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Neuropathy TIMES

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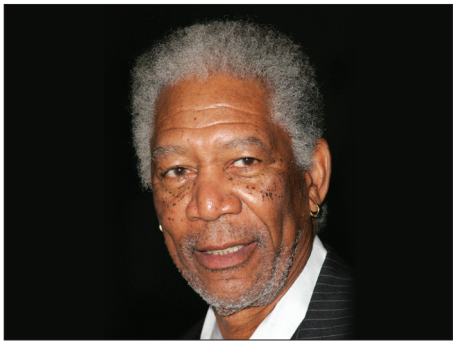
NEUROLOGY AND BRAIN HEALTH

Life does not stop with fibromyalgia: Morgan Freeman opens up about his condition



Morgan Freeman, a successful American actor, director, and narrator, revealed he had fibromyalgia, in an interview with a leading men's magazine. Fibromyalgia is a painful condition characterized by widespread pain, stiffness, numb hands and feet, fatigue, anxiety and depression.

A substantial proportion of the population suffers from fibromyalgia; however, only few reveal it, probably due to a certain stigma associated with it. Therefore, it seems important for celebrities, who suffer from this disorder, to step forward and admit the same. This might be helpful to non-celebrities, as it provides an iconic figure to relate to with the same syndrome from which others may suffer. Celebrity ownership of their disorder also helps raise awareness and funding for research into the less-acknowledged health condition.

During the interview, Freeman discussed not being able to do certain activities anymore, such as sailing and attributed it to fibromyalgia. Yet he wanted others to know that the condition might not be all depressing, and added that there is a point to changes like these. One should move on to other things, to other beginnings, since life doesn't stop with fibromyalgia.

Sources: 1. 10 Celebrities Who Have Fibromyalgia. Available at: http://rmfibromyalgia.com/10-celebrities-fibromyalgia/. Accessed on 18/09/2017. **2.** 5 Celebrities With Fibromyalgia. Available at: http://www.healthline.com/health/celebrities-fibromyalgia#2. Accessed on 18/09/2017.

George Clooney suffers from chronic back pain following an injury in 2005

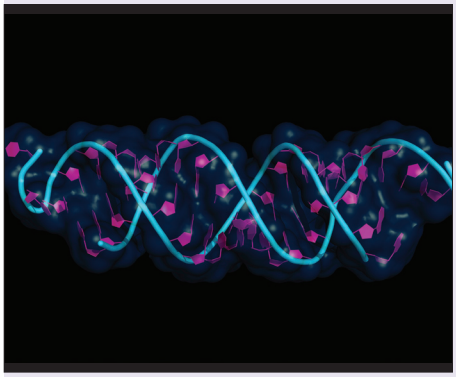
Pain is considered a great equalizer, as it does not discriminate between individuals; chronic pain can hit anyone, at any time. George Clooney, one of the most successful actors in Hollywood, suffers from chronic back pain, which started when he suffered an injury while filming a thriller in 2005. He suffered constant pain and splitting headaches as doctors initially could not identify the problem. At one point, the pain was so severe that he even contemplated suicide. Despite

doctors' initial uncertainty, a neurologist eventually identified the problem and Clooney underwent a series of operations. Besides, he sought to prepare mentally through therapy that taught him to forget his own pain. Although he still struggles with the pain, it has become much more manageable, thanks to some of the most advanced, cutting-edge pain treatments.

Sources: 1. 9 Celebrities Who Suffer With Chronic Pain. Available at: http://www.healthcarepass.com/9-celebrities-that-suffer-with-chronic-pain/. Accessed on 18/09/2017. **2.** Head injury drove Clooney to think of suicide. Available at: https://www.theguardian.com/world/2005/oct/23/film.usa. Accessed on 18/09/2017.

Scientists discover RNA that plays a special role in nerve healing process

The discovery that an 'anti-sense' RNA (AS-RNA) is expressed after nerve injury to regulate the repair of damage to the nerve's myelin coating could lead to novel approaches in the process of healing peripheral nerve damage. Indeed, the ability to control the newly discovered RNA might help in efforts to promote nerve healing. Scientists from Brown University reported that they were able to control the expression of the AS-RNA in the lab and therefore the transcription factor Egr2 that prompts myelin-building Schwann cells into action. Considering that the AS-RNA inhibits the expression of Egr2, which is the central transcriptional regulator of myelin genes, it is likely that inhibiting



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The scientists not only found the AS-RNA, but also that its expression increases markedly and with specific timing after sciatic nerve injury. In further experiments, they discovered which molecules stimulate the expression of the AS-RNA and they also successfully interfered with its activity, which delayed demyelination.

The discovery provides a new factor that can be manipulated to affect when myelin is removed and restored and by how much; this might be translated, with further research, into a novel therapy for nerve injury repair and peripheral demyelinating neuropathies.

Source: Scientists find RNA with special role in nerve healing process. Available at: https://www.sciencedaily.com/releases/2017/08/170822123839.htm. Accessed on 18/09/2017.

Powerful potential pain reliever identified

Scientists at The University of Texas at Austin have discovered a powerful pain reliever that may be as effective at relieving neuropathic pain as gabapentin, a drug widely used for pain relief. The synthetic compound, known as UKH-1114, acts on a previously unknown pain pathway and works at a much lower dose, with longer duration of action than gabapentin.

The scientists tested UKH-1114 on experimental models with nerve damage and found that it alleviated pain as effectively as gabapentin did, but at a much lower dose (one-sixth as much); besides, it was effective for much longer duration (a couple of days versus 4-6 hours, respectively) compared to gabapentin. The pain drug was shown to bind to the sigma 2, which is a receptor on cells throughout the central nervous system. Although sigma 2 was discovered more than two decades ago, scientists remained oblivious of the exact functions of this receptor until now. This research is the first to reveal that the sigma 2 receptor may be a target for treating neuropathic pain.

In developed countries, almost one-third of the population suffer from chronic pain, yet the most effective pain relievers— opioids— are addictive and frequently require increased dosing to maintain efficacy. Alternatives to opioids, such as gabapentin, can cause cognitive impairment in certain individuals. If the scientists can establish that the drug is safe, effective and non-addictive in humans, the

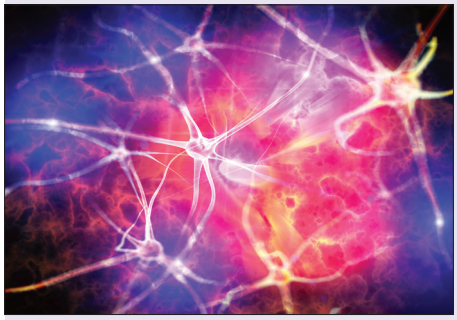
> *The synthetic compound, known as UKH-1114, is as effective at relieving neuropathic pain as gabapentin and works at a much lower dose, with longer duration of action than gabapentin*

discovery could be instrumental in addressing one of today's biggest public health conundrums: the opioid abuse epidemic.

Source: Scientists discover powerful potential pain reliever. Available at: https://www.sciencedaily.com/releases/2017/08/170816160622.htm. Accessed on 18/09/2017.

Unraveling a novel mechanism behind chronic nerve pain

Chronic nerve pain has long been assumed to be a result of hypersensitivity in the neurons that transmit pain. Of late, scientists at Karolinska Institutet in Sweden have revealed that another kind of neuron that normally are responsible for pleasant touch sensation can switch function and instead signal pain after nerve damage. The study, which is published in the journal *Science*, suggests that the novel finding can ultimately lead to more effective pain treatments.



Earlier, it was presumed that certain sensory neurons only transmit pleasant touch sensations, while other specializes to transmit pain. During chronic nerve pain, normal touch can cause pain, but the exact mechanism for this remained elusive. In the present study, scientists have sown that a small RNA molecule (microRNA) in sensory neurons regulates touch perception. Upon nerve damage, levels of this molecule decline

> *Upon nerve damage, levels of a small RNA molecule decline in the sensory neurons leading to raised levels of a specific ion channel that makes the nerve cells sensitive to pain*

in the sensory neurons, which leads to raised levels of a specific ion channel that makes the nerve cells sensitive to pain.

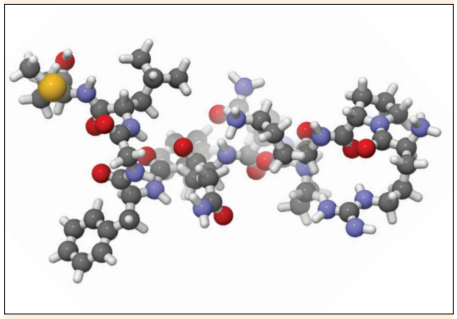
The study revealed that touch-sensitive nerves switch function and start producing pain, which can explain the genesis of hypersensitivity. Also, microRNA regulation could explain the variation in pain thresholds among different individuals. Considering the complex etiology of nerve pain with several underlying mechanisms, the present study holds prominence since it demonstrated that the RNA molecule controls the regulation of majority (80%) of the genes that are known to be involved in nerve pain. A better elucidation of the mechanisms that lead to chronic nerve pain might help discover novel pain treatment methods.

Source: Unexpected mechanism behind chronic nerve pain. Available at: https://www.sciencedaily.com/releases/2017/06/170601151906.htm. Accessed on 18/09/2017.

Tear film substance P: A potential biomarker for diabetes-related nerve damage

Levels of a nerve cell signaling molecule called substance P, which is measured in tear samples, may be a potential biomarker of diabetes-related nerve damage (neuropathy), according to a recent study published in *Optometry and Vision Science*, the official journal of the American Academy of Optometry. Substance P, a neuropeptide that contributes to wound healing, is also involved in maintenance and nutrition of the cornea.

The researchers reportedly measured substance P levels in the natural tear film in the eyes of nine adults with diabetes and a control group of 17 non-diabetic individuals. The results revealed that patients with diabetes had considerably lower levels of substance P in tear film samples, compared to healthy controls. Further, on confocal microscopy, patients with diabetes also had a substantially lower corneal nerve



fiber density, indicating loss of corneal nerve fibers. Substance P levels were moderately correlated with the corneal nerve fiber density assessments.

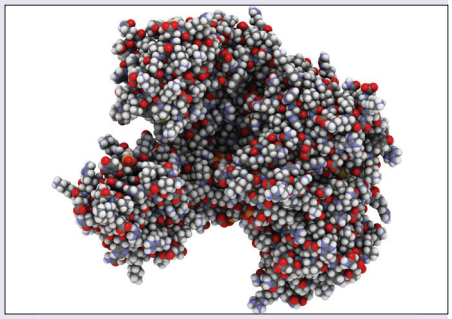
Substance P is expressed at a considerably lower level in the tears of patients with diabetes compared with healthy controls. Besides, the positive correlation between substance P and corneal nerve density suggests that substance P may be a potential biomarker for corneal nerve health. The researchers suggest that measuring substance P levels in the tear film might be an effective, noninvasive test for evaluating the risk of peripheral neuropathy in patients with diabetes.

> *Patients with diabetes had considerably lower levels of substance P in tear film samples, compared to healthy controls*

Source: 'Substance P' in tears: Noninvasive test for diabetes-related nerve damage? Available at: https://www.sciencedaily.com/releases/2017/07/170705151737.htm. Accessed on 18/09/2017.

Novel targets for ameliorating neuropathic pain

A novel therapeutic target called lysophosphatidylcholine acyltransferase (LPCAT)2 may prove effective against pain that is not receptive to the currently available analgesic drugs, according to a recent study. The study published in *The FASEB Journal* also indicates the existence of a platelet alleviating factor (PAF) pain loop, suggesting a possible role for PAF-receptor (PAFR) antagonists. The study was conducted among two groups of experimental models. The first group had a disrupted LPCAT2 gene, which normally encodes the synthesis of PAF, while the other group consisted of normal experimental models. The researchers found that pain-like behaviors resulting from partial sciatic nerve ligation (PSL) were mostly attenuated in the group having a disrupted LPCAT2 gene, as compared to their normal counterparts. These findings underscore a novel concept of analgesic drug development for neuropathic pain through the inhibition of PAF biosynthetic enzyme, LPCAT2, and re-evaluation of the clinical utility of PAFR antagonists.



> *Pain-like behaviors resulting from partial sciatic nerve ligation were mostly attenuated in the group having a disrupted lysophosphatidylcholine acyltransferase (LPCAT)2 gene*

Source: Scientists discover new category of analgesic drugs that may treat neuropathic pain. Available at: https://www.sciencedaily.com/releases/2017/03/170329102442.htm. Accessed on 19/09/2017.

In search of new ways to block nerve cell damage in neurodegenerative diseases

Many neurodegenerative conditions including Parkinson's disease and peripheral neuropathy are characterized by loss of axons as an early defect. Axonal loss hampers normal nerve cells communication, which results in impaired functioning of the nervous system. Degeneration of axons, particularly in peripheral neuropathy, triggers a self-destruct program. Researchers at Washington University School of Medicine have revealed that a specific molecule called SARM1 might be associated with the self-destruction of axons, which are the wiring of the nervous system. Understanding the mechanism of nerve cell damage may help researchers find a way to block it.

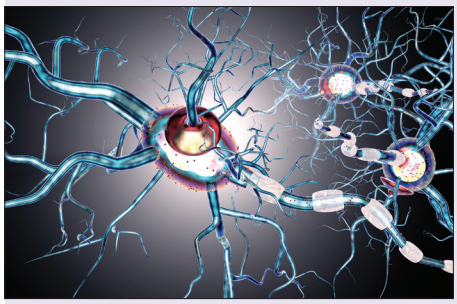
> *SARM1, a specific molecule that provides a passive platform for the assembly of molecules or proteins to perform their work, plays a key role in the self-destruct pathway of axons*

SARM1 and similar molecules that contain the TIR domains are well-known to act as scaffolds for the assembly of molecules or proteins to perform their work. Interestingly, in this new study, researchers revealed that SARM1 does more than simply providing a passive platform and plays a key role in the self- destruct pathway of axons. SARM1 is present in healthy neurons, but remains inactive, and gets activated during an event of injury or disease. Activation of SARM1 triggers a series of events that drains a key cellular fuel called nicotinamide adenine dinucleotide (NAD), and results in the destruction of axons. Specifically, it was found that SARM1's TIR domain acts as an enzyme, which leads to axonal destruction by first burning all their NAD cellular fuel. Researchers are of the opinion that if the pathway that destroys axons could be paused or halted, it would slow or prevent the gradual loss of nervous system function and the debilitating symptoms that ensue.

Source: Surprising culprit in nerve cell damage identified. Available at: https://www.sciencedaily.com/releases/2017/03/170324104924.htm. Accessed on 19/09/2017.

Novel mechanisms to promote sensory neuron growth as a potential treatment for peripheral neuropathy

Researchers have discovered a potential treatment for peripheral neuropathy, according to a study published in the *Journal of Clinical Investigation*. Peripheral neuropathy is a condition that results from damage to the peripheral nervous system, with symptoms ranging from numbness, tingling and muscle weakness to severe pain, paralysis and organ dysfunction.



The researchers have identified a method to promote sensory neuron growth by blocking a specific molecular signaling pathway. Of note, the blockage also prevents or reverses peripheral neuropathy in cell and experimental models of type 1 and 2 diabetes, chemotherapy-induced neuropathy and human immunodeficiency virus.

While looking for key molecules and mechanisms used in sensory neuron growth and regrowth, the researchers observed that the outgrowth of neurites

> *While looking for key molecules and mechanisms used in sensory neuron growth and regrowth, the researchers observed that the outgrowth of neurites was inhibited by activation of muscarinic acetylcholine receptors*

was inhibited by activation of muscarinic acetylcholine receptors; this was a rather interesting finding, since acetylcholine is a neurotransmitter usually associated with activation of cells. With identification of this novel signaling pathway, it might be possible to investigate the utility of anti-muscarinic drugs as a new treatment for peripheral neuropathy.

It is worth considering that a number of anti-muscarinic drugs are already approved for use in various indications and have well-characterized safety profile. Therefore, the novel therapeutic application of anti-muscarinic antagonists suggested by findings of the present study could potentially translate relatively rapidly to clinical use.

Source: Blocking neuron signaling pathway could lead to new treatments for peripheral neuropathy. Available at: https://www.sciencedaily.com/releases/2017/01/170117192708.htm. Accessed on 19/09/2017.

Device to help people with peripheral neuropathy avoid trips and falls

Researchers at RICE University have developed a device that can help people who have impaired sensation in the feet to avoid accidental falls. The innovative device converts pressure applied by the sole of the shoe into a vibration that is more promptly felt by the foot. The vibration, accompanying every step, changes in intensity that is proportional to the pressure on the shoe. It should be noted that people with diabetes, small vessel disease, post-injury, and other conditions may have limited tactile sensation in their feet, and may not be able to feel the ground while walking; this makes them vulnerable to trips and falls. The sensory feedback produced by the device might prevent a tumble and could prove a lifesaver to many elderly and patients with diabetes who might have lost some ability to feel their extremities, probably due to peripheral neuropathy.

> *The innovative device converts pressure applied by the sole of the shoe into a vibration that is more promptly felt by the foot*

Sources: **1.**Device Improves Sensation in Folks with Peripheral Neuropathy. Available at: https://www.medgadget.com/2017/04/device-improves-sensation-folks-peripheral-neuropaty.html. Accessed on 19/09/2017. **2.**Hear the buzz about seniors' sensor-laden shoes. Available at: http://news.rice.edu/2017/04/05/hear-the-buzz-about-seniors-sensor-laden-shoes-2/. Accessed on 19/09/2017.

MOLECULE PREGABALIN

Pregabalin effectively ameliorates pain regardless of duration of neuropathic pain

Neuropathic pain, a common chronic pain condition, can be particularly challenging to treat owing to its severity and associated comorbidities. Neuropathic pain is accountable for a substantial proportion of visits to primary care physicians and pain clinics and represents a significant economic burden on patients and health-care systems. Patients with chronic pain conditions such as neuropathic pain usually do not receive timely diagnosis; besides, they often experience delays in receiving treatment that, when wait times are more than 6 months, have been found to result in considerable deterioration in health-related quality of life and psychological well-being.

Ideally, every patient should be administered appropriate treatment; however, it should be borne in mind that approved treatments remain effective in patients with more established disease. In the present study, investigators conducted a pooled analysis of 19 randomized placebo-controlled trials of pregabalin for peripheral neuropathic pain conditions, including diabetic peripheral neuropathy, postherpetic neuralgia, and post-traumatic/postsurgical pain. Patients were categorized into 5 pain duration categories based on time since onset of pain (<6 months, 6 months to <1 year, 1 year to <2 years, 2 years to <5 years, and ≥5 years). Mean change in pain score at endpoint, versus placebo, was evaluated for each category, along with changes in Patient Global Impression of Change (PGIC) responders.

> *Pregabalin significantly improves pain regardless of the length of time since onset of neuropathic pain*

A total of 5,783 patients (n = 3,619 pregabalin; n = 2,164 placebo) were included in the study. The results revealed similar mean baseline pain scores across the pain duration categories (range 6.3 to 6.5). Further, pregabalin significantly ameliorated pain score at endpoint, versus placebo, in all patients together and similarly in each pain duration category. Of note, there were significantly more PGIC responders with pregabalin, compared to placebo, for all patients (45.0% versus 30.9%, respectively P <0.0001) and each category separately (P <0.001 for each). No consistent, remarkable differences in treatment response were observed between the different pain duration categories. The investigators concluded that pregabalin significantly improves pain regardless of the length of time since onset of neuropathic pain.

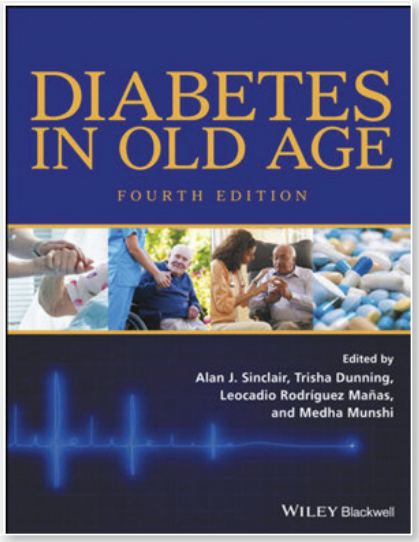
Source: Pérez C, Latymer M, Almas M, Ortiz M, Clair A, Parsons B, *et al.* Does Duration of Neuropathic Pain Impact the Effectiveness of Pregabalin? *Pain Pract.* 2017; 17(4):470-479.

Book Review

Diabetes in Old Age, 4th Edition

Editors: Alan J. Sinclair, Trisha Dunning, Leocadio Rodríguez Mañas, Medha Munshi

Publisher: Wiley-Blackwell, 2017



This fourth edition of the popular and market-leading book, Diabetes in Old Age, features state-of-the-art and comprehensive information about the key features of managing older people with diabetes, primarily type 2 diabetes.

With a robust evidence-based focus throughout, this book encompasses the complete range of issues pertaining to diabetes and its various complications, each with a clear focus on how they relate directly to the older patient. It presents a wide range of approaches to optimize diabetes care in the community, primary care and secondary care health care arenas, and also underscores the importance of comprehensive functional assessment. Coverage of areas unique to an ageing population of older people with diabetes such as falls management, frailty and sarcopenia, and cognitive dysfunction form a special feature of the book. Every chapter is accompanied with best practice points and key learning outcomes, as well as published evidence bases for each major conclusion.

Diabetes in Old Age, 4th edition is an indispensable reading for diabetologists and endocrinologists, diabetes specialist nurses, primary care physicians, general physicians and geriatricians, podiatrists and dieticians with an interest in diabetes, as well as all health professionals associated with the delivery of diabetes care to older people.

Conference Calendar

- **Central Nervous System Disorders & Therapeutics**
  October 02, 2017 – October 03, 2017
  Vienna, Austria

- **MYOPAIN 2017: 10th World Congress on Myofascial Pain Syndrome and Fibromyalgia Syndrome**
  October 04, 2017 – October 08, 2017
  Bengaluru, India

- **17th Global Neuroscience Conference**
  October 16, 2017 – October 17, 2017
  Osaka, Japan

- **NSUKI Annual Scientific Meeting Oxford 2017**
  Joint Meeting of the Neuromodulation Society of the UK & Ireland ASM and the IASP Special Interest
  November 11, 2017 – November 12, 2017
  Oxford, United Kingdom

- **16th Annual Pain Medicine Meeting, 2017**
  November 16, 2017– November 18, 2017
  Florida, United States

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