Board

Aachen/Brussels, 26 August 2011. The social burden of pain is considerable: One in five of the European adult population experienced pain in the previous month and almost two of them reported daily moderate or severe pain. It seriously affects patients' quality of life and leads to high utilisation of healthcare resources and to lower work productivity. This was shown in a recent publication[1] which analysed data of the National Health and Wellness Survey (NHWS) supported by the CHANGE PAIN® Initiative. CHANGE PAIN® – a pan-European initiative launched by the German pain expert Grünenthal and endorsed by the European Federation of IASPv Chapters (EFIC) – aims to enhance the understanding of the needs of patients with severe chronic pain and to develop solutions to improve pain management.[2] At the 5th meeting of the CHANGE PAIN® Advisory Board, a major topic was how a multidisciplinary approach to pain management could improve patients' outcomes.

Approximately 20% of the adult population in five European countries (UK, France, Italy, Germany and Spain) experienced pain in the previous month. This was shown in the National Health and Wellness Survey (NHWS) that evaluated data of over 50,000 pain patients in these five countries.[1] The most frequently reported condition causing pain was back pain, cited by almost two-thirds of respondents, followed by joint pain (~50%) and neck pain (~30%).

Throughout the observed pain conditions, a large majority of the survey participants experienced moderate to severe pain, with many patients suffering daily from their pain. In addition, the results demonstrate the great burden of pain on both, the individual patient and on society – particularly when it is severe and frequent. Survey participants often suffered from additional health conditions associated with their pain such as sleeping disorder, anxiety and depression.

Understanding chronic pain

A further area of interest of the CHANGE PAIN initiative is to improve understanding of the process of pain chronification and its implications.

Traditionally, chronic pain has only been defined by its pain duration. In the SELECT study, another project supported by the CHANGE PAIN group, quantitative interviews were conducted with 1,005 participants of the 2010 NHWS who had reported having suffered from back pain in the past three months. This survey uses different questionnaires assessing not only pain duration and severity, but also variables such as pain-related activity limitations, depressive symptoms and a number of additional pain sites.

This information was then used to define assign the pain in terms of outcome probabilities, applying a Prognostic Risk Score to identify patients

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Central topic discussed at the 5thCHANGE PAIN® Advisory Board

with "possible" or "probable" chronic pain.[3] This approach can help to better understand patients suffering from moderate or severe back pain and to tailor pain management according to the needs of the individual patient. Results of the SELECT Study are expected to be published later this year.

Multidisciplinary team approach

Pain as a multidimensional condition requires the involvement of a multidisciplinary team of healthcare professionals. The CHANGE PAIN group has started working on a booklet to provide guidance to healthcare professionals on how to set up such a team. A multidisciplinary approach to pain management provides benefits for patients, healthcare providers and society as a whole. The integration of multiple treatment modalities results in considerable improvements for patients suffering from chronic pain in terms of a reduction in the use of medications, improved functional ability and increased likelihood of returning to work. Further advantages are better quality of patient care, higher patient satisfaction and reduced healthcare costs.

Preconditions for a multidisciplinary team approach are clear referral guidelines for the primary care physicians and good communication between patients, general practitioners and specialists. A valuable tool that can be used for improving physician-patient communication is the CHANGE PAIN® Scale[4], which has been translated and distributed in 13 countries worldwide and can help to set individual treatment goals for chronic pain patients.

About CHANGE PAIN®

CHANGE PAIN® aims to enhance the understanding of the needs of patients with severe chronic pain and to develop solutions to improve chronic pain management. Initiated by the German pain expert Grünenthal and endorsed by the European Federation of the IASP® Chapters (EFIC), the initiative involves pain experts from across Europe. The international Advisory Board is chaired by Professor Giustino Varrassi, MD, General Director ASL Teramo and past president of EFIC, and Dr. Gerhard H. H. Müller-Schwefe, MD, Head of Centre for Interdisciplinary Pain Therapy & Palliative Care, Goeppingen, Germany and President of the German Pain Association (DGS).

More information:
www.change-pain.com

IMPRINT

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WILEY-BLACKWELL
Blackwell Verlag GmbH
A company of John Wiley & Sons, Inc.
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10245 Berlin, Germany
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Fax: +49(0)30 / 47 0 31-444
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Schröders Agentur, Berlin
www.schroeders-agentur.de

Rate card 25/2011

Subscritpion price for 2011
(45 issues per year):
€ 238 (prices are exclusive of tax)

No. 25/ Volume 35
Berlin, September 2011

ISSN 0934-3148 (Printversion)
ISSN 1439-0493 (Onlineversion)

ZKZ 30371

www.medreports.de

Targeting TRPV1 for pain relief

Should we quench or reignite the fire?

Arpad Szallasi

Arpad Szallasi

Preclinical research has recently uncovered new molecular mechanisms underlying the generation and transduction of pain, many of which represent opportunities for pharmacological intervention. Manipulating TRP (Transient Receptor Potential) channels on nociceptive neurons is a particularly attractive strategy in drug development in that it targets the beginning of the pain pathway. The vanilloid (capsaicin) receptor TRPV1 is a multifunctional channel involved in thermosensation (heat) and taste perception (e.g. peppers and vinegar). Importantly, TRPV1 also functions as a molecular integrator for a broad range of seemingly unrelated noxious stimuli. Indeed, TRPV1 is thought to be a major transducer of the thermal hyperalgesia that follows inflammation and/or tissue injury.

1. TRPV1 antagonists in clinical trials

The cloning of TRPV1 has spurred considerable efforts in the pharmaceutical community to find TRPV1 antagonists. However, side-effects associated with the use of TRPV1 antagonists have so far prevented any compounds from progressing beyond testing in phase II trials. Particular concern has surfaced around the effects of antagonizing TRPV1 on the regulation of body temperature and in the detection of noxious heat.

1.a TRPV1 and body temperature regulation

TRPV1 null and knockdown mice have an apparently normal body temperature despite the fact that they prefer lower ambient temperatures. These characteristics are also seen in rats whose TRPV1-expressing neurons have been ablated by high-dose neonatal capsaicin treatment. Therefore it was somewhat unexpected that some TRPV1 antagonists cause hyperthermia in preclinical studies and humans.

Several studies noted that treatment with antagonists that block the three primary TRPV1 activators (that is, capsaicin, low pH and heat) *in vitro* cause a transient hyperthermia in experimental animals. The severity of this effect varies depending on the compound used but it attenuates after several days of dosing. In human volunteers, AMG517 caused a lasting (1-4 days) and marked hyperthermic reaction (up to 40.2 0C), leading to the withdrawal of this compound from clinical trials. Other clinical studies have also noted hyperthermia associated with TRPV1 antagonists (e.g. ABT-102 and AZD1386) though these effects were not as pronounced as what was observed with AMG517. In rats in was possible to eliminate hyperthermia while preserving analgesic activity by differential blockade of TRPV1 activation. Compounds (e.g. AMG8562) which prevented the activation of rat TRPV1 by capsaicin, but not by low pH or heat, had no effect on body temperature in the rat (though these compounds still caused hyperthermia in dogs). How well this translates to humans remains to be seen. Of note, PHE377 (currently in phase IB trials) did not cause hyperthermia in rats or dogs although it did inhibit all three major modalities of TRPV1 activation.

1,b, TRPV1 antagonists and noxious heat perception in humans

Clinical studies have confirmed the role of TRPV1 as a noxious heat sensor in humans. Indeed, the threshold for detecting painful heat was significantly elevated in non-sensitized skin of healthy volunteers following oral administration of 400 mg *per diem* SB-705498, with subsequent studies reporting blunted heat perception in healthy human subjects which did not desensitize upon repeated dosing. This effect could potentially cause scalding injury during common activities such as taking a hot shower or consuming hot food or beverages. Indeed, some subjects taking MK-2295 perceived potentially harmful temperatures as innocuous. In randomized clinical trials, similar findings were reported using ABT-102 (up to 4 mg twice a day) and AZD1386 (a single daily dose of 95 mg). Of note, no other relevant safety findings were reported in these two trials and it was felt by the investigators that AZD1386 may have a clinical potential to relieve pain associated with gastro-esophageal reflux disease.

2. TRPV1 agonists (capsaicin and resiniferatoxin) in the clinics

Topical TRPV1 agonists (e.g. capsaicin creams) have been employed clinically for many years to alleviate chronic painful conditions such as diabetic neuropathy. An occlusive high capsaicin concentration patch (Qutenza, NeurogesX/Astellas) was recently approved for the treatment of a variety of pain conditions. Injections of resiniferatoxin, an ultrapotent capsaicin analogue, are being evaluated as a so called 'molecular scalpel' to achieve long-term analgesia in patients with cancer who have chronic, intractable pain. Activity-dependent targeting of TRPV1 using permanently charged agonists that permeate the channel core of TRPV1 only when it is open is a novel approach to minimize the burning pain reaction at the application site which is the main adverse effect of capsaicin administration. Such agonists are expected to target (and subsequently desensitize) hyperactive TRPV1 and spare normal nociception.

Summary

Desensitization of capsaicin-sensitive neurons by agonists ("reigniting the fire") and pharmacological blockade of TRPV1 by antagonists ("quenching the fire") are two fundamentally different but complimentary therapeutic approaches for pain relief. Only localized pain is amenable to topical and/or site-specific capsaicin therapy. By contrast, small molecule TRPV1 antagonists may be administered per os to alleviate more generalized pain. The balance between the beneficial actions and adverse effects of TRPV1 antagonists must be carefully and pragmatically evaluated in order to determine if these drugs could emerge as the next generation of pain killers. Regardless of the outcome, the tremendous experience obtained with therapeutic targeting of the TRPV1 receptor should greatly facilitate on-going efforts to capitalize on the additional TRP channels (e.g. TRPA1, TRPV3 and TRPM8) that are present in nociceptive neurons.

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DETAILS OF THE EVENT

Thursday 22nd September 2011
12.15–13.45 h
Hall G2

SATELLITE SYMPOSIUM

Challenges in current treatment of neuropathic pain – Balancing of efficacy and tolerability

Chairman: Prof. Dr. med. Burkhard Gustorff

Insights in neuropathic pain treatment – drugs' mode of action taken into consideration
Prof. Guy Hans

Treatment of localised neuropathic pain with 5 % lidocaine medicated plaster – clinical data giving new insights into mechanism of action
Prof. Burkhard Gustorff

Practical experience and relevant factors for quality of life – the patient´s view and what it could mean for treatment choice
Dr. Uwe Kern

Patient requirements translated into treatment algorithms – consequences for treatment guidelines
Prof. Nadine Attal

In cooperation with Grünenthal

The "Two-Edged Sword" of Narcotics in Pain Management

Powerful Treatment Requires Physician's Diligence to Avoid Abuse

Prescription narcotics are among the most effective treatments for chronic and debilitating pain, but their improper use can have tragic consequences. For proof, look no further than North Carolina, where 1,000 deaths occur annually from misused medications – among the highest rates in the US. "If we all work together responsibly, patients can receive appropriate and effective pain management and we can avoid these needless deaths," said Dr. Mark Romanoff of Southeast Pain Care during an appearance on the program Medicine and Society, produced by University of North Carolina-Charlotte Cable Television. The segment is titled "Prescription Narcotics: A Two-Edged Sword."

An estimated 70 million Americans suffer from chronic pain, and many find relief from narcotics prescribed by their physicians. National studies report that 85 percent of these patients use the medications appropriately. When prescribing narcotics, Romanoff said physicians must be extremely careful to ensure the patient's wellbeing and achieve the desired results while avoiding negative outcomes such as addiction, accidental overdoses or death. He added that patients bear the responsibility to use prescriptions only for their intended purpose; to secure them away from others; never to share medications; and to return unused portions to their physicians for disposal. For more information visit www.sepaincare.com

PAIN Proposal

Improving the Current and Future Management of Chronic Pain

The Pain Proposal Steering Committee is an independent group of European experts, from a range of backgrounds, with a shared interest in chronic pain. The Steering Committee has taken a leading role in the development and implementation of the Pain Proposal initiative.

Committee members have contributed their time and expertise, hosting a meeting with the Executive Committee; reviewing the questions for the patient and primary care physician surveys commissioned for this project; and assisting in the development of content for this report.

The recommendations within this document represent a consensus from the Steering Committee of steps that could be taken to improve the management of chronic pain in Europe for the benefit of all involved.

www.mijnpijn.nl/pdf/PainProposalEuropeanReport.pdf

Musculoskeletal pain, neuropathic pain, and fibromyalgia – the evidence

Prof. Andrew Moore

Prof. Andrew Moore

In musculoskeletal pain, neuropathic pain, and fibromyalgia, the evidence is that all drugs produce at least 50% pain intensity reduction in between 10% and 20% more patients than placebo over 12 weeks, with NNTs in the range of 5-10. That's as good as it gets. There have been significant developments in understanding bias in pain trials, beyond usual sources like randomisation and blinding. Systematic reviews of randomised trials can produce be misleading if the new sources of bias are not considered.

Most trials are done for regulatory purposes – to say that an intervention works, to demonstrate efficacy. What we need is information on clinical effectiveness – how many patients get a good outcome – enabling us to deliver pain relief to the greatest number of patients at the lowest cost and in the shortest time.

These notes spring from the needs of clinical effectiveness over trial efficacy.

1. Distribution of response in chronic pain trials is not Gaussian, but take the form of a bi-modal distribution where some patients obtain very good pain relief while others get very little. The average result represents only a small minority of patients. This has been shown in a number of painful conditions using individual patient meta-analysis. Studies reporting average changes in pain scores are of limited utility: who treats patients with the goal of achieving the average result from a clinical trial?
2. The thrust has been to move to responder analysis, where responder is someone who has ≥30% or ≥50% pain relief over baseline. While these treatment goals have been discussed for some time, the IMMPACT recommendations of 2008 were a very useful support.
3. Chronic pain trials often have large numbers of withdrawals because of lack of efficacy or adverse events (up to 60% in chronic low back pain). It is traditional to use last observation carried forward (LOCF) in the trials, using pain scores from those who cannot or will not take the drug or use the intervention.
4. LOCF is statistically legitimate, but imparts major bias from the clinical effectiveness perspective. Recent evaluations of opioids in chronic non-cancer pain show that statistical benefit using LOCF is lost with other imputation methods, particularly where a withdrawal is considered to produce no pain relief (because patients can't take the medicine), or where a withdrawn patient is considered to be a non-responder.
5. Clinical effectiveness considers withdrawal quite differently, with response from the clinical effectiveness perspective including *both* adequate pain relief *and* ability to continue with the treatment. Using this definition, the proportion of responders in chronic pain therapies is never high in chronic pain – perhaps with NSAIDs 30% in ankylosing spondylitis and 25% in OA or RA, no more than 20% with antidepressants and anticonvulsants in neuropathic pain, and perhaps 10% with treatments for fibromyalgia and CLBP.
6. These figures are in longer duration (3-month) trials. There is also a considerable duration bias with less effective therapies. Duration bias is not noticeable with more effective therapies with NNTs of about 4-5, but typically it becomes more appreciable where NNTs wise above about 7-8, the case in many interventions in chronic pain.
7. For most drug interventions the timescale of response is swift, with response or lack of response established within 2-4 weeks. Initial response generally predicts long term benefit. Lack of initial response is a reason for stopping therapy and not exposing patients to prolonged therapy with potential risk but no benefit. Stopping rules should aid care pathway or guideline development.
8. Higher levels of pain relief give rise to benefits in other symptoms, like sleep, fatigue, and depression, and improve quality of life and ability to work.
9. Making comparisons between competing therapies is difficult, and to be consistent the same outcome, the same duration, and the right imputation method or response criterion has to be used. Like-for-like comparison is essential for care pathways or guidelines to be of value.
10. If the goal is to achieve good outcomes for the most people with a chronic painful condition, then it is certain that a restricted number of drugs will be inadequate. There is virtually no pragmatic research on the effectiveness of serial testing of drugs for efficacy in chronic pain, though what there is encouraging; in patients with OA but inadequate pain relief, 50% obtained it when switching to another drug. In other conditions, like depression, formal studies have been conducted to demonstrate that limited formularies produce overall worse and more costly results.
11. The clinical effectiveness agenda is also important for assessing risk benefit. We now know that in responders, highly important actual benefits come with successful treatment, over and above pain relief. It is these tangible benefits now that have to be balanced against the potential for future risk of harm at a very low level. There is growing evidence that patients regard this type of result as acceptable.

The amount of robust data – based on these criteria, plus sufficient information to make any result reliable – is limited. Current reviews for antidepressants and anticonvulsants are being updated, but older reviews may be misleading. Providing good and useful clinical effectiveness information from good clinical trials is the ambition of evidence-base thinking in 2011.

Tetrodotoxin-sensitive Na+ channels

PD Dr. med. Angelika Lampert

Many known painkillers act on sodium channels. We are all familiar with the effect of an injection at the dentist. Local anesthetics, such as those used in smaller surgeries, inhibit voltage-gated sodium channels effectively in their function. These results in the blockage of the pain stimuli, which is normally passed along the nerves – unfortunately however, the stimuli needed for muscle contraction is also blocked as local anesthetics are not subtype-specific. Side effects occur, whereby the coffee stain on the shirt after visiting the dentist, is still one of the harmless ones.

Nine different sodium channel subtypes are known within humans, two of which are mainly expressed in nociceptors: the tetrodotoxin (TTX) sensitive Nav1.7 and TTX-resistant Nav1.8. If it were possible to selectively block sodium channels, people would profit from reduced pain perception but other body functions, except for olfaction, would not be affected. What is this assumption based on?

A family in Pakistan was recently discovered, whereby the members of this family appear to feel no pain. As previously suspected this condition is not due to a defect in a receptor for nerve growth factor. Surprisingly, it was found that family members have a truncation mutation in the sodium channel subtype Nav1.7, indicating that the mutation carriers can no longer produce any functional Nav1.7 channels[1]. Obviously, the loss of Nav1.7 function is not compensated by a different sodium channel subtype; although on the first glance, the function of TTX-sensitive sodium channels seems quite similar. The Pakistani family members showed normal sensory perception and body functions during a medical examination, apart from analgesia and a loss of the sense of smell.

A sole loss of function of Nav1.7 seems to be sufficient to selectively and completely remove pain perception. This underlines that this sodium channel subtype makes for a very interesting target for the future treatment of pain. So far it is not possible to block certain subtypes selectively, and scientists in industry and academia are working towards a detailed picture of the three-dimensional structure and the physiological function of this nociceptive channel, so as to enable a more targeted drug design.

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By modifying certain areas of the sodium channel one might also alter specific functions of the channel, such as fast or slow inactivation. Especially the latter has shown a promising possibility of alteration, with higher subtype selectivity than other channel functions. Several drugs were developed that now need to be tested thoroughly for the exact subtype specificity, their effects on pain and also on additional systemic effects.

A few weeks ago, the first crystal structure of a voltage-gated sodium channel was published and for the first time it was possible to verify whether our previous assumptions about drug binding sites and their accessibility are likely to be true[2]. Although this channel is derived from bacteria, its sequence homology to mammalian sodium channels is relatively high and their 3D structures are likely to be built up in a similar manner. Interestingly, the new structure of the pore region of the channel, which represents the connection between cell interior and external, has a direct connection to the lateral cell membrane, the so-called "pore portal". Small, fat-soluble substances, such as some local anesthetics could therefore theoretically penetrate laterally into the channel pore through the cell membrane and reach its binding site in the closed state of the channel. Amino acids that are known to be involved in the binding of local anesthetics are very close to this pore portal. With the means of homology modeling it is possible to simulate the path of a drug molecule through this portal and thus make predictions as to whether different drugs will access the channel in a different manner. It might also help to design new drugs which possibly have a higher efficacy or pronounced subtype specificity, so that they would only block the nociceptive sodium channels, but not those needed for proper muscle function.

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Acceptance and Commitment Therapy in chronic pain – how does it work?

Clarifying the change processes in treatment

Dr. Rikard Wicksell

Rikard Wicksell, Stockholm (Sweden)

Recent research has suggested the importance of acceptance as a central link between chronic pain and disability, and the empirical support for interventions emphasizing exposure and acceptance strategies, particularly Acceptance and Commitment Therapy (ACT), has rapidly increased. As for psychological treatments in general, the change processes, or mechanisms of action, in ACT for pain still need to be clarified.

For patients with chronic pain the utility of psychological treatments, and especially cognitive behavioral therapy (CBT), has repeatedly been shown[1]. Nevertheless, further improvements are needed. Patients with significant disabilities due to pain and distress often need more tailored interventions to improve functioning. This is certainly the case for pediatric chronic pain as well. In fact, the rather high prevalence of chronic debilitating pain among youths together with a tendency for these problems to persist into adulthood suggests an even greater need for such efforts.

ACT, as a development within CBT, is aimed at improving the patient's ability to act effectively in concordance with personal values even in the presence of pain and distress (i.e. psychological flexibility). In contrast to most treatments, which emphasize reduction or control of symptoms, ACT promotes acceptance of negative reactions that cannot be directly changed (thoughts, emotions, bodily sensations) in favor of engaging in activities that are meaningful although possibly painful or fear provoking (i.e. exposure).

Research on psychological interventions for chronic pain has primarily focused on effectiveness, with relatively minor attention given to exploring and evaluating change processes in treatment. Thus, the mediators of change in psychological treatments are still unclear and represent central targets for contemporary clinical research. In short, mediators refer to processes through which changes are considered to occur. For example, improvements in functioning may occur as a result of changes in pain but may also be due to other processes such as increased psychological flexibility. From a clinical perspective, clarifying the mediator(s) in successful treatments would help therapists focus on relevant processes that most probably affect changes in functioning. Further implications are more effective yet less extensive treatment programs with obvious financial health care benefits. In addition, information on change processes is required in order to refine theories regarding behavioral interventions for chronic pain.

ACT and similar approaches are sometimes labeled "3rd wave CBT" and the arrival of these treatments has initiated a debate regarding the actual novelty of acceptance-oriented interventions. It is important that the discussion regarding conceptual differences and similarities is based on empirical arguments; how ACT works and if change processes differ from other treatments should be evaluated empirically, by carefully examining the processes through which various interventions affect outcome.

Several studies from our research team and other groups indicate the utility of ACT for chronic pain in adults. To develop and evaluate ACT for children and adolescents we have conducted a series of studies including an RCT comparing ACT with a multidisciplinary treatment approach including pharmacotherapy (amitriptyline), with results supporting the effectiveness of ACT to improve functioning in youths with chronic pain[4]. Recently, additional analyses were conducted to clarify the change processes, or how these improvements in functioning occurred. In short, mediation analyses on the RCT with pediatric chronic pain illustrate that improvements in functioning following ACT occurred as a result of changes in the variables most closely related to psychological flexibility rather than through changes in self-efficacy, kinesiophobia, catastrophizing, or pain intensity[3]. These results are consistent with findings from a similar study with adult pain patients, in which psychological inflexibility but not pain intensity, anxiety, depression, kinesiophobia, or self-efficacy were found to mediate effects on outcome when treated with ACT[5]. These results also correspond with research indicating the relevance of targeting psychological flexibility in treatments of chronic pain and distress[2].

Thus, an increasing amount of research supports the effectiveness of ACT for adult as well as pediatric chronic pain. Recent studies indicate that psychological flexibility may be a central target for interventions aimed at improving functioning in patients with chronic debilitating pain. Undoubtedly, more research on change processes will significantly improve our ability to tailor interventions and develop more effective treatments.

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The Pain Within – a photographic exhibition at EFIC

The Pain Within is a new pan-European campaign that uses the power of specially-commissioned photographic patient portraits by award-winning photographer Alex Telfer to raise awareness of peripheral neuropathic pain (PNP). PNP is a little-known and often invisible condition which can have a devastating impact on the lives of those affected by it.

Sponsored by Astellas Pharma Europe Ltd., an exhibition of *The Pain Within* images will launch here at EFIC on 21 September and will be open for viewings at Booth 2 for the duration of the congress. The exhibition will then tour Europe in the coming months.

Creating portraits of pain with Alex Telfer

Each image featured in *The Pain Within* captures the experiences of a real person living with neuropathic pain. Photographer Alex Telfer worked with patients from across Europe to understand how they feel about their pain and the challenges that they face living with it every day. He then spent time with them in a London studio to capture images that could convey those feelings and experiences to others.

Photographer Alex Telfer says: "My aim for this exhibition was to allow visitors a glimpse into the lives of patients suffering from neuropathic pain, so that they could understand their experience and gain an insight into living with this type of chronic pain. I have tried to capture not just how these people look, but also how they perceive their pain and how they feel about it."

Alex Telfer has received several awards for his work including: The American Photography Annuals 2009 and 2010, Communication Arts Photography Annual 50 and 51, Lurzer's Archive Top 200 Ad Photographers Worldwide 2010, Creative Review Photography Annual and The International Photography Awards. He has also been recognised by *Campaign* Magazine as their Number One Advertising Photographer of 2009.

PNP is invisible but debilitating

PNP, a type of neuropathic pain, results from damage to nerves rather than to skin, muscle or bone and can be caused by a range of diseases, injuries and even some medications. The true burden of the disease is often misunderstood by a patient's friends and loved ones. It can last indefinitely and is often progressive. PNP can have an overwhelming impact on the lives of those who live with it including family life and social life as well as ability to work and to perform day-to-day activities.[1,2,3] Treatment of PNP is considered a great challenge and many patients struggle to find relief from the condition.[1]

Here is what some of the patients photographed said about their condition: *"I find it incredibly hard to be a mother with neuropathic pain"…"It feels like I'm being stabbed with a knife over and over again"…"I wasn't able to work, drive my car or participate in family life" is how just three patients describe their experiences of PNP.*

Increasing understanding of PNP

The aim of *The Pain Within* is to raise awareness of PNP and foster greater understanding of the disease and the burden it places on patients. *The Pain Within* will help the friends and loved ones of those living with PNP, as well as the general public, to understand the patient's perspective and the challenges they face every day. Ultimately, it will help patients living with the condition by creating an environment in which the burden of their disease is recognised and understood.

Astellas is committed to patients with PNP

As part of its commitment to people living with PNP, Astellas is supporting *The Pain Within* to raise awareness of the condition across Europe.

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German Association of the Scientific Medical Societies AWMF

Recommendations for the management of FMS

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Winfried Häuser, M.D.

Due to the multiple controversies on the classification and management of patients with chronic widespread pain without evidence of a somatic disease (so-called fibromyalgia syndrome FMS), two German scientific umbrella organisations, the Association of the Scientific Medical Societies in Germany AWMF and the German Interdisciplinary Association of Pain Therapy DIVS coordinated an evidence-based guideline on the management of FMS.

Thirteen German medical and psychological associations and two FMS-patient self-help organisations participated in the project. A systematic search of the literature including all controlled studies, systematic reviews and meta-analyses of pharmacological and non-pharmacological treatments of FMS was performed in the Cochrane Library, Medline, PsycInfo and Scopus until December 2007. Levels of evidence were assigned according to the classification system of the Oxford-Centre for Evidence Based Medicine. Grading of the strengths of recommendations was done according to the German program for disease management guidelines. Standardized procedures were used to reach a consensus on recommendations. The guideline was reviewed and finally approved by the boards of the societies involved[1]. A short version of the guideline for patients was developed[2].

Classification: The guideline recommends classifying FMS as a functional somatic syndrome rather than a mental disorder. Comorbid mental disorders are to be additionally coded.

Diagnosis: FMS is diagnosed on the basis of the characteristic symptoms[3] and the exclusion of other diseases that can lead to the same symptom pattern. The use of a pain sketch and a thorough medical history are recommended. A complete physical examination is necessary for the diagnostic evaluation of structural diseases associated with chronic widespread pain, e.g. joint swelling in inflammatory rheumatic diseases or skin changes in Fabry disease. Examination of the ACR tender points is optional. A few ancillary tests are recommended as part of the initial evaluation of every patient (C-reactive protein, complete blood count, Creatine kinase, Serum calcium, Basal thyroid-stimulating hormone). There is no reason to test routinely for antibodies associated with inflammatory rheumatic diseases in the absence of clinical evidence. No further ancillary studies (i.e. no further laboratory testing, clinical neurophysiological tests, or imaging studies) are recommended in patients who have the characteristic symptoms of FMS and show no clinical evidence of systemic, orthopaedic, or neurological disease.

Therapy: Based on expert opinion, a stepwise short-term FMS-management is proposed. The diagnosis of FMS should be communicated explicitly to the patient along with information about the treatment options. The level of treatment and the therapeutic options should be chosen by shared decision-making of the patient and treating physician, in the light of the patient's preferences and accompanying illnesses, if any.

Level 1

- Cognitive behavioral therapy and operant therapy for pain, including patient education (grade 1a evidence, grade A recommendation, strong consensus)
- Aerobic endurance training adapted to the patient's individual performance level (grade 1a evidence, grade A recommendation, strong consensus)
- Pool-based exercise / aquatic jogging (grade 1a evidence, grade A recommendation, consensus)
- Spa therapy (bathing in thermal springs) (grade 1a evidence, grade A recommendation, strong consensus)
- Amitriptyline 25-50 mg/d (grade 1a evidence, grade A recommendation, strong consensus)
- Diagnosis and treatment of comorbid physical and mental illnesses (grade 5 evidence, open recommendation, strong consensus)

Level 2

- Multimodal treatment (requirement for medical training therapy or other type of activating movement therapy coordinated with psychotherapeutic methods) (grade 1a evidence, grade A recommendation, strong consensus); Mainly outpatient; (partly) inpatient, when outpatient treatment is inadequate or impossible

Level 3

- Short-term: duloxetine 60–120 mg/d or fluoxetine 20–40 mg/d or milnacipran 100–200 mg/d or paroxetine 20–40 mg/d or pregabalin 150–300 mg/d (grade 1a evidence, grade B recommendation, majority opinion)
- Short-term: hypnotherapy/directed imagery (grade 2b evidence, grade B recommendation, consensus) or therapeutic writing (grade 2b evidence, grade B recommendation, strong consensus)
- Multimodal interval/booster therapy (grade 5 evidence, open recommendation, strong consensus)
- Short-term: complementary therapeutic techniques (homeopathy, vegetarian diet) (grade 2b evidence, open recommendation)

For the long-term treatment, the patient and physician should decide together on an individualized treatment program. In long-term care, it is important to reinforce the patient's assumption of individual responsibility and self-motivated activities (e.g., endurance training, application of heat by himself or herself).

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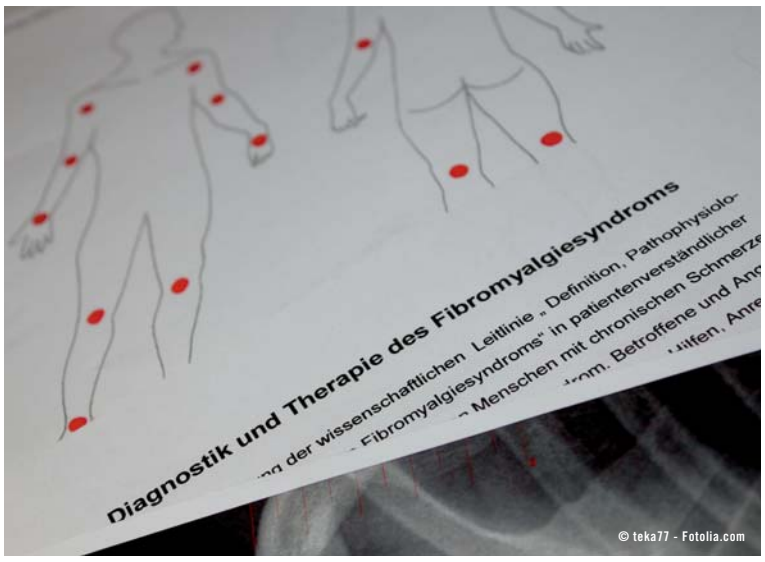

Validating outcomes in pain trials

Choosing trial outcomes

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Priv.-Doz. Sebastian Straube

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Meaningful and validated outcome measures are essential to interpreting clinical trial results. Results of pain trials have commonly been reported as treatment group average data but this is often inappropriate because the underlying frequency distribution of the raw (individual patient) data is not normal (Gaussian, bell-shaped) but rather skewed or bimodal ("U-shaped"). An alternative is to use responder outcomes for pain improvement over the course of a trial and for pain state (pain intensity) at trial end.

For pain improvement, evidence-based expert consensus exists that a 10–20% decrease in pain scores corresponds to "minimally important", at least 30% decrease to "moderately important" and at least 50% decrease to "substantial" improvement [4]. For pain state, scoring more than 30 mm on the 0–100 mm visual analogue scale (VAS) corresponds to at least "moderate" pain and scoring above about 50 mm to "severe" pain[2]. Patients rating their pain treatment as "very good" or "excellent" also tend to have pain less than 30 mm on the VAS[8]. Furthermore, pain less than 30 mm corresponds to "very much" improvement on the Patient Global Impression of Change scale. Therefore, achieving at least 50% decrease in pain scores and pain less than 30 mm on the VAS appear to be meaningful outcomes to identify *responders*. In order to validate these pain-related responder outcomes, we need to investigate how they correspond to outcomes in other domains of life. Patients with chronic painful conditions often experience a range of other symptoms in addition to pain, and interference with many aspects of their lives.

Key questions are: Is having at least 50% improvement in pain intensity scores typically accompanied by improved sleep, less anxiety, more time at work and generally an improved quality of life, or is there no consistent relationship? How large are the benefits in other domains of life that can be expected for pain state or pain improvement responders? Do pain state and improvement responders approach "normal" population reference values for sleep disturbance, depression, anxiety etc.?

Pain improvement responders

Evidence now exists across a range of painful conditions that those patients with the greatest improvements in pain scores also experience the greatest improvement in other domains of life. For example in hand osteoarthritis, those with ≥50% improvement in pain intensity and especially those with ≥70% improvement also experienced the most benefit in function, stiffness, and global rating of disease[1]. Patients with painful diabetic neuropathy who had ≥50% pain improvement also experienced the largest improvements in mood, sleep, and enjoyment of life, among other outcomes[6].

We found that in fibromyalgia patients with 30–50% and especially those with ≥50% improvement in pain scores also benefitted most with regard to a range of other outcome measures including sleep disturbance, depression, anxiety, as well as all eight Short Form 36 Health Survey (SF-36) domains[9], approaching population norm values for these outcomes [3,5,6].

Pain improvement and pain state responders

In fibromyalgia we investigated patients who were either improvement responders (≥50% pain improvement over the duration of the trial), state responders (≤30 mm on the VAS at trial end), "double responders" (state and improvement responders), or non-responders (nei-

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Interventional procedures for non-spinal pain and cancer pain

Bart Morlion, Pellenberg (Belgium)

Bart Morlion

Interventional pain management (IPM) has to be viewed as part of a multimodal pain management strategy. Most IPM procedures are not supported by strong evidence and the use of diagnostic test blocks to predict outcome of interventional procedures is debated because of the high rate of false positive tests. Despite the lack of prospective, randomized, placebo-controlled trials IPM can offer a substantial benefit in pain control and a reduction of systemic analgesics and their side effects in selected cases.

IPM for non-spinal pain

The blockade of nerves with local anaesthetics, with or without corticosteroids, leads in some patients to prolonged pain reduction, far beyond the expected time based on the pharmacokinetic properties. Nerves commonly targeted for blocks include, among others, inguinal, ileohypogastric and genitofemoral nerves for groin pain, occipital and supraorbital nerves for headache and suprascapular nerve for shoulder pain. According to American practice guidelines, issued by ASA and ASRA, peripheral somatic nerve blocks should not be used for long-term treatment of chronic pain[1].

More permanent blockade of nerve tissue can be carried out using neurolytic techniques. Meticulous care is needed to prevent damage to other nervous functions, including motor function. Physical neurolytical modalities include the use of heat (radiofrequency ablation) and cold (cryoneurolysis). Phenol (7–12%) and ethanol (50–100%) are the most frequently used and studied chemical substances for neurolytic blocks[2]. Chemical neurolysis is debated as obsolete for the treatment of chronic non-cancer pain because of the risk of neuritis and deafferentiation pain. Nevertheless, in some rare indications, these might be considered[3].

The authors of a recent Cochrane review conclude that the practice of chemical cervico-thoracic or lumbar sympathectomy for neuropathic pain and CRPS is based on very little high quality evidence[4]. They advise to use sympathectomy cautiously in clinical practice, in carefully selected patients, and probably only after failure of other treatment options. In particular, neurolysis of the sympathetic chains can be a treatment option in peripheral vascular disease.

IPM for cancer pain

According to many handbooks, most patients suffering from cancer pain can be managed effectively by the WHO stepladder methods. Only 5–14% remain poorly controlled and are in need of more interventional procedures to adequately control the pain. However, recent research indicates that these figures are often underestimated[5]. For this group of patients, mostly suffering from neuropathic pain and bone pain, the access to a pain specialist, mostly anaesthetists, is recommended in recent guidelines.

Often, pain specialists are called in only at a late stage for their advice. Indeed, mostly they are confronted with poorly controlled patients on high dose opioids and adjuvant medication leading to cognitive impairment. Interventional procedures may lead to excessive sedation once the pain is better controlled. In addition, fast reduction of the opioids can lead to acute withdrawal symptoms. Therefore, a close observation after interventional procedures is mandatory in order to prevent these problems, and to titrate systemic medications downwards according to their response.

A wide range of interventional procedures can be applied in poorly controlled cancer pain[6–8]. These include, neuraxial pharmacotherapy, neurolytic procedures and nerve blocks. In neuraxial analgesia, drugs are administered by the epidural or intrathecal route. Drugs widely used for this purpose alone or in combination, include opioids like morphine, local anesthetics and clonidine. In contrast to non-cancer pain, neurolytic procedures can be appropriate in cancer pain. Lifetime expectancy, comorbidity and the patient's wishes will influence treatment decisions more than the fear for late complications. Indeed, in palliative situations, more destructive interventions such as neuraxial and sympathetic neurolytic blockades, and percutaneous cordotomy will be offered to patients in an effort to improve pain control at the end of life. Among all procedures, the neurolytic coeliac plexus block is the most applied technique with high efficacy (70–90%) to for patients with visceral pain arising from an upper abdominal malignancy, especially for pancreatic cancer.

A recent Cochrane review concluded that despite minimal statistical evidence for the superiority of pain relief over analgesic therapy, the fact that coeliac plexus block causes fewer adverse effects than opioids is important for patients[9]. The efficacy of neurolytic blocks of the superior hypogastric plexus for the treatment of cancer-related pelvic pain was also demonstrated[10]. In patients with end-stage pelvic tumours intrathecal sacral phenolization can be considered. However, this technique should be reserved to patients whose bladder and rectum function is no longer existent or bypassed already[11].

In conclusion, interventional procedures for non-spinal pain and cancer pain should be used only in highly selected patients and only as part of a multimodal pain management strategy.

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Choosing trial outcomes

ther state nor improvement responders). Across a range of outcomes, double responders consistently benefitted most and non-responders benefitted least, with state only responders and improvement only responders in-between.

Work is a good example to illustrate this further because being able to work and do so without interference caused by chronic disease is an important outcome, both on an individual and a societal level. We examined the relationship between pain response and work by analysing a type of work-related data commonly collected but infrequently analysed as such in clinical trials: work-related component questions from a number of commonly used questionnaires (Fibromyalgia Impact Questionnaire (FIQ), SF-36, Sheehan Disability Scale, and Multidimensional Assessment of Fatigue). Work-related outcomes of interest included *time off work* and *interference with work*. We found that double responders gained about 1.4 days of work per week and experienced substantially less interference with work when answers to FIQ questions about work at trial beginning and end were compared. Non-responders did not experience meaningful improvement. State only responders and improvement only responders were in-between, with the former achieving greater benefit than the latter. Analysing answers to a number of other questions about interference with work from the other questionnaires yielded similar results indicating that our findings are robust and that this methodology can be applied to other trials[10].

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Advertorial

QUTENZA™ provides lasting pain relief to patients living with peripheral neuropathic pain

QUTENZA (capsaicin 8% w/w dermal patch) is a new topical treatment option for peripheral neuropathic pain (PNP) that enables the rapid delivery of high-dose capsaicin directly to the hyperactive pain receptors that are the source of neuropathic pain. A single application of QUTENZA delivers prolonged and reversible defunctionalisation of cutaneous nociceptor nerve endings, effectively making them unresponsive to stimuli that normally cause pain and resulting in significant pain relief for up to three months.

Neuropathic pain is a complex and difficult to treat condition[1], and is a consequence of damage to nerves caused by a range of different diseases, medications, or surgical or traumatic injuries. It can be differentiated into peripheral neuropathic pain (PNP), which results from damage to or dysfunction of the peripheral nervous system or, less commonly, central neuropathic pain (CNP), which results from damage to or dysfunction of the central nervous system.

No definitive figures for the prevalence of the neuropathic pain exist but estimates for the percentage of the European population affected by it range from 3% to 8%.[2,3] The condition, which can last for months or years, has an adverse impact on health and quality of life, including important aspects of physical and emotional functioning such as mobility and the ability to work.[4,5] Neuropathic pain is also associated with a poorer quality of life than chronic conditions including cancer, heart failure, type 2 diabetes, Parkinson's disease and stroke.[6]

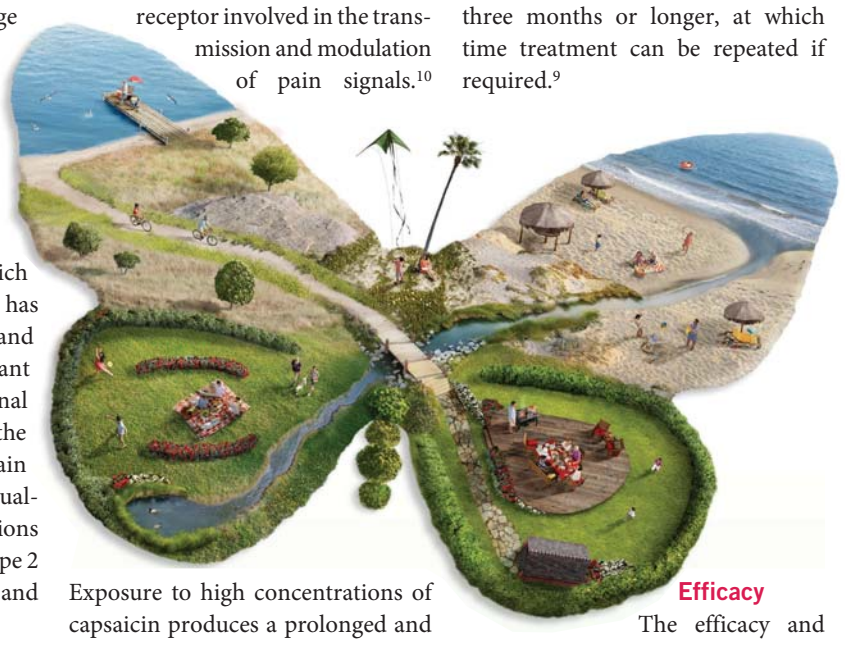
While a variety of medicines can be used to treat neuropathic pain, their use is often limited by unwanted side effects (such as sedation and dizziness) as well as drug-drug interactions, slow onset of action, the need for potentially complex titration and dosing multiple times a day.[7] Research suggests that two-thirds of patients do not achieve adequate pain relief with current treatment options.[8]

Introduction to QUTENZA

QUTENZA is an advanced dermal application system designed to deliver prolonged pain relief directly to the source of peripheral neuropathic pain while avoiding the problems of systemic treatments, such as unwanted side effects, drug-drug interactions and addictive potential. QUTENZA is approved by the European Medicines Agency (EMA) for the treatment of peripheral neuropathic pain in non-diabetic adults either alone or in combination with other medicinal products for pain. This approval followed an EMA review of data from the comprehensive QUTENZA clinical trial programme.[9] The product is already available in several European countries and launches in additional countries will take place over the coming months.

Mechanism of action of capsaicin

QUTENZA enables rapid delivery of high-dose capsaicin directly to the hyperactive pain receptors (nociceptors) that are the source of neuropathic pain. Capsaicin, a substance found in chilli peppers, is a highly selective agonist for Transient Receptor Potential Vanilloid 1 (TRPV1), which has been identified as a key receptor involved in the transmission and modulation of pain signals.[10]



Exposure to high concentrations of capsaicin produces a prolonged and reversible defunctionalisation of hyperactive nociceptors, effectively making them unresponsive to stimuli that normally cause pain.[11] Exposure to high concentration capsaicin does not permanently alter nociceptors and function returns naturally with time. Low dose capsaicin (0.075%) when applied topically as a cream also activates the TRPV1 receptors. However, nociceptor defunctionalisation can only be achieved with repeated exposure to capsaicin, meaning that the capsaicin cream must be applied three-to-five times daily for up to six weeks before significant pain relief is achieved. These creams are inconvenient to apply, are associated with a burning sensation on each application and may lead to contamination of sensitive areas of the body (e.g. eyes or mucous membranes), which may result in poor patient compliance.[11]

Administration

QUTENZA is designed to be administered by a physician or by a health care professional under the supervision of a physician. The high concentration capsaicin contained in QUTENZA is delivered to the site of pain via a microreservoir monolithic dermal patch. QUTENZA is in the form of a thin transparent film with a protective backing layer, which can be cut to size for easy application to hands, feet and other parts of the body. After pre-treating the painful area with a local anaesthetic to minimise any treatment-related discomfort, QUTENZA is applied to the area of pain and left in place for either 30 minutes (when used on the feet) or one hour (when used elsewhere on the body).[9]

Each application of QUTENZA can provide pain relief for up to three months or longer, at which time treatment can be repeated if required.[9]

Efficacy

The efficacy and safety of QUTENZA has been investigated in a comprehensive clinical trial programme involving 1327 patients who received at least one QUTENZA application.[9]

QUTENZA has been shown to significantly reduce neuropathic pain caused by both post-herpetic neuralgia and HIV-associated neuropathy.[7,9] Pain relief with QUTENZA is rapid in onset and long-lasting following a single application. Forty four percent of patients with post-herpetic neuropathic pain (PHN) treated with QUTENZA reported ≥30% decrease in neuropathic pain.[7] In the same study, twelve weeks post treatment, 55% of patients treated with QUTENZA still reported improvement in pain.[7] Reductions in pain were achieved with QUTENZA treatment when used as monotherapy or in combination with other treatments.[7]

Safety and tolerability

The only commonly reported side effects with QUTENZA are transient and related to the QUTENZA application procedure.[7,9,12,13] A very common side effect is application site discomfort, which is usually mild to moderate in intensity and resolves within seven days.[7,9,14]

Because QUTENZA acts topically to reduce pain, systemic absorption of capsaicin is minimal and it is not associated with side effects such as sedation and dizziness that may be experienced with other treatments currently prescribed for neuropathic pain.[9] QUTENZA has no known drug-drug interactions (no formal interaction studies with other medicinal products have been performed as only transient low levels of systemic absorption have been shown to occur with QUTENZA).[9] Lack of drug-drug interactions is important for this patient population as neuropathic pain can be caused by underlying conditions which require ongoing treatment. In addition, research suggests that people living with neuropathic pain are in poorer health and more likely to suffer from chronic comorbidities including osteoarthritis, depression and coronary heart disease.[14]

Patient benefits

For patients, QUTENZA offers the possibility of lasting and effective pain reduction with limited side effects and the convenience of application once every three months. Since conventional treatments can only offer a compromise between pain relief and the burden of medication, QUTENZA provides a new option for patients seeking relief from this chronic and debilitating condition.

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DETAILS OF THE EVENT

Friday 23 September 2011
12.15–13.45 (lunch provided)
Hall G2

SATELLITE SYMPOSIUM

Revealing the need for a new approach to neuropathic pain

Chaired by Prof. Dr med. Rolf-Detlef Treede

12.15–12.20
Welcome and introduction
Prof. Dr med. Rolf-Detlef Treede (Chair)

12.20–12.30
Layers of suffering: Key challenges in the management of peripheral neuropathic pain
Dr Albert van Wijck

12.30–12.40
Lifting the burden of disease: The science behind QUTENZA in the management of peripheral neuropathic pain
Prof. Dr med. Rolf-Detlef Treede

12.40–13.20
A tale of three cities: Uncovering the real world evidence for a new approach
Dr Uwe Kern, Dr Concepción Pérez, Dr Albert van Wijck

13.20–13.45
Getting beneath the skin of difficult clinical cases
Faculty discussion led by
Prof. Dr med. Rolf-Detlef Treede

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