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# MIGRAINE

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# NEWS

Patient focused, research driven

THE JOURNAL OF

the  
**migraine**  
trust

Special EHMTIC edition



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A registered charity in England and Wales  
(no. 1081300) and Scotland (no. SC042911)

The Migraine Trust was founded in 1965  
primarily to promote medical research into  
migraine.

#### Currently The Migraine Trust:

- Provides a comprehensive information service to the general public, health professionals, employers and the media. We have a comprehensive website and produce a journal called Migraine News
- Holds workshops and courses for GPs, nurses, health professionals and the general public
- Jointly holds the European Headache and Migraine Trust International Congress (EHMTIC) every two years for leading experts in migraine from all over the world to meet and exchange research results and ideas
- Funds research, fellowships and studentships in hospitals and universities.

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## LETTER FROM THE CHIEF EXECUTIVE

Photo credit: Wellcome Library London



### Dear Readers,

**Happy New Year and welcome to this edition of Migraine News.**

This year marks a special anniversary for The Migraine Trust as the charity was founded 50 years ago in 1965. It is a time for us to reflect on what the charity has achieved and what our focus needs to be going forward. We have created a dedicated area on our website that we invite you to visit for further information as well as opportunities to get involved ([migrainetrust.org/50-years](http://migrainetrust.org/50-years)).

In the previous edition of Migraine News we wrote about migraine research being

at the heart of The Migraine Trust's work. Funding and promoting research was in fact the primary reason for the charity's creation in 1965. In more recent years, migraine research in the UK has suffered from a lack of interest and support, but we were keen to halt the decline and with your help we are gradually improving the situation.

Our fundraising appeals in 2013 and 2014 that specifically sought funds towards The Migraine Trust's research programme have to date raised a combined total of over £57,000. Thank you to everyone who contributed to these appeals and to the many individuals who continue to support our work with regular donations. Your generosity makes all the difference and has helped us to fund both a Research Fellow and a Clinical Training Fellow.

The Migraine Trust is so passionate about research being the key to a better quality of life for people with migraine that, to mark our 50th anniversary, we have set the ambitious goal of finding a cure for migraine within 25 years. Yes we have made progress in understanding migraine and developed treatments such as triptans - but it is not enough. Migraine research still needs much more investment so that we can significantly increase the numbers of researchers involved.

There are still far too many people struggling to live with this misunderstood, debilitating and often disabling condition. We will continue to lobby the government to fund migraine research, but in the meantime we seek to build the momentum and expand our programme. Finding a cure within just one generation is achievable – if we can substantially increase research funding.

Research is indeed the focus for this issue of Migraine News. The 4th European Headache and Migraine Trust International Congress (EHMTIC) took place in Copenhagen, Denmark from 18-21 September 2014 and I had pleasure in attending along with a number of our Trustees and our Research Fellows. Over the coming pages we will share with you a roundup of news from the Congress to update you on current worldwide research.

With best wishes for 2015.

A handwritten signature in black ink that reads "Wendy". The signature is written in a cursive, flowing style.

**Wendy Thomas**  
Chief Executive

## Neurological Alliance calls for further review of neurology services

In November last year our Chief Executive, Wendy Thomas, co-signed a letter to members of the House of Commons Public Accounts Committee calling for a further review of neurological services.

The letter, organised by the Neurological Alliance and co-signed by 27 organisations working in the field of neurological conditions, sets out ongoing issues affecting neurological services and calls on the Committee to pursue its previous recommendation made in 2012 of a follow-up progress review of neurology in 2014-15.

Services for people with neurological conditions, such as migraine, continue to be neglected by the health service. Whilst there have been some significant improvements, there is much more to do in order to meet the needs of people with neurological conditions. To see a copy of the letter please visit [bit.ly/neuroreview](http://bit.ly/neuroreview).

## Prescription Charges Coalition responds to plans to strengthen policing of prescription exemption claims

The Department of Health is planning to tighten control on claims for exemption from prescription charges. The news was widely circulated by the media over the Christmas and New Year period.

In response, the Prescription Charges Coalition, of which The Migraine Trust is a member, said that the system of prescription charge exemption in England is confusing for people with long term conditions and the recent clamp down proposal on incorrect claims will cause more hardship. It will result in anxiety and deter people from collecting essential medications. To read the full position statement please go to [migrainetrust.org/news](http://migrainetrust.org/news)

## Nasal spray migraine treatment research



Researchers at the Roseman University of Health Sciences in the USA believe that prochlorperazine, an anti-nausea medication already available in tablet and injection form, could provide better pain relief than other medications currently used to treat migraine symptoms. They suggest that a nasal spray version of prochlorperazine would not only be effective, but fast acting and more patient-friendly as nasal sprays tend to have fewer side effects than oral alternatives. Details of the new research were presented at the 2014 American Association of Pharmaceutical Scientists (AAPS) Annual Meeting and Exposition, held in San Diego from 2-6 November. The next stage of this research is to test the safety and efficacy of the nasal spray.

## Obituary – Professor Merton Sandler

Professor Merton Sandler, one of the pioneers of modern neuropharmacology, died on 24 August 2014 at the age of 88. After serving in the Army and at the Royal Free Hospital as a junior pathologist, he was appointed first as Consultant Chemical Pathologist at Queen Charlotte's Hospital, and from 1973 until 1991 he was Professor of Chemical Pathology at the University of London's Royal Postgraduate Medical School Institute of Obstetrics and Gynaecology. Throughout his time at Queen Charlotte's Hospital he led a 20-strong team of laboratory and clinical researchers. Over many years he did very influential work on post-natal depression, alcoholism, schizophrenia and Parkinson's disease as well as on headache and migraine.

For the full obituary please see [migrainetrust.org/news](http://migrainetrust.org/news)

## A new approach to migraine management



Last year we reported that Curelator Inc. is working with The Migraine Trust during development of Curelator's new approach to migraine management, called Curelator Headache™. This novel digital platform (website and app) aims to allow people with migraine to quickly and scientifically find out which triggers and other factors might cause or prevent their migraine attacks and guide them to make changes that could help manage their migraine more effectively.

Since then more than 500 people have signed up to test Curelator Headache and the first users will soon start receiving their personal Trigger Maps™. Based on feedback from these users, Curelator Inc. recently upgraded their product to make it even easier to register and use Curelator Headache.

Curelator is now looking for more people to try Curelator Headache: if you sign up before **15th March 2015** there will be **no charge for** using it and, when enough daily information has been entered, for receiving your Individual Trigger Map, showing you triggers associated with your attacks. You can find out more, and watch a short introductory video, at the website: [curelator.com](http://curelator.com)

To register now for free use of Curelator Headache go to: [curelator.com/studies](http://curelator.com/studies)

**Please note** that, at this time, you would need use of an iPhone or iPad as it is currently only available on iOS. Curelator will make an introductory offer to Android users when the Android version is available.



## European Headache and Migraine Trust International Congress (EHMTIC)

The European Headache and Migraine Trust International Congress (EHMTIC) was held on the 18th to 21st September 2014 in Copenhagen, Denmark. EHMTIC is the opportunity for doctors and other health professionals, researchers and medical students, to hear about the latest headache research, new treatments and to attend training programmes.

EHMTIC 2014 was attended by more than 1,000 delegates, whilst the session for members of the public was organised by four Danish Headache Societies and over 100 people attended.

EHMTIC started on the morning of Thursday 18th September with teaching courses on: headache diagnosis in general practice; patients with primary headache and facial pain; diagnostic tools in practise; management of migraine and medication overuse headache; management of non-migraine headaches and trigeminal neuralgia; trigeminal autonomic headaches (such as cluster headache); secondary facial pain and uncommon headaches. Teaching courses also included a basic science migraine

course with the title 'The road to a new era in migraine research'.

The day finished with the opening ceremony and Macdonald Critchley Lecture. Dr Macdonald Critchley, (2 February 1900 – 15 October 1997) was an internationally known neurologist who helped form The Migraine Trust and was its founding Chairman.

Friday 19th started with a lecture entitled 'Headache Therapy – Where After Medicines?'. Two poster discussions followed: on Genes and Environment, and Non-Migraine Headache. A lecture on the biological function of the pain genes, and a lecture on interesting headache cases finished the day.

Saturday 20th began with lectures on Neuromodulation in Chronic Headache including: 'What is Medically Intractable Chronic Headache?' and 'Mechanisms of Action and Future Perspectives on Neuromodulation', followed by The Migraine Trust lecture given by J. Olesen entitled 'CGRP [calcitonin gene related peptide] Past Present and Future'. Poster discussions followed: on the human science of migraine and headache; the Optimization of Headache Services; Headache Care; Basic Science; Relevance of the Multidisciplinary Team.

The afternoon included a meeting of the International Forum of Headache Nurses.

Sunday 21st started with a breakfast symposium on Headache Management, followed by a lecture on the subject of Controversies in Headache, then a poster discussion on Migraine Therapy and a talk on paediatric (child) headache. The Enrico Greppi Award was given to Professor Anne MacGregor for her work on the genetics of menstrual migraine (more information about this research on page 14). The morning finished with a lecture on cluster headache, the presentation of awards and the Closing Ceremony.

The afternoon of Sunday 21st was devoted to an event for members of the public with headache conditions, or an interest in headache conditions, to hear from expert researchers about new knowledge in the field.

We are fortunate that doctors at the conference have written an account of the papers presented for inclusion in Migraine News.

# New outcomes from preclinical research in migraine

by Ms Margarida Martins Oliveira

**Ms Margarida Martins Oliveira describes new research into migraine looking at what causes migraine symptoms and opportunities to develop new treatment.**

At the centre of migraine preclinical research (preclinical research is a stage of research before clinical trials - testing in humans - can begin), and besides the important headache pain phase, there is the complex and exquisite premonitory (or warning) phase of the attack. Recently, it was shown that the hypothalamus, a brain area with a prominent role in fatigue, thirst, appetite and sleep control, is active in the early phase of a migraine attack. Therefore, this new exciting data prompted scientists to investigate how the hypothalamus might lead to the activation of the brain's pain pathway and the generation of the migraine headache attack. For example, studies by Andreou et al. on specific parts of the hypothalamus (such as the AI1 nucleus) showed a significant involvement in the pathophysiology of migraine. In addition, findings on specific hypothalamic neuropeptides that convey information between hypothalamic and extra-hypothalamic neurons (such as neuropeptide Y) demonstrate a link between the potential origin of disturbed feeding and sleep regulation in migraine, as reported by Martins-Oliveira and colleagues.

Furthermore, new scientific techniques that have been used to study other major neurological conditions are now

being used in the laboratory to study migraine. A great example of this is the use of optogenetics and the study by Baca et al. of cortical spreading depression (CSD; slowly propagating wave of neuronal inhibition) in animals, considered to be the neurophysiological correlate of the migraine aura in humans. Optogenetics was recently developed and uses light with a specific wavelength to control neurons that have been genetically sensitized to light.

Indeed, CSD is one of the most widely used animal models of migraine and this was no exception at the EHMTIC 2014 presentations. Specifically, a study by Filiz et al. using CGRP receptor (increased levels of CGRP have been reported in migraine patients) antagonists showed attenuated CSD pain- and anxiety-related behaviours. Hansrivijit and colleagues reported that CSD impairs memory processes (amnesia is actually manifested by some chronic migraine patients) by possibly disrupting glutamate (important neurotransmitter) actions. Interestingly, a study by Suprongsinchai et al. demonstrated that acute harmful stimuli can facilitate the development of CSD regardless of where the painful stimulus was applied. In clinical studies, on the other hand, infusion of the nitric oxide (NO) donor, glyceryl trinitrate (GTN), provokes a delayed (4 to 6 hours after) migraine-like attack in migraineurs. Therefore, this method is likewise used in basic studies to investigate migraine pathophysiology. One study performed by Hougaard and colleagues in Denmark showed that GTN caused significant inflammatory

responses on the dural membrane 30 minutes to at least 6 hours after infusion, which might explain the delayed migraine-like attack when given to migraine patient research volunteers. These results aim to support one of the proposed theories that migraine pain may originate from inflammation of the meninges, particularly the dural membranes that surround the brain. However, the cause of migraine pain is still controversial, as recent basic and clinical studies point to a central nervous system origin of the migraine attack.

Regarding potential therapeutic options for migraine under basic research, a study performed by Greco and colleagues in Italy, using URB937 (a peripheral fatty acid amide hydrolase inhibitor that plays a role in the endocannabinoid biological system), which is known to induce relief in animal models of pain, reported a significantly reduced neuronal activation in areas responsible for the migraine attack in the animal models of migraine.

In summary, the latest studies presented at the EHMTIC 2014 proved that basic research still has a lot to overcome but seems to be on the right track in order to provide a better knowledge of the complex pathophysiology of migraine and optimize pharmacological treatment.

## New clinical investigations on the pathophysiology of headaches

by Dr Marta Vila

A crucial issue covered by presentations at the EHMTIC 2014 has been the clinical investigations of the pathophysiology [disordered physiological processes associated with a disorder] of headache. Several interesting studies analysed different subtypes of headache using various approaches. Results from these studies are presented here according to the type of headache: headache in general, migraine and cluster headache.

### Pathophysiology of headache

Studies with healthy volunteers (people **without** headache disorders)

Studies performed with volunteers without headache disorders are able to determine whether potential triggers and provokers of headache have the same effect in people who do not have a headache disorder, as for those that do have headache disorders. It is worth noting that recruiting such healthy volunteers is usually harder than recruiting patients who do suffer from the disorder.

Arngrim and colleagues used acetazolamide, a drug that causes dilation of cerebral small arteries and may be used to treat glaucoma, epileptic seizure, and altitude sickness, in healthy volunteers and were able to show that this drug induces both immediate and delayed headache in people who do not usually suffer headache, and also dilation of intracranial arteries.

Two studies by Baschi and colleagues, and by Naegel and colleagues, analysed the effects of activating and inhibiting the cortex of the brain (outer layer of neural tissue) with the application of direct current over the scalp. Using this method, they were able to show how the volunteers had a lower response to pain caused by heat, which is of interest for preventing migraine in patients.

### New methodologies in headache research

Researchers aimed to find better methods to study or to treat headache, a field that is crucial to improve the quality of life of patients. Schulte and colleagues studied a part of the brain called the brainstem, which is involved in processing and modulating pain and is thought to be implicated in various headache disorders. Compared to previous studies, they used better quality brain imaging techniques which allowed them to better analyse the brainstem, concluding that this technique would be very useful to study the mechanisms involved in headache. Voitcovschi-Iosob and colleagues developed a standardised protocol based on a different technique, called infrared thermography, to evaluate the localization and lateralization of pain. Göbel and colleagues described a new computer-based imaging method to improve a neuromodulation technique based on stimulating the occipital nerve. Occipital nerve stimulation is used as a preventive treatment of migraine and cluster headache patient and this computer-based technique has already been proven to be effective in the treatment of other pain disorders.

## Pathophysiology of migraine

The vast majority of the studies presented at EHMTIC were based on the study of migraine. A study by Shapiro and colleagues analysed factors in the sociological perception of persons with migraine, concluding that the stigma towards migraineurs increases with work absenteeism although gender is not an influencing factor.

It is known that a positive family history of migraine increases the individual's risk of suffering migraine. Coppola and colleagues tested the idea that migraine patients process information in the cortex of their brain (this is the outer region of the brain) in a different way depending on whether they had relatives with migraine or not. Their results suggested that patients with a positive family history of migraine had a reduced response of the cortex of the brain to visual information.

Two different studies examined the differences in the brain in two periods: during a migraine attack and between two attacks. Coppola and colleagues reported that there exist differences between both periods. Their results indicate that these differences are related to changes in the grey matter of some areas of the brain that are important for multisensory integration and memory processing. However, in contrast, results from a study by Uglem and colleagues reported no differences in the excitability of the cortex of the brain in these two periods. Ruiz and colleagues studied the differences in pressure-like head pain in patients with one-sided or two-sided migraine pain, but without finding differences between either group.

Another study included 47 migraine patients and 43 subjects without migraine to assess whether the presence of depression, anxiety, stress and the level of quality of life was different in migraineurs when compared to those without migraine. Thirty per cent of the migraine patients presented some of these symptoms, especially depression, which in turn contributes to the worsening of their quality of life. In

the same study, Majláth and colleagues aimed to determine if these differences were due to a specific molecular mechanism, however they were unable to confirm this.

Interestingly, there was one study, carried out by Messina and colleagues, which explored the presence of abnormalities in the white matter of paediatric (child) patients compared to those without migraine. Their positive results might be explained by a hyperexcitability of the brain in migraine patients.

Razeghi Jahromi and colleagues studied the relation between the body fat composition and the likelihood of suffering migraine. They recruited 1510 women who were diagnosed with migraine and whose body fat was determined by analysing different parameters. They concluded that lower levels of fat in the body could be protective in relation to a predisposition to migraine. Another study, performed by Di Lorenzo and colleagues, studied the effects of administering a ketogenic diet in migraine. The results of this study suggest that a ketogenic diet could be a promising preventive therapeutic option for migraine.

## Migraine with aura

Approximately one third of migraineurs experience migraine aura. The aura is a stage that usually precedes the headache and that includes a wide range of neurological symptoms, most commonly, visual symptoms.

Wang and colleagues examined if there were differences in some areas of the brain that are involved in the modulation of the visual system between migraine with and without aura. They were able to show the existence of differences in the brain region involved in the generation of auras.

Another study, performed by Hougaard and colleagues, aimed to determine if patients with migraine aura had differences in the connectivity of their brain when compared to people without migraine. Their results indicated no differences in the brain connectivity of these patients.





## Brain activity induced by visual stimuli

Five different studies presented at EHMTIC were based on the analysis of the brain activity induced by visual stimuli in migraineurs. Amrosini and colleagues analysed the response of migraineurs to visual stimuli between attacks. They recorded the brain activity induced by visual stimuli in 22 volunteers without migraine, 23 migraineurs without aura and 21 migraineurs with aura between attacks, and 24 patients during an attack. Their results showed that, between attacks, migraineurs have a different brain activity induced by visual stimuli compared to people without migraine and to patients during an attack.

In a different study, Coppola and colleagues examined the brain activity after exposure to high intensity light in 43 migraine patients and 14 volunteers without migraine. They were able to determine that, under the influence of an imminent attack, migraine patients show an alteration of brain activity when compared to people without migraine.

Magis and colleagues presented their work where brain activity was

analysed in a group of 37 migraineurs with and without exposure to a visual stimuli. Interestingly, they showed that between attacks the cortex of the brain of migraineurs is less preactivated than during the attacks.

## Episodic migraine

Episodic migraine is a subtype of migraine defined when headaches are present on fewer than 15 days per month.

Oliveira and colleagues performed a study in a group of 24 patients with episodic migraine and 24 volunteers without migraine. Their objective was to determine if there were differences in the concentration of a molecule called anandamide after performing aerobic exercise training between both groups. Anandamide is a molecule that is involved in the endocannabinoid system (a pain inhibitory system in the brain) which, it has been suggested, may be dysfunctional in migraine. Their results showed that the levels of this molecule were reduced in volunteers without migraine after performing the training, but not in migraineurs. These results could confirm the hypothesis of a dysfunction of the endocannabinoid system in migraine.

Another study focused on episodic migraine was conducted by Chai and colleagues. In this work, they studied the levels of two different molecules (adiponectin and leptin) that are involved in inflammation processes in two different situations: before and after treatment with acute abortive drugs sumatriptan and naproxen. Their results indicated that adiponectin, but not leptin, was modulated by this treatment in episodic migraineurs.

## Chronic migraine

Chronic migraine is defined when headaches occur on 15 or more days per month for more than three months. However, there exist some discrepancies related to this classification. A study presented at EHMTIC by Pozo-Rosich and colleagues is an example of it. In this work they separated migraine patients into three different groups, according to the frequency of their attacks: low-frequency migraine (0-9 days per month), high-frequency migraine (10-14 days per month) and chronic migraine (15 days or more per month) and analysed and compared their clinical characteristics. Their results allow them to conclude that the high-frequency migraine and the chronic

migraine groups have the same clinical characteristics and differ only in the frequency and the duration of the attacks, suggesting that both groups should be studied together.

Yu and colleagues analysed if the chronification of migraine was related to changes of brain grey matter volume. They studied 60 patients with chronic migraine (44 with medication over-use headache and 16 without), 18 patients with episodic migraine and 32 volunteers without migraine, and found differences in some brain structures that could be related to migraine chronification.

In work presented by Cady and colleagues, a local anaesthetic called bupivacaine was administered to 41 patients with chronic migraine. Their objective was to block the sphenopalatine ganglion, also called the nasal ganglion due to its close proximity to the nose. A ganglion is a nerve cell cluster or a group of nerve cell bodies located in the peripheral nervous system. The sphenopalatine or nasal ganglion has been implicated in migraine mechanisms. Their results suggested that the long-term administration of this anaesthetic reduced the number of days of headache and improved the quality of life of migraine patients.

An important issue that is constantly researched in the study of migraine is for a predictor of the efficacy of a specific treatment for each patient. The aim is to know if a treatment will be effective for a particular migraineur before starting it. With this objective, Cernuda-Morellón and colleagues studied whether two molecules that have been implicated in migraine (called CGRP or calcitonin gene related peptide and VIP or vasoactive intestinal peptide) could be used to predict the efficacy of onabotulinumtoxinA, commonly known as Botox. They compared the levels of these two molecules in chronic migraine patients according to their positive- or non-response to the treatment. They found that the levels of both molecules between attacks, especially of CGRP, helped to predict the response to onabotulinumtoxinA.

## Pathophysiology of cluster headache

Cluster headaches are attacks of excruciating pain in one side of the head, often localised behind the eye, that begin unexpectedly. They are more painful and debilitating than other types of headache. There were some studies presented at EHMTIC that aimed to better describe this condition.

Two of these studies analysed specific treatments for cluster headache. In one study, Bratbak and colleagues injected onabotulinumtoxinA in 10 patients with cluster headache to explore the safety aspects and therapeutic potential of this drug. They presented positive preliminary results obtained with the first 5 patients, suggesting that further studies with more patients should be performed.

In another study, Miller and colleagues treated 4 patients with cluster headache by stimulating an area of the brain called the posterior hypothalamic region, which has been implicated in this condition. Their results indicate that this treatment may be useful in cluster headache patients, but that further studies are needed.

Three interesting studies had the objective of a better characterization of cluster headache. One study, conducted

by Cosentino and colleagues, compared the excitability of the cortex of the brain of 25 patients with cluster headache with 13 volunteers without cluster headache. They concluded that cluster headache patients show an increased cortical excitability during and between attacks. Due to the connection of cluster headache and sleep, Barloese and colleagues investigated sleep in 40 cluster headache patients and 25 volunteers without cluster headache. Their results showed differences between the two groups in some of the parameters analysed during the different sleep phases. Their results indicated a role of a brain nucleus called hypothalamus and of the arousal systems in cluster headache. Related to these results, the same authors investigated for the first time the levels of a molecule called hypocretin (also called orexin) in 26 patients with cluster headache while having an attack, and 27 volunteers without cluster headache. The interest in this molecule for cluster headache is based on the fact that it is produced in the hypothalamus and it is involved in the regulation of arousal and pain. The results of these analysis indicated that the levels of hypocretin are lower in cluster headache patients, showing again a relation between the hypothalamus and cluster headache.



# Migraine & genetics

by Dr WPJ van Oosterhout

**Dr van Oosterhout explains DNA and genes, how some people can have a predisposition for certain health conditions such as migraine, and how new research in this area hopefully will lead to new anti-migraine treatments.**

Migraine is a brain disorder, characterised by attacks of headache. Clinically, migraine is divided into two main subtypes that are based on the presence or absence of an aura: migraine without aura, and migraine with aura. Over the past years, scientific studies have shown the importance of genetic factors, the DNA, in why some people have migraine attacks and others not. Slight changes in the DNA can also predispose for different conditions, including migraine. Genetics appear to play an important role in migraine. Many patients have first-degree relatives who also suffer from migraine. Family studies have shown that indeed relatives of migraine without aura patients have almost double the risk of getting migraine themselves. Here, I will try to discuss the role of these genetic factors in migraine and give an update on the new studies into migraine and genetics that were presented at EHMTIC 2014.

## What is genetics?

The base of genetics is formed by DNA, deoxyribonucleic acid. This is a molecule that encodes the genetic instructions used in the development and functioning of all known living organisms and many

viruses. In the nucleus of every cell, DNA is organised into long structures called chromosomes, in a total of 23 paired chromosomes in every human cell.

The biological information is coded by molecules known as nucleobases. It is the sequence of the four different types of nucleobases that actually encodes the information. This is called the genetic code. A strand of nucleobases that codes for a protein with a specific function, is called a gene. These proteins are derived from the DNA via a complex molecular reading and translating system in the cell. Humans have approximately 24,000 genes in their DNA, few more than a chimpanzee or a mouse. More surprisingly, scientists discovered that large parts of our DNA do not code for genes.

## Changes in the DNA

Several types of differences or changes in the DNA can occur that are linked to or can predispose individuals for a certain disease.

A mutation is a permanent change in the nucleobase sequence. Mutations result from unrepaired damage to the DNA, errors in replicating the DNA or from insertion or deletion of a part of the DNA. Mutations in the DNA are passed to the offspring. Mutations in genes can either have no effect on the functioning of the cell, alter the product of the gene, or prevent the gene from functioning properly or completely. Mutations are therefore only found in the DNA of

patients, not in healthy controls (people who don't have the health condition in question).

A single-nucleotide polymorphism (SNP) is a DNA variation occurring commonly within a population (~1%) in which a single nucleobase differs between people or between the two paired chromosomes in every cell within one individual. Specific SNPs can occur both in patients and in healthy individuals and be linked to having a higher risk for a certain disease. Within the DNA, SNPs may fall within genes, or between genes, and can affect how the cell functions.

Variations in the DNA sequences of humans can affect how humans develop diseases and respond to pathogens, chemicals, drugs, vaccines and other agents. However, their greatest importance in biomedical research is for comparing regions of the genome between groups of people with and without a certain disease. Also in migraine, SNPs have been studied using genome-wide association studies (GWAS). In these studies the whole DNA of patients is screened against the DNA of healthy volunteers for potential changes in their DNA.

## Genetics in migraine with and without aura

In the most common forms of migraine, migraine with and without aura, there is not a single mutation responsible for the

condition. It is the combination of genetic susceptibility (= variability in the DNA, caused by multiple genetic factors each with a small effect) and environmental factors that means that some individuals get migraine and others do not. Since the disease is not caused by a single mutation in a single gene (in contrast to familial hemiplegic migraine, a rare type of migraine with aura, where single mutations have been identified in three different genes) but might be linked with broad genetic variability (as measured by the so-called polymorphism in SNPs), a different scientific approach needs to be used to look into the genetics of these common migraine subtypes.

This different scientific approach is known as genome-wide association studies (GWAS). For GWAS in migraine, large groups (well over a thousand migraine patients and non-headache controls or people without headache conditions) are needed. In GWAS, DNA from blood samples from patients and controls is compared to detect genetic factors (SNPs) that are associated with an increased chance of having migraine. Recently, analyses of international GWAS studies performed in migraine using DNA samples from over tens of thousands of individuals have identified multiple SNPs. These SNPs might be involved in several different cellular processes, so-called pathways.

At the latest EHMTIC, several investigators presented new data on recently discovered polymorphisms in SNPs associated with migraine. Dr. A. Esserlind and colleagues discussed their data on differences in genetic variability between patients with severe and mild migraine. Barbanti and colleagues reported on an association between signs of oxidative stress (SOD1 and SOD2 genes) and migraine, whereas F. Haghdoost and colleagues showed promising data from a cohort of Iranian migraine patients on a gene that is known as a predictor for coronary heart disease. Two groups (A. Sergeev and colleagues; K. Skorobogatikh and colleagues) reported on genetic variability in genes that are involved in dopamine, a hormone and neurotransmitter that is an important messenger molecule

in the brain. Many more ongoing and future studies are needed to clarify the exact importance of all the genetic variability that has been reported. As it is of utmost importance to compare large cohorts of patients, the already ongoing international cooperation in this field will be continued.

## Is there more than genetics?

Recent developments in science have enabled researchers to not only look into the genetic material, the DNA, itself, but also in other interesting mechanisms that are involved in the process from DNA to how a cell functions.

One of them is the so-called transcriptome. This is the set of all messenger molecules in a cell that intermediate between the genetic material and the end product of a gene, i.e. the protein that has a specific function in the cell. Using different complex techniques, this transcriptome can be measured and compared between patients with and without migraine. At EHMTIC 2014, A. Oterino and colleagues presented data on differences in the transcriptome between patients with migraine with aura and non-headache controls. As this is a complex and developing field, more studies are needed to correctly interpret all these findings.

Another very interesting field of research is epigenetics. Epigenetics (epi = over, outside, around) focusses not on the DNA itself, but it studies heritable changes that are not caused by the DNA sequence, but rather how the genetic material itself is wrapped within the cell. How the DNA is packed and compacted depends on several factors. Active DNA, which means DNA from which proteins are being made, is organised from different in-active DNA. Furthermore, the environment around and in the cell affects the way the DNA is organised. For example, malnutrition or stress induces a different epigenetic signature.

Important mechanisms in epigenetics are DNA methylation and histone modification. DNA methylation means that an extra molecule is added to the

genetic material, thereby impeding the use of that specific area of DNA. It also helps in keeping the inactive DNA in a compact form. Histones are little protein balls in the nucleus of the cell and they act as spools around which DNA coils. This enables very efficient compaction of the DNA, necessary to fit the large amount of genetic material inside the cell nucleus. The compacted DNA molecule is 40,000 times shorter than an unpacked molecule! Several histone modifications (= changes) exist, that each alter the way the DNA is compacted in a slightly different way and thereby change how genes are used.

In migraine, epigenetics is considered a promising new avenue. Researchers hope that epigenetic mechanism may explain how non-genetic factor such as female sex hormones, stress hormones and inflammation triggers may modulate for example migraine attack frequency. Developing drugs that specifically target these mechanisms may bring new prophylactic treatment in the future.

Not only the genetic material, the DNA itself, is important in understanding how the DNA determines how a cell, and thus the human body, functions. Also other factors such as the transcriptome and the way the DNA is compacted in each cell are relevant.

## Into the future!

To conclude, genetic factors are important in migraine. This includes on one hand the changes in the DNA that directly cause the disease (so-called mutations) or are associated with a higher risk of getting it (polymorphism; SNPs). On the other hand, both the messenger molecules and the way the DNA is compacted in each cell affect how certain genes function. At EHMTIC 2014 meeting preliminary research promises to combine these different approaches, and bring more insights in how migraine attacks start, and hopefully this will lead to new anti-migraine drugs.

# Enrico Greppi Award

Professor Anne MacGregor was awarded the Enrico Greppi Award at the 2014 European Headache and Migraine Trust International Congress (EHMTIC) for her research on the genetics of menstrual migraine which was part funded by The Migraine Trust.

Menstrual migraine encompasses pure menstrual migraine and menstrually-related migraine which have been recognised as subtypes of migraine without aura in the International Classification of Headache Disorders (a classification system to help to standardise headache research). Pure menstrual migraine is diagnosed when a woman has a diagnosis of migraine without aura and confirms that migraine attacks occur within the two days before her period starts or within the first few days of bleeding (days -2 to +2 of the cycle) and at no other time of the month. This coincides with the phase of the menstrual cycle when the concentrations of the hormones oestrogen and progesterone fall to their lowest levels. Menstrually related migraine has the same characteristics as pure menstrual migraine but attacks occur additionally at other times of the cycle.

Hormonal fluctuations throughout a woman's life may contribute to the cause of menstrual migraine. Menstrual migraine has been linked to the fluctuations in oestrogen levels that occur naturally during the menstrual cycle. The drop in oestrogen is thought to be an important trigger in menstrual migraine which was first suggested in 1972 as the 'oestrogen withdrawal' theory.



## // In this study, the researchers investigated genetic variants in 14 genes in a population of women with menstrual migraine matched with women without migraine //

Different genetic variants have already been identified in migraine. Three genes have been identified in studies of individuals with familial hemiplegic migraine, a type of migraine with aura. Other genes have been associated with migraine recently in Genome Wide Association Scan studies (GWAS) in common migraine populations. In addition, there are other genes with variants that have been associated with migraine without aura and these represent special concern for researchers into menstrual migraine, due to their role in hormonal processes. However results from these studies have been contradictory and they need to be replicated in different populations. In particular, it is unclear as to the effect of these genes in different migraine subtypes, including menstrual migraine. In this study, the researchers investigated genetic variants in 14 genes in a population of women with menstrual migraine matched with women without migraine.

The population who took part in this research were 437 women, recruited to the research by the City of London Migraine Clinic, including both women with pure menstrual migraine and those with menstrually related migraine. Women with no personal or family history of migraine, matched to the

women with menstrual migraine by age and ethnicity where possible, were also recruited. The diagnosis of migraine was made in accordance with the International Classification of Headache Disorders 2nd edition. Saliva and blood samples were taken, and a medical questionnaire was completed that surveyed migraine family history, symptoms, triggers, medication use and contraceptive use.

Results may indicate that migraine without aura and menstrually related migraine may have different causative genes, and showed genes that are associated with menstrually related migraine in the population taking part in the research.

The researchers showed a correlation of four expressed genes in patients with pure menstrual migraine or menstrually related migraine. Further studies should be focused on the validation of these results in larger populations with more collection timepoints for blood samples, and on the understanding of protein interaction in different stages of the menstrual cycle and its effect on migraine.

### Source:

Astrid J Rodriguez-Acevedo, Robert A Smith, Bishakka Roy, Heidi Sutherland, Rod A Lea, Alison Frith, E Anne MacGregor and Lyn R Griffiths 'Genetic association and gene expression studies suggest that genetic variants in the SYNE1 and TNF genes are related to menstrual migraine' The Journal of headache and pain 2014, 15:62

[www.thejournalofheadacheandpain.com/content/15/1/62](http://www.thejournalofheadacheandpain.com/content/15/1/62)

# Meet

## Professor Peter Goadsby

Director of the NIHR-Wellcome Trust King's Clinical Research Facility and Professor of Neurology, King's College London. **Trustee of The Migraine Trust**

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### 1. What first motivated you to work in neurology and then specialise in headache?

What first attracted me to neurology and particularly to be interested in headache was my mentor, Professor James Lance. I got into medicine a little bit by accident and I was floundering, looking for something that would excite me. Jim Lance gave a lecture about migraine and explained the current thinking of the time. I remember very distinctly, and he remembers me, approaching him after the lecture with a quizzical look on my face and suggesting the explanations for migraine weren't very good; he very politely pointed out to me that maybe I could help make them better by doing research. About a year and a half later I took up the challenge of doing that. What got me excited was the unique opportunity to study something that was really interesting, really troublesome and quite open in terms of there being a lot to discover. So I think it was good advice from Jim Lance and good timing at the end of the day.

### 2. When did you first get involved with The Migraine Trust and what inspired you to become a trustee?

What got me involved in The Migraine Trust and led me to be a trustee was firstly an invitation from the late Frank Clifford Rose to be involved in the scientific committee at The Migraine Trust. I was really impressed that

the Trust was leading both in patient advocacy and supporting research so I was happy to be part of the committee. Eventually Frank Rose then asked me to become a trustee and I thought it was quite a privilege really. I was very happy to join something which seemed to be exactly in line with what I wanted to do with my life.

### 3. You are a Director of EHMTIC and have been involved in attending and organising worldwide headache congresses over many years. How have they changed in that time?

Yes, I'm a Director of EHMTIC, European Headache and Migraine Trust International Congress, and I've been involved in the International Headache Society and in regional meetings for probably more than twenty years now. I think that they've changed in a few ways. They've become bigger, more engaged from a scientific dimension in terms of understanding the disorder and understanding its mechanisms, and less driven by small debates over differences between medicines, which perhaps got carried away a little bit at some point. I think there's been a really healthy trend in recent years to have more early career investigators involved in all aspects of the meetings. I also have to say that at the meetings I go to where there are patient organisations represented or involved in the following day, it's a very

**// Every time I sit down to do a clinic and someone comes in and I see that they've had such a dreadful time of it and I know that I can help, but I also know it's not perfect, I want to redouble my efforts to make things better. //**

important transition. There's no point in doing research in isolation without telling particularly those who are involved what's happening.

**4. As Director of the NIHR-Wellcome Trust Clinical Research Facility based at King's College London, what does your current role involve?**

The role involves encouraging everyone in King's Health Partners and, frankly, broadly across the NHS to be involved in translational research in everything from mental health and neurology including headache problems through to liver and renal, cardiology, dermatology, and respiratory medicine. It's a really impressive portfolio of research. What's important to me in these Clinical Research Facilities, and what's important to my Clinical Research Facility, is the reality of studying patient based problems with a real expectation that understanding of a clinical problem and better therapeutic approaches will come from those studies. So it's a very ideal job for me. I get to promote the thing that I think is really important to making change.

**5. What motivates you to continue research into migraine and other headaches?**

Why do I continue doing headache research, migraine research, research on the trigeminal autonomic cephalalgias, cluster headache in particular? Because while we've made great progress, we understand things better and our treatments are better, at the end of the day far too many people have disabling headache problems, disabling migraine, dreadful cluster headache, and there just isn't enough understood or done for them. There's

not enough treatment and there's not enough broad understanding of the disorders. So what motivates me is every time I sit down to do a clinic and someone comes in and I see that they've had such a dreadful time of it and I know that I can help, but I also know it's not perfect, I want to redouble my efforts to make things better.

**6. In your experience, what are the main barriers in headache research? What difficulties do you face?**

The biggest barrier is simply funding. If we had twice as much money we'd do four times as much work and you can work out the rest of that mathematic progression. What is the barrier to the funding? A big problem is things coming of their age, it's been difficult to study migraine and the other primary headache disorders like cluster headache. It's becoming easier and as it becomes more plausible, then our ability to use resources becomes better. Science will always be ahead of common understanding, and shall we say particularly from funders, and so it's important that we translate our understanding of the disability so that funders will understand we need more resources to do this. The biggest difficulty we face is the challenge of convincing the funders that we can do things that will make big differences to patient outcomes. We can and we will and I hope the funders listen.

**7. What do you think is behind the worldwide lack of interest in headache disorders – it seems that they are not generally taken seriously?**

I think that was generally true twenty years ago, I think it's becoming less

true. I think one of the problems is we're living the dream, we're living the change. We're living in an era when headache disorders, migraine, cluster headache, as we understand them there's a transition from an era where they were not taken seriously, and were thought of as very soft mechanistically, and we're watching that transition. It never seems fast enough, it certainly never seems fast enough to the patients and I can understand that, and it's not fast enough for me either but we're living the transition. I think the direction is the right direction it's just too slow and it's too slow really because of resources and those two things feed into each other.

**8. What developments do you think we'll see in the next five years and what are you most excited about?**

Certainly in the next five years there will be new treatments, there will be specific preventive treatments for migraine that we've never had before, and when I went to medical school weren't even thought about, so that's wonderful. We will not have treatments for everybody so we will have to continue the pursuit of new therapy. We will get a better understanding of the disorder from physiology, meaning brain imaging, and we will get a better understanding from the genetic side and we'll get a better understanding from the laboratory side because all the technologies are available now to start to ask questions about these problems and get real answers. So with a fair wind, good will and reasonable funding we'll make great progress. I have to say that one of the key things that keeps me involved in this, and I'm sure means there will be progress, is the dedication of patients and patient groups which help us with our research and so if I'd like to say anything for myself, it's thank you. Thank you for being patient that we haven't done better, thank you for helping us with what we've done and thank you for the things you will do in the future to help us make it better. **Thank you.**

# Fundraising round-up

If you would like to fundraise for us please contact our Fundraising Team on **020 7631 6976** or email [fundraising@migrainetrust.org](mailto:fundraising@migrainetrust.org). To see what fundraising opportunities we have coming up, visit [www.migrainetrust.org/fundraising](http://www.migrainetrust.org/fundraising).

## Help us celebrate our 50th Anniversary as a Migraine Trust fundraiser in 2015

This year we are celebrating our 50th Anniversary at The Migraine Trust and we would like to invite you to be part of our special year of activities.

Every year several dedicated supporters sign up to take on events from 5Ks to marathons, or organise their own events like bake sales and open gardens to raise money. As a small charity, we are very grateful to these individuals.

During our 50th Year we are aiming to recruit 50 such fundraisers – could you be one of them? If you raise money for The Migraine Trust during 2015, we will add your name to our special '50th Hall of Fame' list and update people with your progress.

You can keep your fundraising simple, such as giving up something for Lent, organising a coffee morning or holding a 50p whip round. If you're more daring, you could do a sponsored sky dive or if you would prefer a sporting challenge, there are lots of events to choose from and our fundraising team will support you every step of the way. Visit [migrainetrust.org/50-fundraisers](http://migrainetrust.org/50-fundraisers) for more information.

## Sponsored Cycles

As well as those taking part in sponsored runs and walks last year we also had supporters take part in sponsored cycles. In July Marie did a sponsored cycle around Warwick Racecourse, whilst Grant took part in the Wiggle Wight Ferry Sportive. Between them they raised over £150. If you'd like to get involved in a cycling event go to [migrainetrust.org/fundraising/cycling](http://migrainetrust.org/fundraising/cycling).

## 40th Wedding Anniversary Celebrations

Long time supporter of The Migraine Trust Ron Flegg and his wife Susan celebrated their ruby wedding anniversary in 2014. Instead of having gifts they asked for any money to be donated to The Migraine Trust. Their generosity resulted in over £750 being donated to us and we would like to thank not only them for this kind gesture, but also all their friends and family who donated.



## Charity of the year

In 2014 we had two golf clubs nominate us for their charity of the year and several events were held in order to raise money for The Migraine Trust. Nicki Vincent and her team at Bognor Regis Golf Club raised £2,000 through a series of events including raffles, fun days and a mixed open. Fundraising and Events Officer Holly went to meet her in November to be presented with the cheque.

The ladies at Lindfield Golf Club, led by Karen Spicer, organised several activities including a fashion show, a bridge event and the Longest Day Challenge where a team were challenged to play four rounds of golf on the longest day of the year! All together they were able to raise just over £3,500.

We would like to say a huge thanks to both golf clubs for their continued effort and hard work over the course of 2014 – we really appreciate it!



## Virgin Money London Marathon

The first fundraisers to join our 50th Hall of Fame will be our London Marathon runners. On April 26th they will take to the streets of the capital to raise funds and awareness for The Migraine Trust. We would like to wish our runners Nicho, Rebecca, and sisters Debbie and Tracey the best of luck! You can find out more about our team and sponsor them by visiting [migrainetrust.org/events](http://migrainetrust.org/events) and selecting the London Marathon.

If you would like to apply for a guaranteed Migraine Trust place in the 2016 London Marathon please email [fundraising@migrainetrust.org](mailto:fundraising@migrainetrust.org) to register your interest.



## London Bupa 10,000

In May Anne ran the London Bupa 10,000 for us for the fifth year in a row. She managed to complete the race despite cracked ribs and a sore knee from a fall she had during training. We would like to say thank you to her for her continued support over these past five years and for the £125 she raised from this latest event.



## Great North Run

In September 2014 we had two people take on the Great North Run for us. Jonathan took on the challenge after being diagnosed with Hemicrania Continua. He managed to complete the run without stopping or walking and raised over £1,000 for The Migraine Trust!

Our second runner, Terry, took part in the race (whilst wearing a blue wig!) on behalf of his wife, Sarah, who has had chronic migraine for a number of years. This is the second year in a row Terry has taken part in the Great North Run and we would like to thank him for the £400 he raised this year.

## Thames Path Challenge

Back in September Anna took on the Thames Path Challenge. As if the 100km walk wasn't tough enough for her, she actually took on the challenge with a badly twisted ankle and even started out using a crutch! We really appreciate Anna's determination in the face of adversity and her efforts raised us £540. Thanks Anna.

## A week of Scottish events

In late September and early October two of our dedicated Scottish supporters took on running events for us. Firstly Gemma took on the Loch Ness Marathon raising £340 and one week later Fiona took part in the Great Scottish 10K raising £271. We would like to thank Gemma and Fiona for all their hard work fundraising and training.

## Yorkshire Three Peaks Challenge

Last September Tony and his partner Sue tackled the Yorkshire Three Peaks Challenge. We would like to thank them both for taking on such a huge challenge and for raising £400!



## Vitality British 10K London Run 2015

Once again we are looking for a team of enthusiastic volunteers to take part in the British 10K in London this July. The British 10K is the UK's most prestigious and sought-after 10km road race which is staged on the world's greatest route through the heart of central London. 25,000 runners fill the streets of the nation's capital and get the unique chance to run past many of the country's greatest landmarks including Big Ben, The London Eye, St Paul's Cathedral, Trafalgar Square and Westminster Abbey. Last year, our 6-strong 10K team raised £1,200 for The Migraine Trust. Join our special 50th anniversary team by visiting [migrainetrust.org/events](http://migrainetrust.org/events) and selecting British 10K.

# CALENDAR OF EVENTS

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If you have any questions regarding events, please email [events@migrainetrust.org](mailto:events@migrainetrust.org) or call **020 7631 6976**.

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## March

### **16-22 – Brain Awareness Week**

A global campaign to increase public awareness of the progress and benefits of brain research. Visit [dana.org/BAW](http://dana.org/BAW) to find out more.

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## April

### **26 – Virgin Money London Marathon**

Our team takes to the streets to run a gruelling 26.2 miles to raise money for migraine. Sponsor one of our marathon runners at [justgiving.com/migrainetrust](http://justgiving.com/migrainetrust). To register your interest for the 2016 London Marathon please contact The Migraine Trust.

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## May

### **2 – Isle of Wight Challenge**

Take on this epic walking challenge and take in some wonderful scenery all whilst raising money for The Migraine Trust.

### **23 – London 2 Brighton Challenge**

One of the UK's most popular endurance events. Walk, jog or run the 100km between London and Brighton.

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## June

### **27 – Grand Union Challenge**

A unique endurance event along an historic route! It's 100, 50, or 25km on the Grand Union Canal towpath - a 'hidden green corridor' that winds its way from the heart of London out towards the Chilterns.

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## July

### **12 – British 10K 2014**

Put on your running shoes and join our 10K team to raise money for migraine and awareness of this debilitating condition. Contact us to apply for a place today.

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## August

### **22 - RIDE 24**

A cycling challenge from Newcastle to London – in less than 24 hours! Join 300 fellow riders with full support en route, tackling the Yorkshire hills, straight flat roads and quiet villages, before hitting the bustle of the nation's capital.

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## September

### **6-12 – Migraine Awareness Week**

An annual awareness-raising week to draw attention to migraine, educate people and reduce stigma.

### **TBC – Managing Your Migraine: London**

A special event as part of The Migraine Trust's 50th Anniversary Year. Hear from migraine experts, meet Migraine Trust staff, share experiences and learn more about migraine.

## I want to help find a cure for migraine. I'd like to make a donation of:

- £35.63**, which would pay for one hour's dedicated migraine research.
- £71.26**, enough to pay for two hours' work by one of our Research Fellows.
- £249.40**, which would pay for a whole day's research.
- £1247.05**, enough to keep one research project running for a whole week.
- My choice of amount: £ \_\_\_\_\_

I enclose a cheque payable to The Migraine Trust  
**OR**  Please debit my credit/debit card

Card type:  Maestro  Visa  Mastercard  Delta  CAF

Card holder's name: \_\_\_\_\_

Card number: \_\_\_\_\_

Expiry date: \_\_\_\_\_ Start date: \_\_\_\_\_ Security code: \_\_\_\_\_ Issue number (Maestro only): \_\_\_\_\_

Signature(s): \_\_\_\_\_ Date: \_\_\_\_\_ / \_\_\_\_\_ / **2 0 1 5**

### Your details:

Title: \_\_\_\_\_ First Name: \_\_\_\_\_

Surname: \_\_\_\_\_

Address: \_\_\_\_\_

\_\_\_\_\_ Postcode: \_\_\_\_\_

Telephone: \_\_\_\_\_

Email: \_\_\_\_\_

### Please treat as Gift Aid Donations all qualifying gifts of money made:

*giftaid it*

Today  in the past four years  in the future (Please tick all that apply)

I confirm I have paid or will pay an amount of Income Tax and/or Capital Gains Tax for each tax year (6 April to 5 April) that is at least equal to the amount of tax that all the charities or Community Amateur Sports Clubs (CASC's) that I donate to will reclaim on my gifts for that tax year. I understand that other taxes such as VAT and Council Tax do not qualify. I understand the charity will reclaim 25p of tax on every £1 that I give.

Signature: \_\_\_\_\_ Date: \_\_\_\_\_

The Migraine Trust will keep your name and contact details on our database and use this information to inform you about events, news or ways to support The Migraine Trust that might be of interest to you. If you do not wish for your details to be used in this way please tick the box:

Funds raised will be used in accordance with the aims of the charity as set out in its governing document, namely to help improve the lives of people with migraine in the UK, and work towards our vision of a world where people can live free of the condition.

Please return this form to: **FREEPOST RSRB-ZYSK-GGCC,  
The Migraine Trust, 52-53 Russell Square, London WC1B 4HP**

For every donation we receive, we send a letter acknowledging receipt and thanking the giver. We are delighted to do this, but if you would prefer us not to send an acknowledgement, please tick the box:

Registered charity in England and Wales (1081300) and Scotland (SC042911).

**Thank you**





The Migraine Trust is the health and medical research charity for migraine in the United Kingdom. The Migraine Trust is committed to supporting all those affected by migraine and disabling headache. We seek to raise awareness of migraine and headache as a serious public health problem. The Migraine Trust funds and promotes research into migraine and disabling headache for the purposes of better understanding, improved diagnosis and treatment and, ultimately, to find a cure for these debilitating conditions.

Information and Enquiry Service: we can help with questions you may have about migraine, other headaches and their management. All our information is based on the best available evidence.

**Telephone:** 020 7631 6975 please leave a message if necessary and we will get back to you or

**Email:** [info@migrainetrust.org](mailto:info@migrainetrust.org)

**Advocacy Service:** We can provide advocacy support to empower migraine sufferers to assert their rights and claim their entitlements in the areas of healthcare, employment and education. (See website for further details and resources.)

**Telephone:** 020 7631 6973

**Email:** [advocacy@migrainetrust.org](mailto:advocacy@migrainetrust.org)

**Events:** throughout the year we organise a variety of educational events around the UK that cater for both health professionals and the public. (See website for details of upcoming events.)

**Website:** information about migraine and headache is available at our website including downloadable factsheets and packs. You can also subscribe to The Migraine Trust's ebulletin. The Migraine Trust is a registered charity funded entirely by voluntary donations from individuals, charitable trusts and corporate sponsors. Without your support we would be unable to continue our work. Please give your support by making a donation or become a regular supporter and receive our journal *Migraine News*.

Find us on Facebook, Twitter and Justgiving.com

**Telephone:** 020 7631 6970

**Fax:** 020 7436 2886

**Email:** [info@migrainetrust.org](mailto:info@migrainetrust.org)

**Website:** [www.migrainetrust.org](http://www.migrainetrust.org)

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