The New Paradigm in Sports Injuries & Performance

Proven Protocols for Optimised Success

Dr. Robert Silverman

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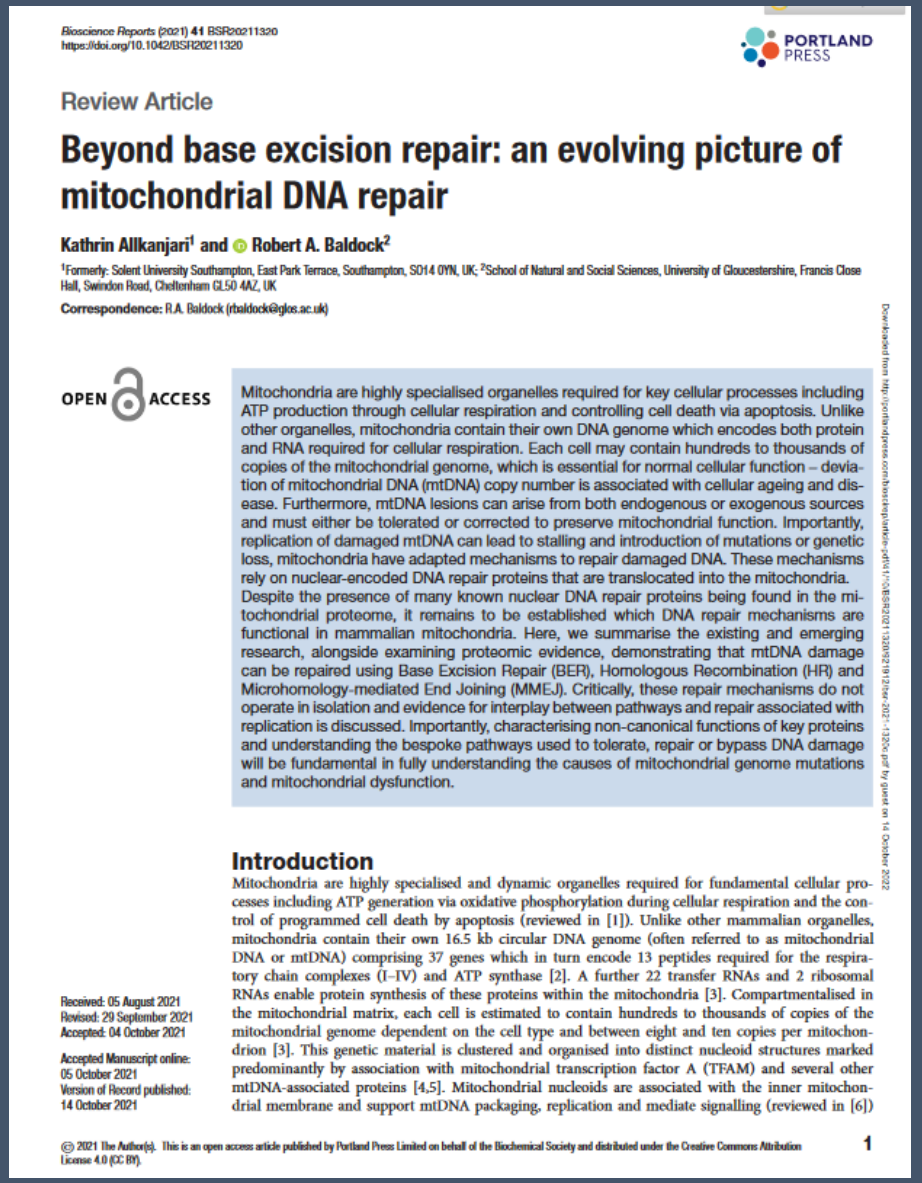
“Let there be light”

Vicious circle of mitochondria dysfunction

- Mitochondria contains own DNA (mtDNA)
- Replication of damaged mtDNA can lead to stalling and introduction of mutations or genetic loss
- Dysfunctional mitochondria survive longer than healthy mitochondria



Bioscience Reports (2021) **41** BSR20211320
https://doi.org/10.1042/BSR20211320

PORTLAND PRESS

Review Article

Beyond base excision repair: an evolving picture of mitochondrial DNA repair

Kathrin Allkanjari[1] and Robert A. Baldock[2]

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Correspondence: R.A. Baldock (rbaldock@glos.ac.uk)

OPEN ACCESS

Mitochondria are highly specialised organelles required for key cellular processes including ATP production through cellular respiration and controlling cell death via apoptosis. Unlike other organelles, mitochondria contain their own DNA genome which encodes both protein and RNA required for cellular respiration. Each cell may contain hundreds to thousands of copies of the mitochondrial genome, which is essential for normal cellular function – deviation of mitochondrial DNA (mtDNA) copy number is associated with cellular ageing and disease. Furthermore, mtDNA lesions can arise from both endogenous or exogenous sources and must either be tolerated or corrected to preserve mitochondrial function. Importantly, replication of damaged mtDNA can lead to stalling and introduction of mutations or genetic loss, mitochondria have adapted mechanisms to repair damaged DNA. These mechanisms rely on nuclear-encoded DNA repair proteins that are translocated into the mitochondria. Despite the presence of many known nuclear DNA repair proteins being found in the mitochondrial proteome, it remains to be established which DNA repair mechanisms are functional in mammalian mitochondria. Here, we summarise the existing and emerging research, alongside examining proteomic evidence, demonstrating that mtDNA damage can be repaired using Base Excision Repair (BER), Homologous Recombination (HR) and Microhomology-mediated End Joining (MMEJ). Critically, these repair mechanisms do not operate in isolation and evidence for interplay between pathways and repair associated with replication is discussed. Importantly, characterising non-canonical functions of key proteins and understanding the bespoke pathways used to tolerate, repair or bypass DNA damage will be fundamental in fully understanding the causes of mitochondrial genome mutations and mitochondrial dysfunction.

Introduction

Mitochondria are highly specialised and dynamic organelles required for fundamental cellular processes including ATP generation via oxidative phosphorylation during cellular respiration and the control of programmed cell death by apoptosis (reviewed in [1]). Unlike other mammalian organelles, mitochondria contain their own 16.5 kb circular DNA genome (often referred to as mitochondrial DNA or mtDNA) comprising 37 genes which in turn encode 13 peptides required for the respiratory chain complexes (I–IV) and ATP synthase [2]. A further 22 transfer RNAs and 2 ribosomal RNAs enable protein synthesis of these proteins within the mitochondria [3]. Compartmentalised in the mitochondrial matrix, each cell is estimated to contain hundreds to thousands of copies of the mitochondrial genome dependent on the cell type and between eight and ten copies per mitochondrion [3]. This genetic material is clustered and organised into distinct nucleoid structures marked predominantly by association with mitochondrial transcription factor A (TFAM) and several other mtDNA-associated proteins [4,5]. Mitochondrial nucleoids are associated with the inner mitochondrial membrane and support mtDNA packaging, replication and mediate signalling (reviewed in [6])

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Version of Record published: 14 October 2021

Common mitochondrial disorders

- **OA:** decreased activity of Complexes I, II and III
- **NSAIDs** (Ibuprofen, aspirin): able to inhibit mitochondrial complex I
- **Acetaminophen:** inhibited activities of complexes I and IV in cerebral cortex
- **Aging** – skeletal muscle: decline in activities of complexes I, II and IV
- **Brain**: decline in complex I and in complex IV
- **Obesity**: significantly fewer complex I and IV components

References in appendix

Mitochondria Health is Linked to InflammAging

The Mitochondrial Basis of Aging

Nuo Sun,[1] Richard J. Youle,[2] and Toren Finkel[1]

Review

Cell Death and Inflammation: The Role of Mitochondria in Health and Disease

Anna Picca [1,2], Riccardo Calvani [1,2,*], Hélio José Coelho-Junior [3] and Emanuele Marzetti [1,3]

Mitochondria and Inflammation: Cell Death Heats Up

*Esmee Vringer[1,2] and Stephen W. G. Tait[1,2]**

[1] Cancer Research UK, Beatson Institute, Glasgow, United Kingdom, [2] Institute of Cancer Sciences, University of Glasgow, Glasgow, United Kingdom

Review article

Inflammation and mitochondrial dysfunction: A vicious circle in neurodegenerative disorders?

Jack van Horssen*, Pauline van Schaik, Maarten Witte

Dept. of Molecular Cell Biology and Immunology, VU University Medical Center, Amsterdam, The Netherlands

Mitochondrial DNA in inflammation and immunity

Joel S Riley[1,2,*] & Stephen WG Tait[1,2,**]

The Aging Mitochondria

Pierre Theurey [1], Paola Pizzo [2] [3]

This Technology Vastly Decreases Opioid Use Chronic Pain & Non-Thermal Laser

FDA Grants 510(k) Market Clearance for Whole Body Postoperative Pain to World Leader in Low Level Laser Technology

Efficacy of 635nm Red Low-Level Laser on Nociceptive Musculoskeletal Pain Compared to NSAIDS, Opioids, and Other Light Sources

Erchonia's Published Peer-Reviewed Results Reveal Promising Treatment for Musculoskeletal Pain

A sample size of over 400 subjects, a p-value of .00001, multiple blinded & controlled studies shows 635nm red lasers are an effective treatment

Two Randomized, Double Blind, Placebo-Controlled Trials Evaluating the Efficacy of Red 635nm Low Level Laser for the Treatment of Low Back Pain

Low-Level Laser Therapy for Treating Low Back Pain: 12-Month Follow-Up

Trevor S. Berry[1], Paul J Quarneri[2], Gregory Roche[3] and Travis M Sammons[4]*

[1]South Mountain Chiropractic Center, Chandler, AZ, USA
[2]Quarneri Chiropractic Inc., San Mateo CA, USA
[3]Bloomfield Laser & Cosmetic, Bloomfield Hills, MI, USA
[4]Erchonia Corporation, Melbourne, FL, USA

Non-Thermal Low-Level Laser & Brain Health

Low-level Laser Therapy for Beta-Amyloid Toxicity in Rat Hippocampus

Protection against neurodegeneration with low-dose methylene blue and near-infrared light

May 2015 · Frontiers in Cellular Neuroscience 9(36)
DOI:10.3389/fncel.2015.00179

Low-Level Laser Therapy Applied Transcranially to Mice following Traumatic Brain Injury Significantly Reduces Long-Term Neurological Deficits

AMIR ORON,[1] URI ORON,[2] JACKSON STREETER,[2] LUIS DE TABOADA,[2] ALEXANDER ALEXANDROVICH,[3] VICTORIA TREMBOVLER,[3] and ESTHER SHOHAMI[3]

Assessing The Autonomic Effect Of Vagal Nerve Stimulation With Low Level Lasers By Heart Rate Variability

C Machado, Y Machado, M Chinchilla, Y Machado, H Foyaca-Sibat

Vagal Nerve Stimulation With Low Level Lasers Of Two Different Frequencies, Assessed By QEEG

C Machado, Y Machado, M Chinchilla, Y Machado, H Foyaca-Sibat

Treating cognitive impairment with transcranial low level laser therapy

Jack C. de la Torre

Non-Thermal Laser is Promising for Neurodevelopmental and Mental Health Disorders

Article

Transcranial Photobiomodulation for the Treatment of Children with Autism Spectrum Disorder (ASD): A Retrospective Study

Stefano Pallanti [1,2,*], Michele Di Ponzio [1], Eleonora Grassi [1], Gloria Vannini [1] and Gilla Cauli [3]

Effects of Low-Level Laser Therapy in Autism Spectrum Disorder

Gerry Leisman, Calixto Machado, Yanin Machado, and Mauricio Chinchilla-Acosta

Follow-Up Assessment Of Autistic Children 6 Months After Finishing Low Lever Laser Therapy

C Machado, Y Machado, M Chinchilla, Y Machado

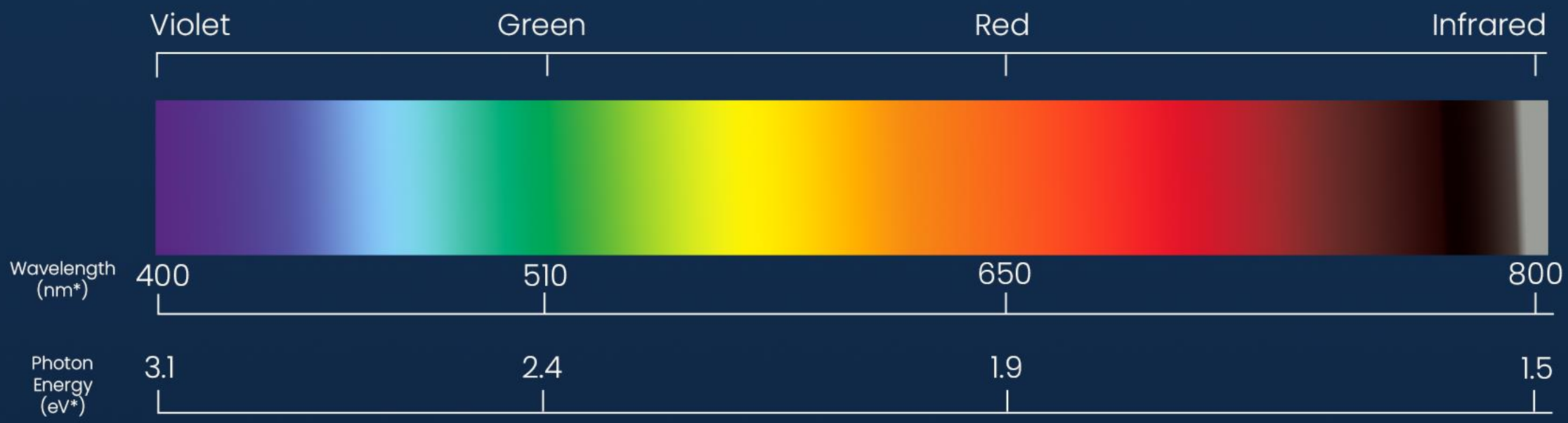
Follow-Up Assessment Of Autistic Children 12 Months After Finishing Low Lever Laser Therapy

C Machado, Y Machado, M Chinchilla, Y Machado

Low-Level Laser Irradiation Improves Depression-Like Behaviors in Mice

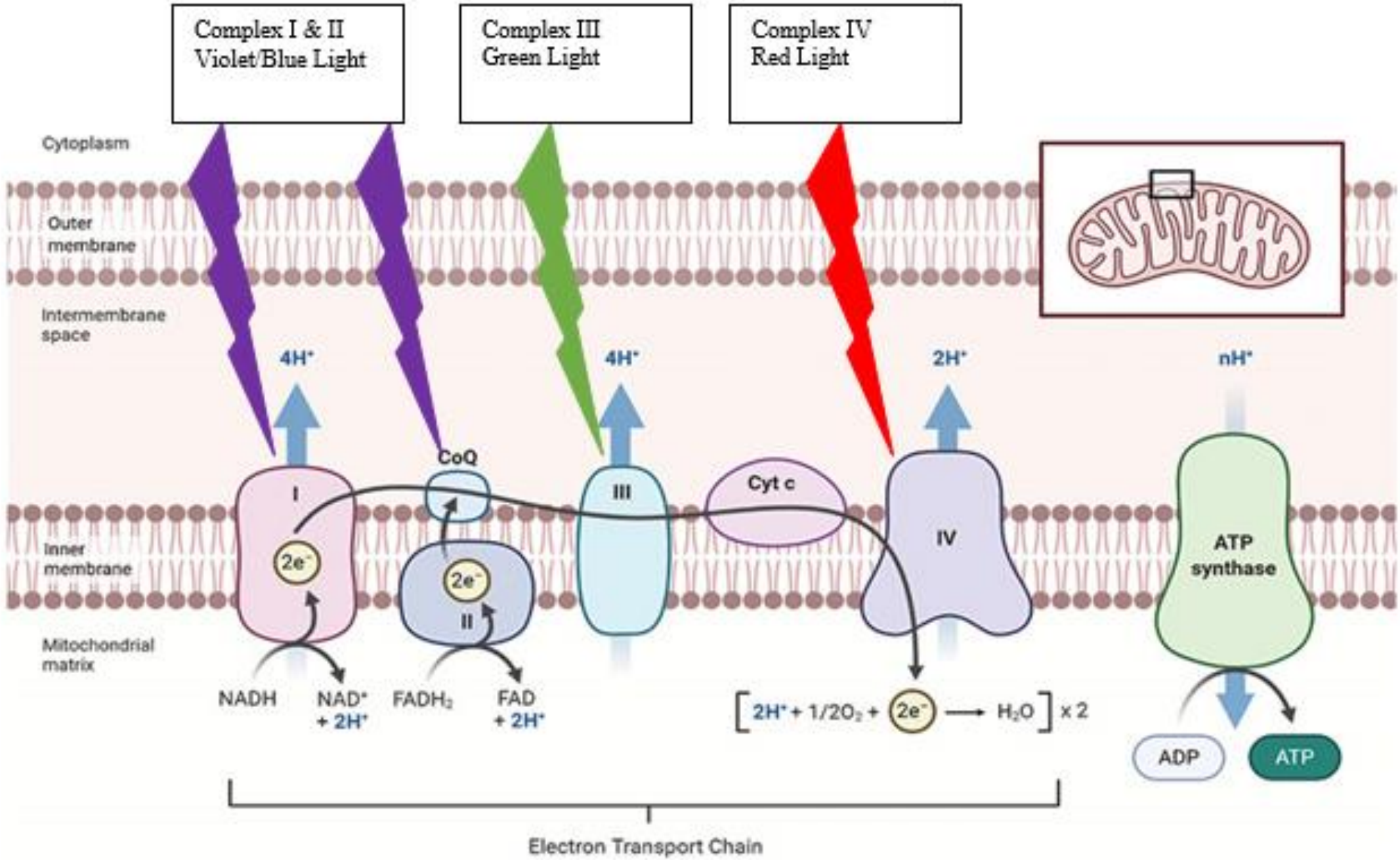
Zhiqiang Xu [1 2], Xiaobo Guo [2], Yong Yang [3], Donovan Tucker [4], Yujiao Lu [4], Ning Xin [1], Gaocai Zhang [1 2], Lingli Yang [1], Jizhen Li [5], Xiangdong Du [3], Quanguang Zhang [6], Xingshun Xu [7 8]

The most **energetic** laser in the world.



Photochemistry is dependent on the Photon Energy **(Electron Volts).. NOT POWER**

Key Concept: A minimum Photon Energy of 1.7 eV is required to cause electrons to jump to higher orbits. You can NOT make up for a lower eV by increasing the wattage (power) to trigger the same reactions.


Complex I & II
Violet/Blue Light
Complex III
Green Light
Complex IV
Red Light
Cytoplasm
Outer membrane
Intermembrane space
Inner membrane
Mitochondrial matrix
4H+
4H+
2H+
nH+
CoQ
I
II
III
IV
Cyt c
2e-
2e-
ATP synthase
NADH
NAD+ + 2H+
FADH2
FAD + 2H+
[2H+ + 1/2O2 + 2e- → H2O] x 2
ADP
ATP
Electron Transport Chain

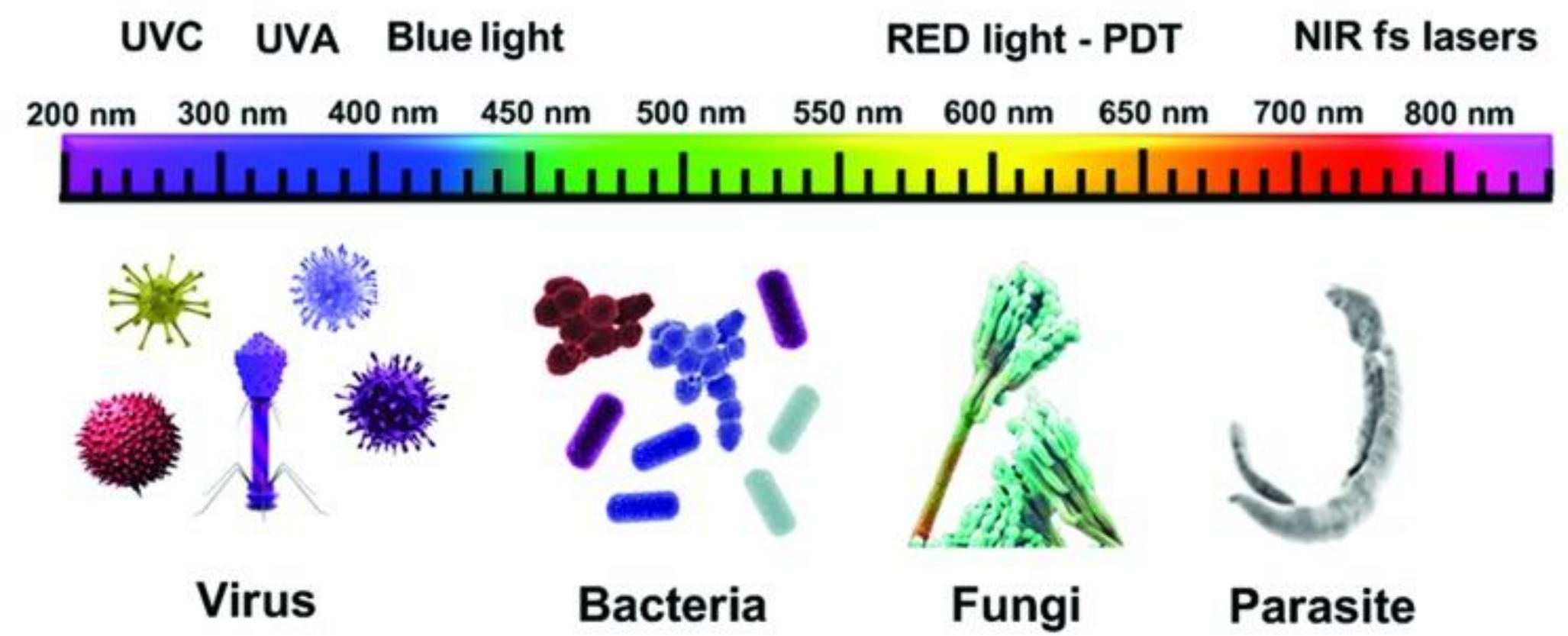
Could Non-Thermal Laser (NTL) be the answer and why?

- Non-invasive
- No downtime
- No pain
- Short treatment time
- Pain-relieving properties
- Decreases swelling
- Improves blood flow
- Enhances energy production
- Optimizes mitochondrial function
- Anti-inflammatory
- Immune boosting properties
- Promotes stem cell production
- Decreases stress hormones
- Neuroprotective
- Down-regulates stress responses in brain
- Accelerates wound-healing
- Upregulates collagen production
- Fat loss
- Cellulite reduction
- Skin conditions

Non Thermal Laser (NTL) Improves Cellular Function and Stability of Mitochondria

- NTL – concentrated light that delivers highly energetic photons of energy into cell, optimizing overall cellular function
- Primary effect of NTL believed to affect **Cytochrome C Oxidase** (*CCO/Complex IV of Electron Transport Chain*), which is a rate-limiting mechanism for production of ATP within the mitochondria
- Mitochondria – cell's powerhouse that are master controllers of cellular function, immune responses, and controlling inflammation:
  - ***NLT can dampen inflammation, improve mitochondrial function, and optimize our genetic expression to enhance overall quality of life***

Electromagnetic spectrum and its physiological effects on various microorganisms



Can biowarfare agents be defeated with light?. *Virulence*. 2013;4(8):796-825

Photomedicine and Laser Surgery
Volume 34, Number 11, 2016
© Mary Ann Liebert, Inc.
Pp. 556–563
DOI: 10.1089/pho.2015.4025

Mesenchymal Stem Cells Synergize with 635, 532, and 405 nm Laser Wavelengths in Renal Fibrosis: A Pilot Study

Megan O'Connor, MS,[1] Rachana Patil, MS,[1] Jiangzhou Yu, MD, PhD,[1] Richard Hickey, BS,[1] Kavitha Premanand, MS,[1] Andre Kajdacsy-Balla, MD, PhD,[2] Enrico Benedetti, MD,[1,3] and Amelia Bartholomew, MD, MPH, FACS[1]

Abstract

Objective: To address whether a single treatment of one of three visible light wavelengths, 635, 532, and 405 nm (constant wave, energy density 2.9 J/m^2), could affect the hallmarks of established renal fibrosis and whether these wavelengths could facilitate mesenchymal stem cell (MSC) beneficence. ***Background data:*** Chronic kidney disease is a global health problem with only 20% receiving care worldwide. Kidneys with compromised function have ongoing inflammation, including increased oxidative stress and apoptosis, peritubular capillary loss, tubular atrophy, and tubulointerstitial fibrosis. Promising studies have highlighted the significant potential of MSC-based strategies to mitigate fibrosis; however, reversal of established fibrosis has been problematic, suggesting that methods to potentiate MSC effects require further development. Laser treatments at visible wavelengths have been reported to enhance mitochondrial potential and available cellular ATP, facilitate proliferation, and inhibit apoptosis. We hypothesized that laser-delivered energy might provide wavelength-specific effects in the fibrotic kidney and enhance MSC responses. ***Materials and methods:*** Renal fibrosis, established in C57BL6 mice following 21 days of unilateral ureter obstruction (UUO), was treated with one of three wavelengths alone or with autologous MSC. Mitochondrial activity, cell proliferation, apoptosis, and cytokines were measured 24 h later. ***Results:*** Wavelengths 405, 532, and 635 nm all significantly synergized with MSC to enhance mitochondrial activity and reduce apoptosis. Proliferative activity was observed in the renal cortices following combined treatment with the 532 nm laser and MSC; endothelial proliferation increased in response to the 635 nm laser alone and to the combined effects of MSC and the 405 nm wavelength. Reductions of transforming growth factor-β were observed with 532 nm alone and when combined with MSC. ***Conclusions:*** Specific wavelengths of laser energy appear to induce different responses in renal fibrotic tissue. These findings support further study in the development of a customized laser therapy program of combined wavelengths to optimize MSC effects in the treatment of renal fibrosis.

Keywords: kidney fibrosis, laser wavelength, mesenchymal stem cell, tissue regeneration

Background

Chronic kidney disease is considered a worldwide health crisis; only 20% of affected individuals are treated worldwide.[1,2] The financial burden of ongoing treatment remains a significant obstacle to care. Strategies aimed at facilitating permanent endogenous recovery of kidney function may circumvent this obstacle. Kidneys with compromised function have developed structural changes in response to ongoing inflammation, including increased oxidative stress and apoptosis, peritubular capillary loss, tubular atrophy, and tubulointerstitial fibrosis.[3–5] Transforming growth factor-β (TGF-β) has been implicated as a key player in epithelial–mesenchymal transition, a process that contributes pathologically to fibrosis and excessive deposition of extracellular matrix.[6–8]

While mesenchymal stem cell (MSC) have shown to improve acute kidney injury, their effect in chronic fibrotic kidney disease has been less effective.[9] MSC have been reported to suppress some of the underlying inflammatory responses and oxidative stress associated with fibrosis, improve regulation of matrix deposition and remodeling, and inhibit the TGF-β pathway.[9–14] Encouraging findings have shown reduced albuminuria, collagen IV deposition, and loss of peritubular capillaries, but MSC alone could not completely reverse or restore function, despite their abilities to facilitate endothelial and epithelial proliferation.[15,16]

Departments of [1]Surgery, [2]Pathology, and [3]Transplant Surgery, University of Illinois at Chicago, Chicago, Illinois.

University of Illinois at Chicago

635nm
Mitochondrial Activity
Proliferative activity
Production of IL-10

405nm
Reduction of Apoptotic cells on fibrous tissues
Improved breakdown of scar tissue due to high eV

532nm
Reduction of TGF-B
Biggest stimulation of stem cells

SUMMARY

- For a photon to work it has to be absorbed; if it's not being absorbed it's not working
- To allow electrons to move to higher orbit, the wavelength must be between 380 nm – 683 nm
- High power vs. low power; less is proven more effective
- The lower the wavelength, the more electromagnetic transfer of energy
- Photochemistry cannot be achieved with infrared light or thermal laser

EVRL

THE MOST ENERGETIC LASER OUTSIDE THE US!

A NON-THERMAL LASER CLINICALLY PROVEN FOR REDUCING CHRONIC OR ACUTE PAIN, PROMOTE HEALING AND REDUCING INFLAMMATION VIA FDA CLEARED LEVEL ONE (510k) STUDIES

Red 635nm & Violet 405nm

Also...

- Plethora of Health/Wellbeing Advantages
- Mitochondrial Stimulation
- Promote ATP & Nitric Oxide Production
- in Damaged Tissue
- Improve overall Efficacy in Treating Skin Conditions
- Anti-Microbial Effects
- Stimulate Vagal Nerve & Gut Function

"The addition of the violet light application with the red light has revolutionized my approach to treating musculoskeletal injuries. The lights synergy has increased my clinical outcomes substantially."

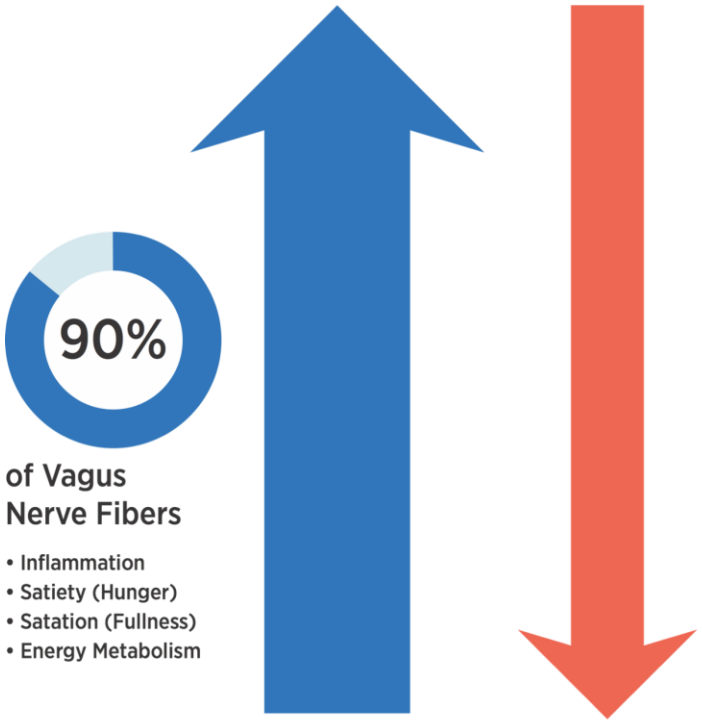
- Dr. Robert Silverman

https://www.prweb.com/releases/erchonia_receives_first_ever_fda_510k_pain_indication_using_a_violet_laser/prweb16626933.htm

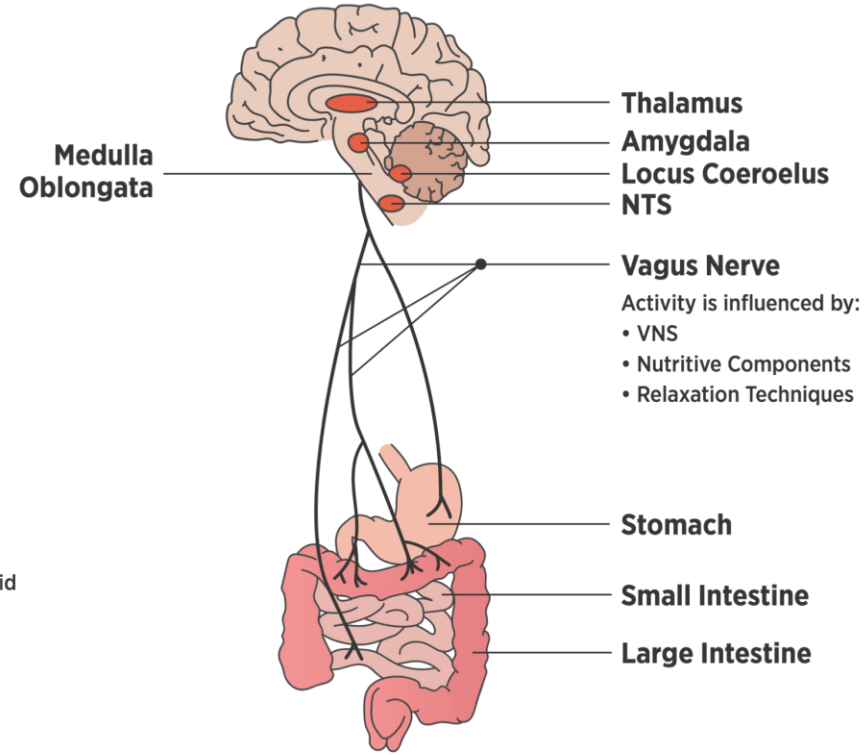

NEXT
BIG THING
AHEAD

BASIC ANATOMY AND FUNCTIONS OF THE VAGUS NERVE

AFFERENT & EFFERENT CONNECTIONS



ANATOMY

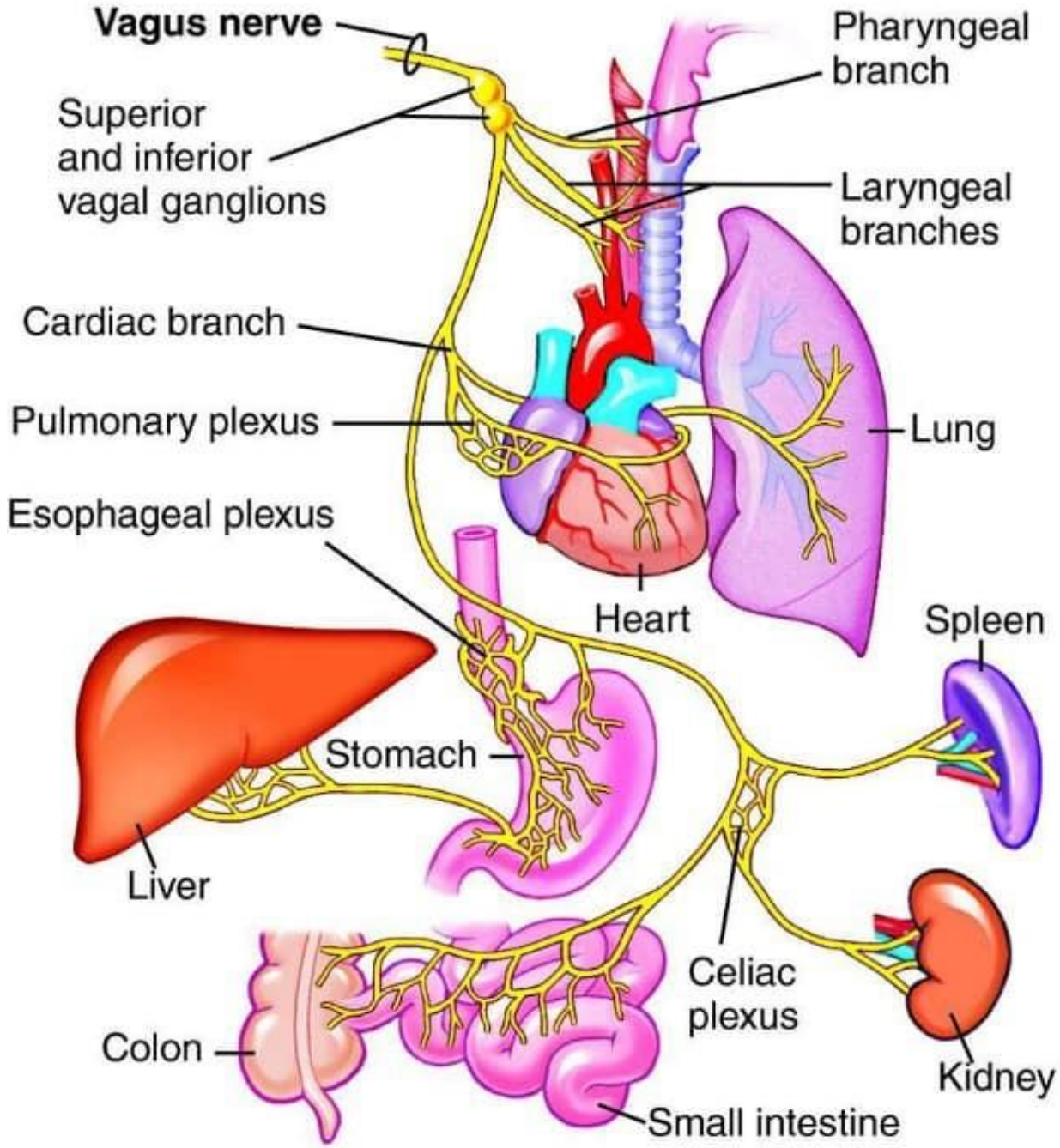


DISORDERS

Psychiatric Disorders
- Major Depression
- PTSD

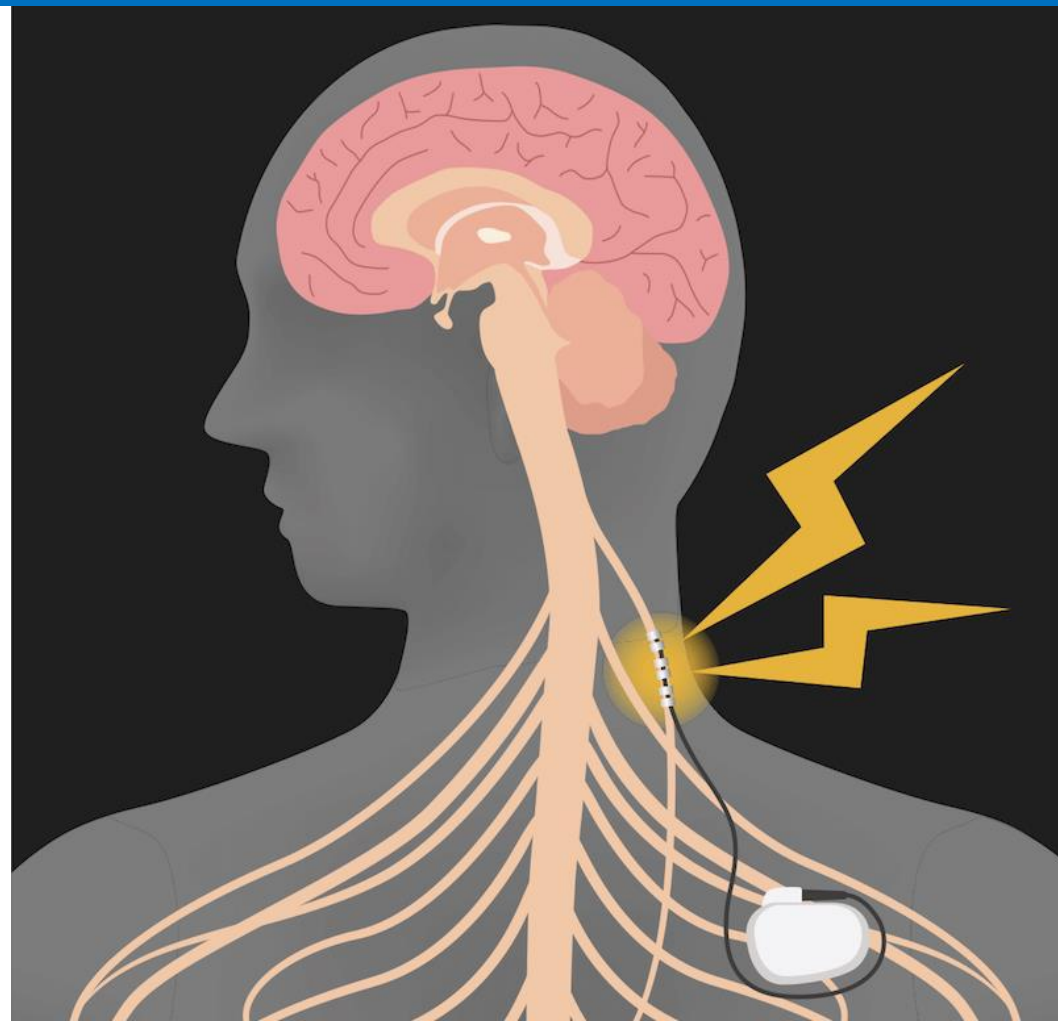
Inflammatory GI Disorders
- Ulcerative Colitis
- Crohn's Disease

Frontiers in NeuroScience. Feb 7, 2018;12:1-8


Vagus nerve
Superior and inferior vagal ganglions
Pharyngeal branch
Laryngeal branches
Cardiac branch
Pulmonary plexus
Lung
Esophageal plexus
Heart
Spleen
Stomach
Liver
Celiac plexus
Kidney
Colon
Small intestine

VAGUS NERVE STIMULATION DRAMATICALLY REDUCES INFLAMMATION

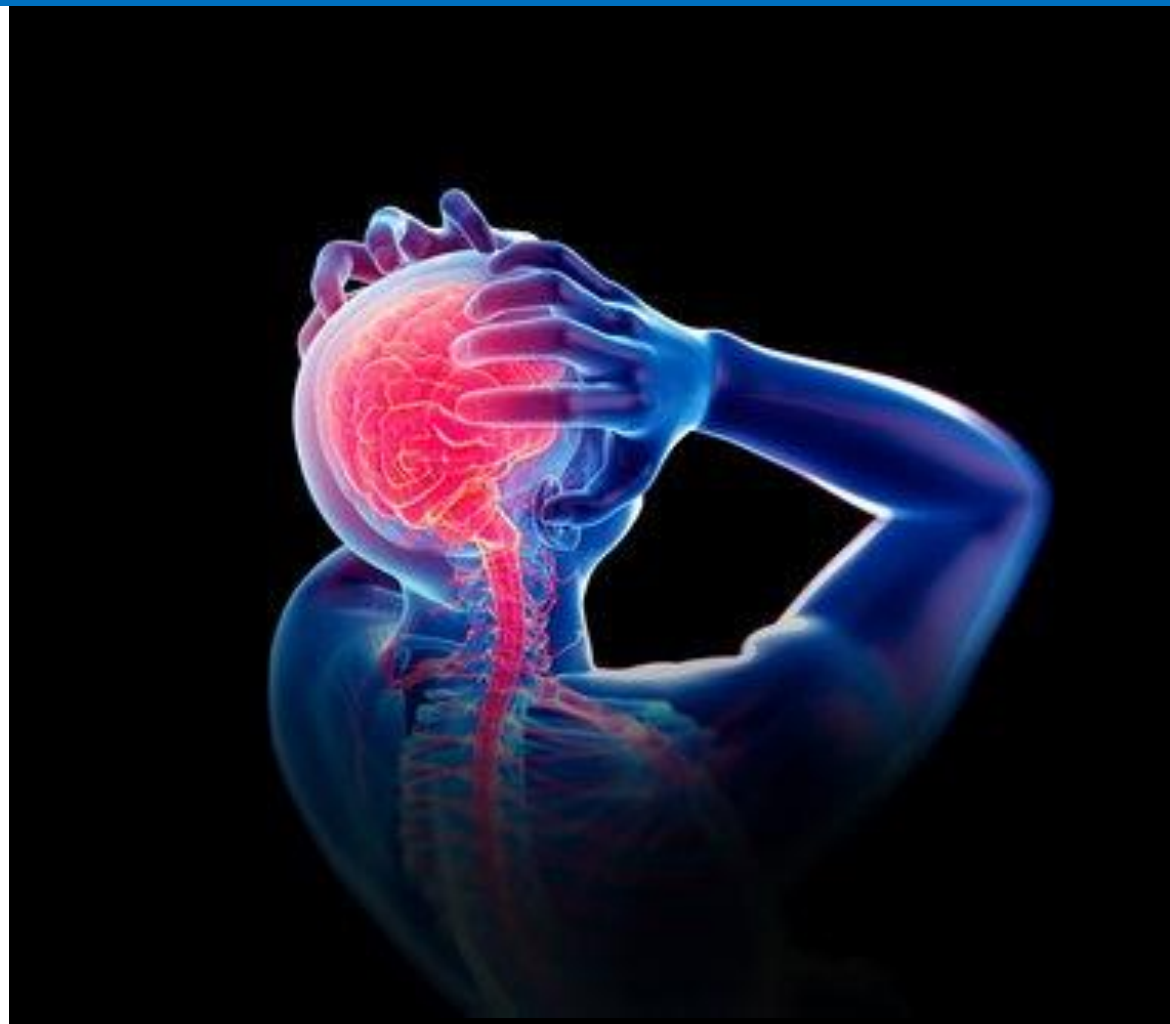
- Stimulating vagus nerve:
  - Acetylcholine
  - Reduces inflammation
  - Improves outcomes in RA
  - Inhibits cytokine production



Psychology Today. July 6, 2016

TBI - VAGUS

- Vagus nerve “rest and digest”
- PNS and SNS cannot both be dominant at the same time
- Following TBI patients find themselves in sympathetic state dominance:
  - Shutting down PNS
  - Affecting normal functionality of vagus nerve
  - Slowing digestion dramatically through mechanism of **MMC**

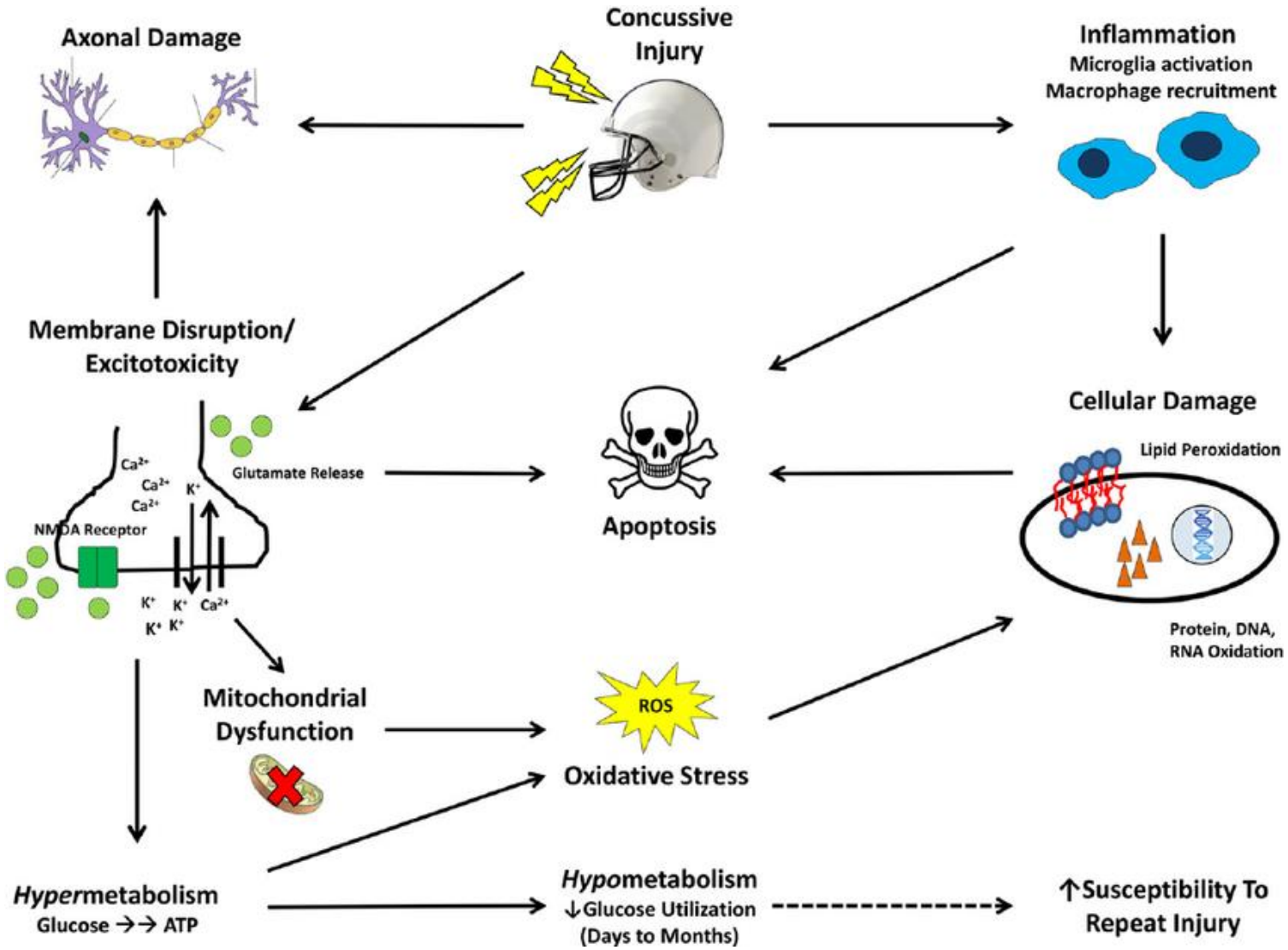


Frontiers in NeuroScience. Feb 7, 2018;12:1-8

Vagus nerve demo

The perfect 10

Molecular cascade of events after a mild traumatic brain injury



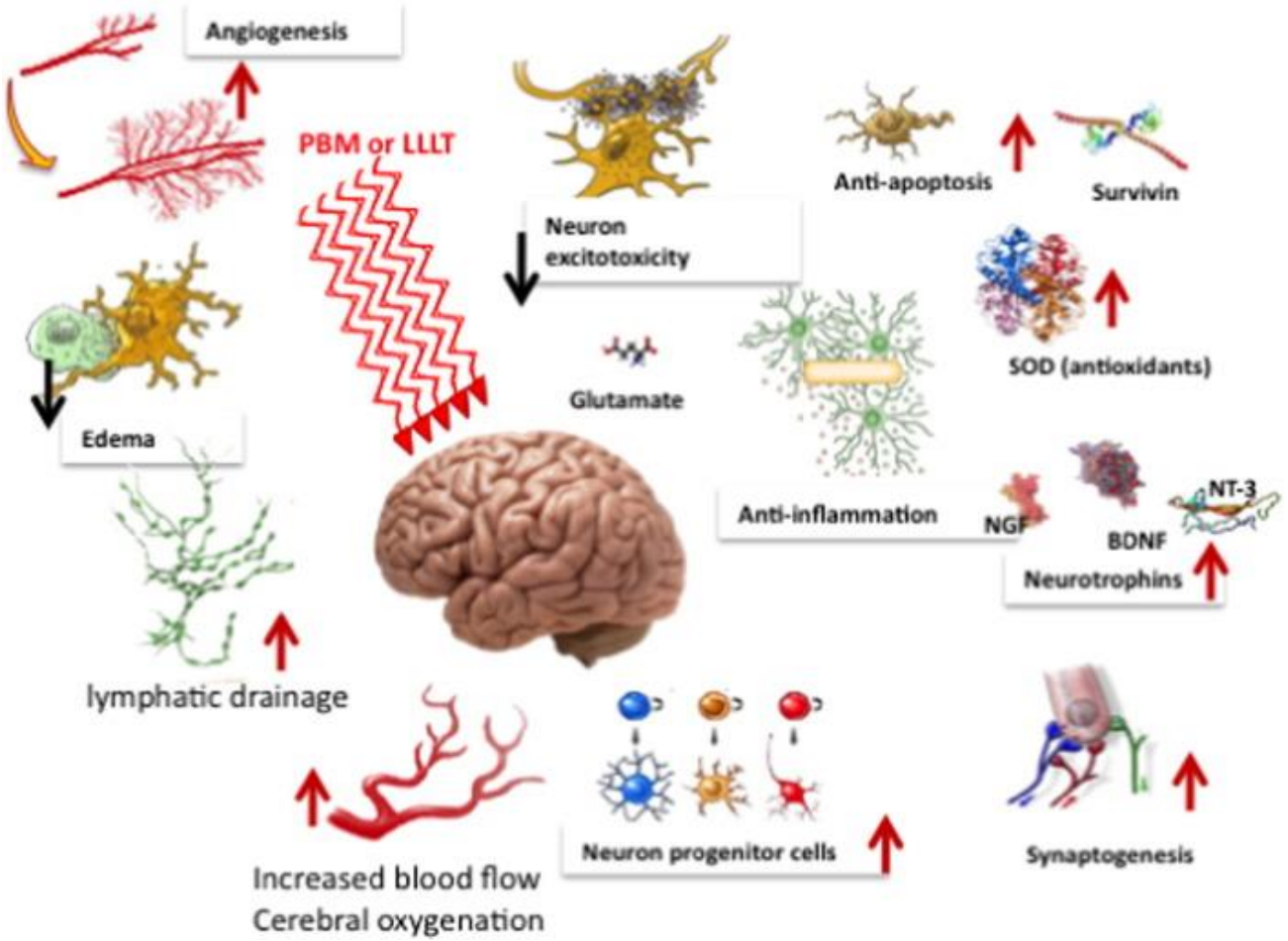
Erin Cernkovich Barrett et al. *Adv Nutr* 2014;5:268-77

Dr. Rob's Concussion Protocol

Multisystem approach:

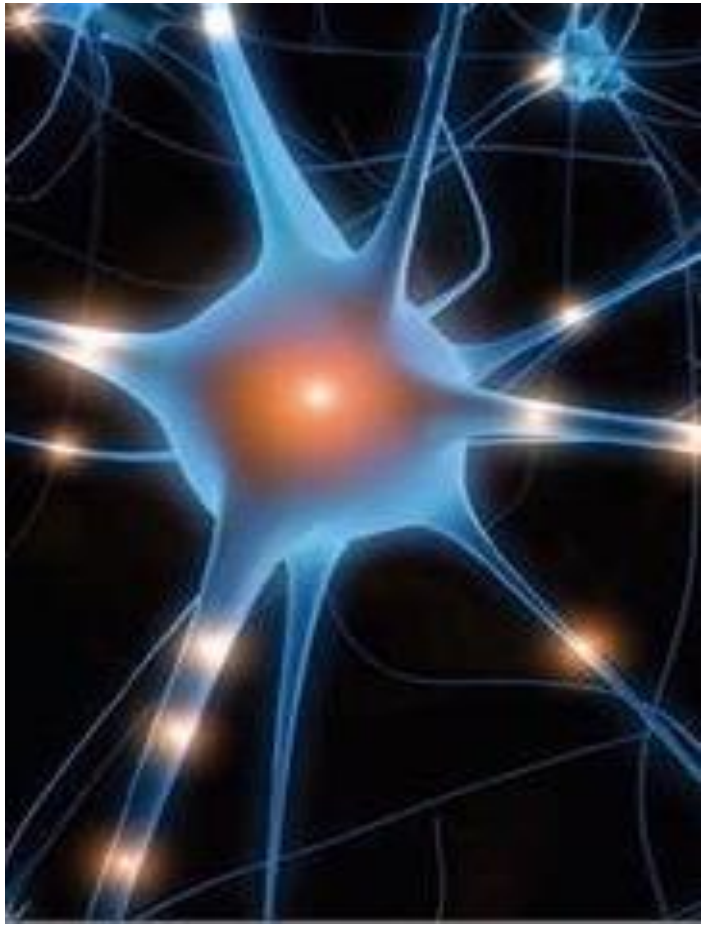
- Musculoskeletal system
- Balance
- Visual disturbances
- Laser
- Nutrition support

Shining light on the head: Non-thermal laser for brain disorders



BBA Clin. 2016 Dec;6:113-124. Published online 2016 Oct 1*Journal of Neuroscience Research*, first published 13 November 2017; 96(4):731-43

“NTL therapy suppressed pro inflammatory cytokine expression of IL-1b and IL-6… The protective effect of NTL may be ascribed to enhanced ATP production and selective modulation of pro inflammatory mediators.”



Low-level Laser effectively prevents second brain injury induced by immediate early response gene X-1 deficiency. Zhang, J *Cereb Blood Flow Metab*. 2014

Macrophages

- NTL modulates ratio of M1 & M2 macrophage phenotypes, reducing proinflammatory cytokines and chemokines, increasing anti-inflammatory cytokines, thus balance inflammation process

A Liebert, B Bicknell, W Markman, H Kiat. **A Potential Role for Photobiomodulation Therapy in Disease Treatment and Prevention in the Era of COVID-19**. *Aging and disease*, 2020/12/01;1352(11)

Violet light/NMDAR

Key takeaway:

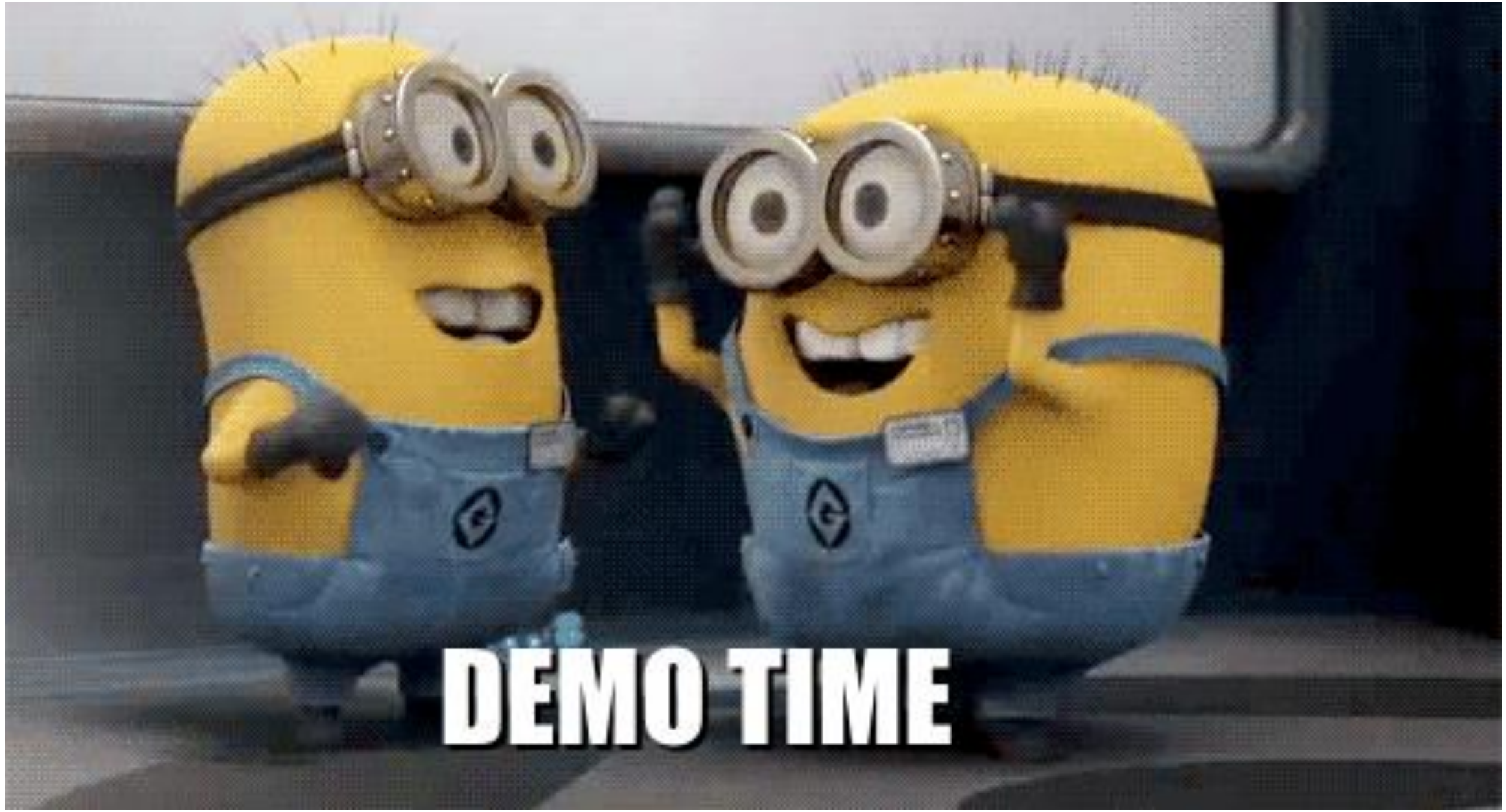
405 Nm violet light shown to effectively target NMDAR (glutamate) receptor sites in both CNS and PNS allowing for the modulation of glutamate. Ultimately, both pain and excitotoxicity were decreased

eLife 2017;6:e23545 DOI: 10.7554/ELIFE.23545

Brain facts – don’t use hot laser!

- 2% of human body mass
- 25% of body’s total glucose utilization
- 20% of O_2 consumption
- Most cerebral processes are sensitive to temperature fluctuations
- Temperature fluctuations intrinsically modulate behavioral changes and reflexively generate autonomic responses
- Hypothermia shown to protect against excitotoxicity

Wang H, Wang B, Normoyle KP, et al. **Brain temperature and its fundamental properties: a review for clinical neuroscientists**. *Front Neurosci*. 2014 Oct 8;8:307


DEMO TIME


NTL therapy for
chronic
low-back pain

FX635

- Double-blind and placebo
- 255 patients
- 49% average pain reduction post-treatment protocols
- No other therapies used
- Comparison (JAMA 2018) – 119 patients:
  - Opioids – 20%
  - Non-opioids – 26% (mainly NSAIDs)
- Implemented adjunctive therapies

FX405 – the world's MOST ADVANCED laser

1st and Only

Noninvasive Technology to receive FDA Clearance for Overall Nociceptive Musculoskeletal Pain

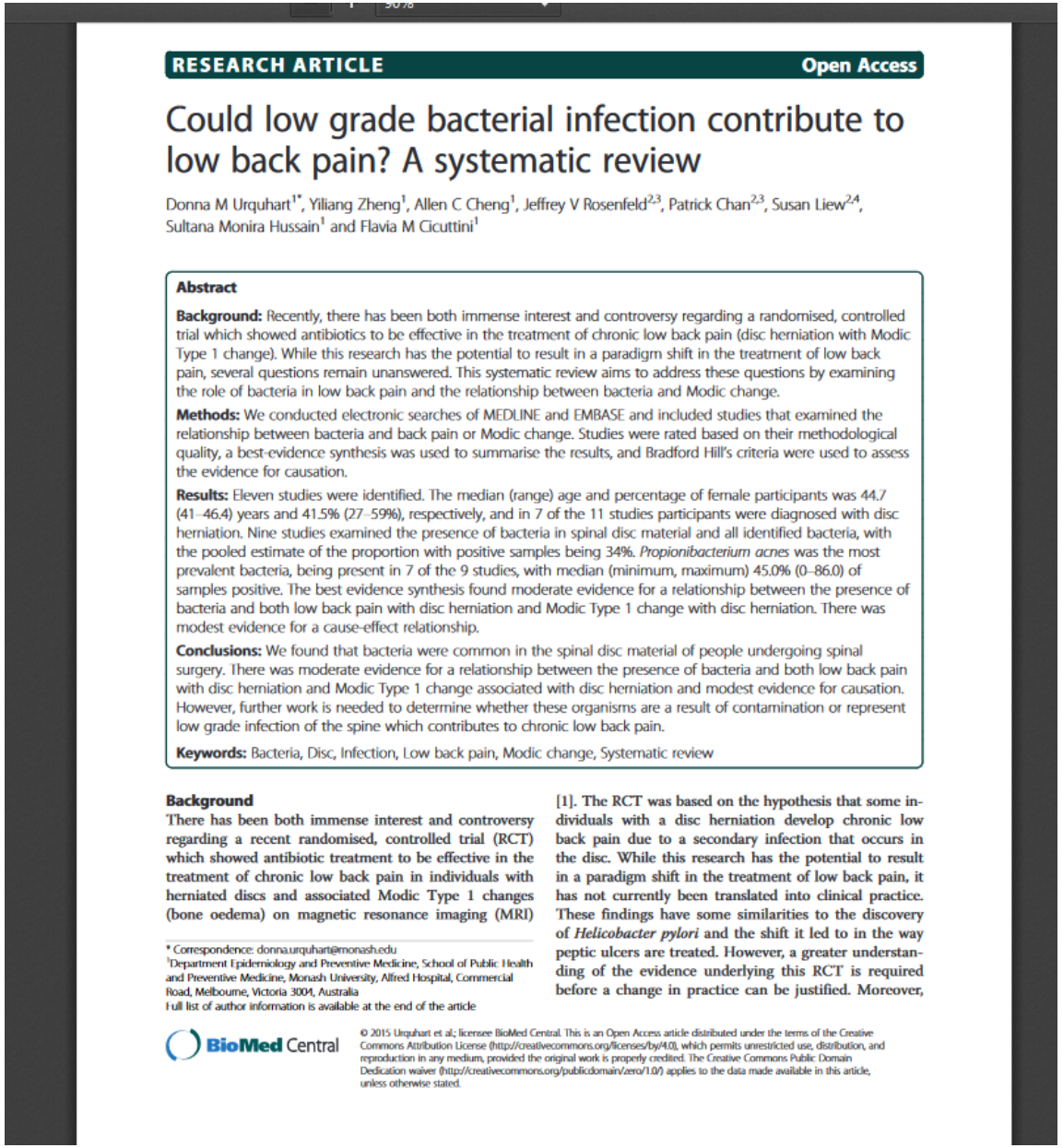
- 3 red diodes
- 1 violet diode (new)

Dr. Rob's take:

- 20% improvement in outcome
- In half the time

Testing a theory

Laser using FX635 and Violet to Treat Low Back Pain



RESEARCH ARTICLE Open Access

Could low grade bacterial infection contribute to low back pain? A systematic review

Donna M Urquhart[1*], Yiliang Zheng[1], Allen C Cheng[1], Jeffrey V Rosenfeld[2,3], Patrick Chan[2,3], Susan Liew[2,4], Sultana Monira Hussain[1] and Flavia M Cicuttini[1]

Abstract

Background: Recently, there has been both immense interest and controversy regarding a randomised, controlled trial which showed antibiotics to be effective in the treatment of chronic low back pain (disc herniation with Modic Type 1 change). While this research has the potential to result in a paradigm shift in the treatment of low back pain, several questions remain unanswered. This systematic review aims to address these questions by examining the role of bacteria in low back pain and the relationship between bacteria and Modic change.

Methods: We conducted electronic searches of MEDLINE and EMBASE and included studies that examined the relationship between bacteria and back pain or Modic change. Studies were rated based on their methodological quality, a best-evidence synthesis was used to summarise the results, and Bradford Hill's criteria were used to assess the evidence for causation.

Results: Eleven studies were identified. The median (range) age and percentage of female participants was 44.7 (41–46.4) years and 41.5% (27–59%), respectively, and in 7 of the 11 studies participants were diagnosed with disc herniation. Nine studies examined the presence of bacteria in spinal disc material and all identified bacteria, with the pooled estimate of the proportion with positive samples being 34%. *Propionibacterium acnes* was the most prevalent bacteria, being present in 7 of the 9 studies, with median (minimum, maximum) 45.0% (0–86.0) of samples positive. The best evidence synthesis found moderate evidence for a relationship between the presence of bacteria and both low back pain with disc herniation and Modic Type 1 change with disc herniation. There was modest evidence for a cause-effect relationship.

Conclusions: We found that bacteria were common in the spinal disc material of people undergoing spinal surgery. There was moderate evidence for a relationship between the presence of bacteria and both low back pain with disc herniation and Modic Type 1 change associated with disc herniation and modest evidence for causation. However, further work is needed to determine whether these organisms are a result of contamination or represent low grade infection of the spine which contributes to chronic low back pain.

Keywords: Bacteria, Disc, Infection, Low back pain, Modic change, Systematic review

Background

There has been both immense interest and controversy regarding a recent randomised, controlled trial (RCT) which showed antibiotic treatment to be effective in the treatment of chronic low back pain in individuals with herniated discs and associated Modic Type 1 changes (bone oedema) on magnetic resonance imaging (MRI) [1]. The RCT was based on the hypothesis that some individuals with a disc herniation develop chronic low back pain due to a secondary infection that occurs in the disc. While this research has the potential to result in a paradigm shift in the treatment of low back pain, it has not currently been translated into clinical practice. These findings have some similarities to the discovery of *Helicobacter pylori* and the shift it led to in the way peptic ulcers are treated. However, a greater understanding of the evidence underlying this RCT is required before a change in practice can be justified. Moreover,

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[1]Department Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Alfred Hospital, Commercial Road, Melbourne, Victoria 3004, Australia
Full list of author information is available at the end of the article

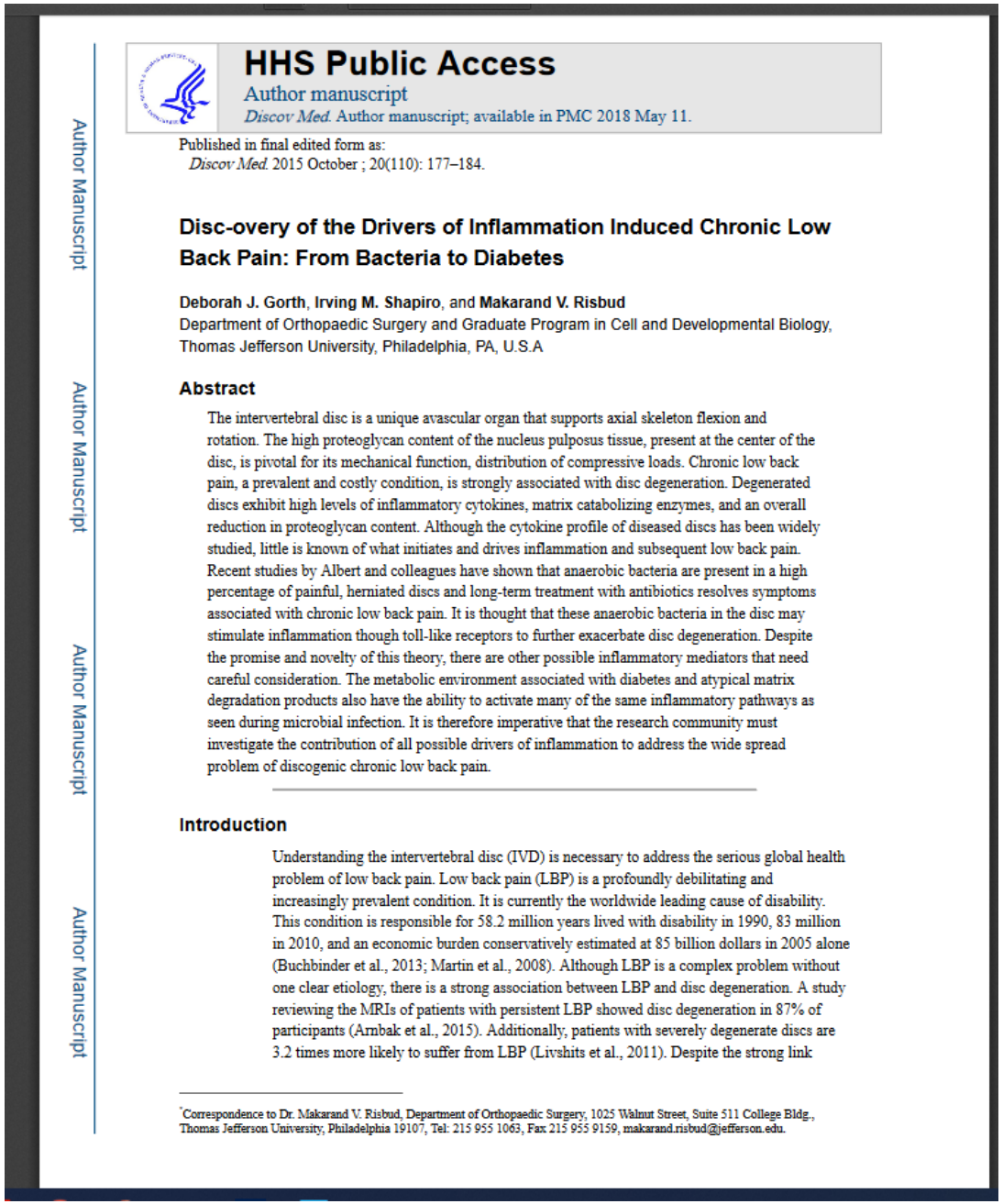
Conclusion:

- Bacteria common in spinal disc material of people undergoing spinal surgery

- Moderate evidence for relationship between presence of bacteria and both low back pain with disc herniation and Modic Type 1 change associated with disc herniation

- Modest evidence for causation

Urquhart, D.M., Zheng, Y., Cheng, A.C. *et al.* Could low grade bacterial infection contribute to low back pain? A systematic review. *BMC Med* **13,** 13 (2015)



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Disc-overy of the Drivers of Inflammation Induced Chronic Low Back Pain: From Bacteria to Diabetes

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Abstract

The intervertebral disc is a unique avascular organ that supports axial skeleton flexion and rotation. The high proteoglycan content of the nucleus pulposus tissue, present at the center of the disc, is pivotal for its mechanical function, distribution of compressive loads. Chronic low back pain, a prevalent and costly condition, is strongly associated with disc degeneration. Degenerated discs exhibit high levels of inflammatory cytokines, matrix catabolizing enzymes, and an overall reduction in proteoglycan content. Although the cytokine profile of diseased discs has been widely studied, little is known of what initiates and drives inflammation and subsequent low back pain. Recent studies by Albert and colleagues have shown that anaerobic bacteria are present in a high percentage of painful, herniated discs and long-term treatment with antibiotics resolves symptoms associated with chronic low back pain. It is thought that these anaerobic bacteria in the disc may stimulate inflammation though toll-like receptors to further exacerbate disc degeneration. Despite the promise and novelty of this theory, there are other possible inflammatory mediators that need careful consideration. The metabolic environment associated with diabetes and atypical matrix degradation products also have the ability to activate many of the same inflammatory pathways as seen during microbial infection. It is therefore imperative that the research community must investigate the contribution of all possible drivers of inflammation to address the wide spread problem of discogenic chronic low back pain.

Introduction

Understanding the intervertebral disc (IVD) is necessary to address the serious global health problem of low back pain. Low back pain (LBP) is a profoundly debilitating and increasingly prevalent condition. It is currently the worldwide leading cause of disability. This condition is responsible for 58.2 million years lived with disability in 1990, 83 million in 2010, and an economic burden conservatively estimated at 85 billion dollars in 2005 alone (Buchbinder et al., 2013; Martin et al., 2008). Although LBP is a complex problem without one clear etiology, there is a strong association between LBP and disc degeneration. A study reviewing the MRIs of patients with persistent LBP showed disc degeneration in 87% of participants (Arnbak et al., 2015). Additionally, patients with severely degenerate discs are 3.2 times more likely to suffer from LBP (Livshits et al., 2011). Despite the strong link

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Conclusion:

- Data suggests anaerobic p. acnes could induce inflammatory effects on intervertebral disc through TLR signaling

- Understanding contribution and interplay between all inflammatory drivers - responsible and effective treatment for low back pain

Gorth DJ, Shapiro IM, Risbud MV. **Discovery of the drivers of inflammation induced chronic low back pain: from bacteria to diabetes**. *Discov Med.* 2015 Oct;20(110):177-84

Is infection the possible initiator of disc disease?

Conclusion:

Study demonstrates bacterial specific proteins and host defense proteins to infection which strengthen hypothesis of infection as possible initiator of disc disease

S Rajasekaran, C Tangavel, SN Aiyer, *et al.* ISSLS PRIZE IN CLINICAL SCIENCE 2017: **Is infection the possible initiator of disc disease? An insight from proteomic analysis**. *Eur Spine J*, 6 Feb 2021;26:1384–1400

Low level light therapy (LLLT) modulates inflammatory mediators secreted by human annulus fibrosus (AF) cells during intervertebral disc degeneration in vitro

Key Takeaway:

- Inflammatory microenvironment in AF cells suppressed by LLLT (IL-6 and 8 levels)
- Results indicate LLLT is potential method of IVD treatment
- 405 NM – most positively affected IL-6

Photochem Photobiol 2015, Mar-Apr;91(2):403-10

Effectiveness of LLLT in patients with discogenic lumbar radiculopathy

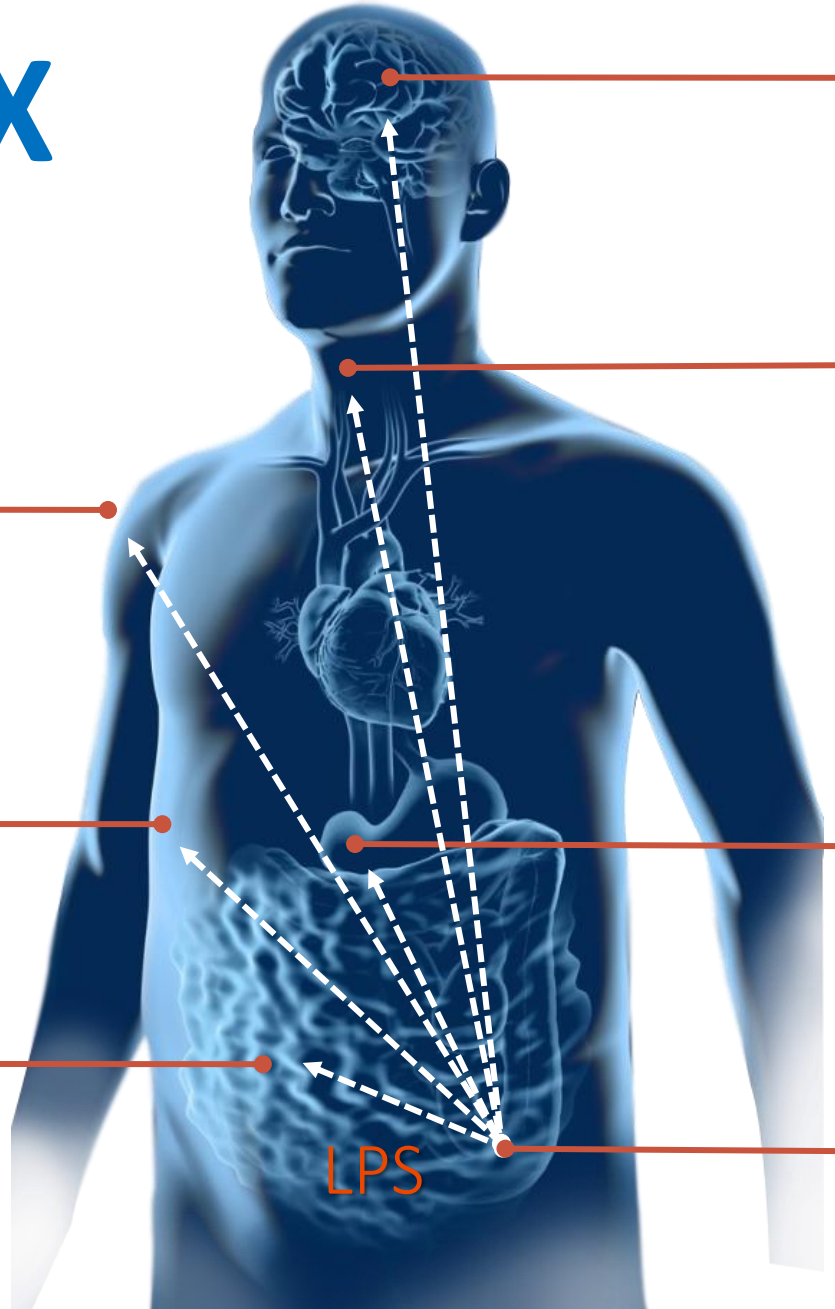
- 110 patients
- 55 patients treated with LLLT and conventional PT
- 55 patients treated with conventional PT alone
- Both groups received 18 treatment sessions

Results: LLLT/PT group had significant improvements over PT alone:

- Local trunk movements
- Pain intensity
- Related functional disability
- No side-effects after LLLT use

Ahmed I, Bandpei MAM, Gilani SA, et al. **Effectiveness of Low-Level Laser Therapy in Patients with Discogenic Lumbar Radiculopathy: A Double-Blind Randomized Controlled Trial**. *J Healthc Eng*. 2022 Feb 27;2022:6437523

Dr. Rob's GUT MATRIX



BRAIN
- ↓ Satiety
- ↑ Inflammatory
- ↑ Neurodegeneration

THYROID
- ↑ Hashimoto's disease
- ↓ Thyroid hormone levels

MUSCULOSKELETAL SYSTEM
- ↑ Arthritis/Joint pain
- ↑ Soft-tissue injury
  - Cytokines, MMPS

LIVER
- Liver dysfunction
- Toxins/chemical overload

BODY COMPOSITION
- Obesity

GI TRACT
- Food sensitivities
- Leaky gut syndrome
- Yeast/Fungus
- Dysbiosis (↓ Good bacteria)

INSULIN
- Blood sugar problems
- Insulin resistance
- Pre-diabetes/diabetes

Photobiomics ability to alter microbiome

- Laser light can affect the microbiome indirectly through the daily circadian rhythm
- Circadian clock regulating levels of metabolites, including those from the microbiome, which in turn can affect metabolome
- Disrupted circadian rhythm on microbiome shows that bacteria responsible for decreased gut integrity and increased LPS occurs
- Favorable improvement in good bacteria (400 fold)
- Significant difference in microbial diversity between PBM and sham

Liebert A, Bicknell B, Johnstone DM, et al. **"Photobiomics": Can Light, Including Photobiomodulation, Alter the Microbiome?**. *Photobiomodul Photomed Laser Surg*. 2019;37(11):681-693

Laser light inhibits biofilm formation in vitro and in vivo by inducing oxidative stress

- Blue (violet) light – efficacy in decreasing viability of various bacterial species:
  - *Pseudomonas aeruginosa*
  - *Porphyromonas gingivalis*
  - *Helicobacter pylori*
  - *Staphylococcus aureus* (MRSA)

Result:

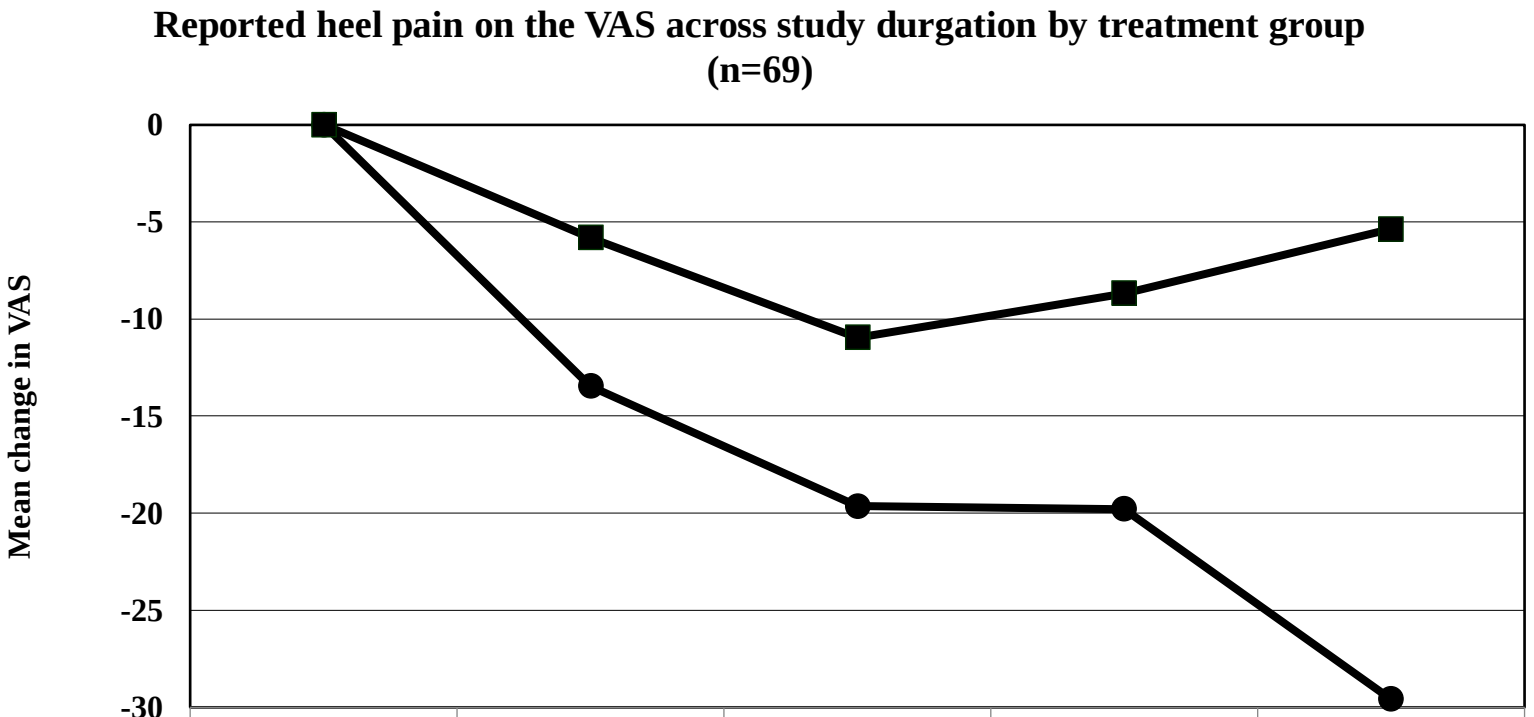
- Blue (violet) laser light exerts direct antimicrobial activity on *P. aeruginosa* grown in planktonic state, on solid surfaces and as biofilms

K Rupel, L Zupin, G Ottaviani, *et al.* **Blue laser light inhibits biofilm formation in vitro and in vivo by inducing oxidative stress**. *npj Biofilms Microbiomes,* 9 Oct 2019;5:29

Plantar Fasciitis Laser Protocol

- 2 treatments a week for 3 weeks
- Area- top of foot (Dorsal Aspect), the myofascial junction of the heel and the plantar aspect of the heel
- All treated simultaneously. 10 minutes per area

Chronic Heel Pain Plantar Fasciitis



	Baseline	Week 1	Week 2	Week 3	Endpoint
Test	0	-13.47	-19.65	-19.79	-29.58
Placebo	0	-5.82	-10.96	-8.68	-5.38

Efficacy of LLLT with lower extremity tendinopathy or PF

Conclusion:

LLLT significantly reduces pain and disability in lower extremity tendinopathy and plantar fasciitis in the short and medium term

Naterstad IF, Joensen J, Bjordal JM, et al. **Efficacy of low-level laser therapy in patients with lower extremity tendinopathy or plantar fasciitis: systematic review and meta-analysis of randomised controlled trials**. *BMJ Open*. 2022 Sep 28;12(9):e059479

LLLT treatment in patients with frozen shoulder

Results: Laser vs. placebo group

- Significant decrease in overall, night, and activity pain scores at end of 4, 8, 16 weeks
- Significant decrease in shoulder pain and disability index (SPADI) scores end of 4, 8, 16 weeks
- Significant decrease in disability of arm, shoulder, and hand questionnaire (DASH) scores at the end of 8 and 16 weeks
- Significant decrease in HAQ scores at end of 4 & 8 weeks

Stergioulas A. **Low-power laser treatment in patients with frozen shoulder: preliminary results**. *Photomed Laser Surg*. 2008 Apr;26(2):99-105

Efficacy of LLLT for shoulder tendinopathy

Conclusion:

- 17 randomized controlled trials (RCTs)
- Optimal LLLT can offer clinically relevant pain relief and initiate a more rapid course of improvement, both alone and in combination with physiotherapy interventions

Haslerud S, Magnussen LH, Joensen J, et al. **The efficacy of low-level laser therapy for shoulder tendinopathy: a systematic review and meta-analysis of randomized controlled trials**. *Physiother Res Int*. 2015 Jun;20(2):108-25

LLLT combined with exercise for subacromial impingement

Conclusion:

LLLT combined with exercises:

- Reduce pain intensity
- Improve shoulder function
- reduces medication intake over 3 months

Alfredo PP, Bjordal JM, Junior WS, et al. **Efficacy of low-level laser therapy combined with exercise for subacromial impingement syndrome: A randomised controlled trial.** *Clin Rehabil*. 2021 Jun;35(6):851-860

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Is Transcranial Laser Therapy effective in acute phase recovery post TBI?

Low level laser therapy (LLLT) effective in reduction of pain, swelling and inflammation Chung. Ann *Biomed*, 2012, improves cerebral circulation Tian. *Lasers Surg Med* 2016 and
may "significantly improve neural function, decreased lesion volume, augment cell proliferation and even protect the brain against neuronal damage." Xuan W, et al. *Transcranial LLLT improves neurological performance in TBI in mice*, PlosOne

Is Transcranial Laser Therapy efficacious in acute phase recovery post TBI?

- Low Level Laser therapy improves neurological performance in TBI (PLoS One, 2013)
- Treatment can stimulate growth of new nerve tissue (Xuan W, et al. *Transcranial LLLT enhances learning, memory, and neuroprogenitor cells after TBI in mice*, J Biomed Opt, 2014 Oct(10);19)
- Also been shown to modulate oxidative stress and nitric oxide production (Manchini. PLoS One, 2014. Chen. PLoS One, 2011)
- LLLT down-regulates pro-inflammatory microglial cytokine expression (Song, 2012)

Is Transcranial Laser Therapy efficacious in acute phase recovery post TBI? (cont'd)

- 635 nm LLLT modulates NF-kB signaling pathways (Lim, 2013)
- Laser shown to mitigate cell apoptosis (Moreira, 2011)
- Transcranial Laser Therapies researched in stroke injury (Naeser, 2011and Lampl 2007) and in clinical trials (Stemer, 2010)
- LLLT improves cognitive deficits and inhibits microglial activation after controlled cortical impact in mice (*J Neurotrauma*, 2012 Jan 20)

LLLT for BDNF

Conclusion: Benefit of LLLT to the brain is mediated by stimulation of BDNF production, which may in turn encourage synaptogenesis.

LLLT may have applications for neurodegenerative conditions

Xuan W, Agrawal T, huang L, et al. *J Biophotonics*. 2015 Jun;8(6):502-11

Study suggests upregulation of BDNF with LLLT can ameliorate AB-induced neurons loss and dendrite atrophy. Thus, identifying a novel pathway by which LLLT protects against AB-induced neurotoxicity

J Mol Neurosci 2013 Aug 14;33(33):13505-17