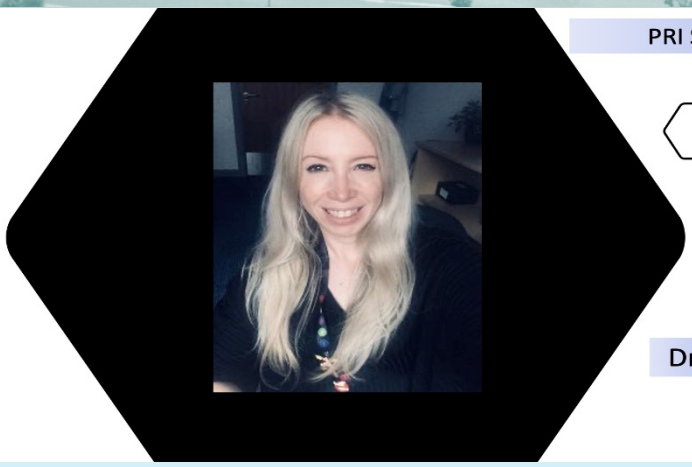
UNIVERSITY OF LIVERPOOL
The Walton Centre NHS
NHS Foundation Trust
Excellence in Neuroscience
November 2021

Pain Research Institute

This is the Pain Research Institute newsletter, the purpose of which is to keep researchers and clinicians informed of the current research going on in the institute. We hope this will enable clinicians to identify areas of research that they may be interested in whilst keeping informed about studies opening to recruitment as they may have pain patients they wish to refer.



PRI SPOTLIGHT

Dr Katie Herron

Dr Katie Herron (Consultant Clinical Psychologist) has recently joined the Pain Management Programme (PMP) Department at The Walton Centre. In addition to her clinical work, she is PMP Research Lead with a key agenda to drive PMP themed projects within the service well as establish external collaborations across academic institutions and other NHS departments. After attaining a Psychology Undergraduate Degree at The University of Liverpool and working for a year as a part-time research assistant in cognitive neuroscience and health care assistant, she was awarded an ERSC grant to study for MSc and PhD at The University of Surrey. Her PhD thesis explored the role of sleep in post-stroke rehabilitation. In order to pursue her chosen career directly working psychologically with patients, she completed a Doctorate in Clinical Psychology at Royal Holloway, University of London. Her enthusiasm for working in pain services sparked during her final year placement at The Pain Management Centre, University College London Hospitals, where she stayed for 6 years. The North West drew her back in 2018 where she took a Principal Clinical Psychologist post within The Pain Medicine Department at The Royal Liverpool prior to her consultant post at Walton. Her main research interests include specialist PMP development and outcomes, opioid management, inpatient pain management psychology (acute & chronic pain), prehabilitation and prevention, pain management in primary care, sleep management in chronic conditions and neuroplasticity in the context of behavioural change.


Dr. Andreas Goebel, Reader in Pain Medicine & Director of the PRI


Francis McGlone, Professor in Neuroscience, School of Natural Sciences & Psychology, Liverpool John Moores University


Dr. Bernhard Frank, Consultant in Pain Medicine and Anaesthesia
Walton Centre NHS Foundation Trust


Selina Johnson, Clinical Research Fellow


Manohar Lal Sharma, Consultant in Pain Medicine, Walton Centre NHS Foundation Trust

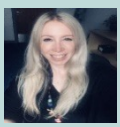

Andy Marshall, Senior Lecturer UOL & Consultant in Pain Medicine, Walton Centre NHS Foundation Trust


Uazman Alam, senior Clinical Lecturer in Diabetes & Endocrinology


Francis O'Neill, Senior Lecturer and Honorary Consultant in Oral Surgery


Helen Poole, Prof. in Applied Health Psychology, Liverpool John Moores University


Serena Sensi, Research Technician at the Rheumatology Laboratory, U**niversity** Hospital Aintree


Katie Herron Specialist Clinical Psychologist & Research Lead for Pain Management Programmes


Hayley McCullough, PRI Administrator

If you would like to add to our newsletter please contact Hayley.McCullough@Liverpool.ac.uk

NIHR Grant success

The Utility Of Frequency-Modulated Electromagnetic Neural Stimulation (FREMS) As A Third Line Treatment In Patients With Painful Diabetes-Related Peripheral Neuropathy: A Randomised Controlled Trial (FREMS-PDPN)

NIHR have now accepted the final submission for funding with Dr Bernhard Frank as new chief Investigator

Scientific Abstract

Research question: Is Frequency Rhythmic Electrical Modulated System (FREMS) an effective treatment in patients with painful diabetic peripheral neuropathy (PDPN) and persistent pain despite trying at least two PDPN medications?

Background. PDPN affects 25% of people with diabetes and 70% of sufferers have moderate-to-severe pain. PDPN is associated with sleep disruption, poor quality of life (QoL), unemployment and depression. The average health care cost of PDPN in the UK is £2,511per patient per year, which increases with greater pain severity. The burden of PDPN is likely to increase with increasing diabetes prevalence.

National Institute for Health and Care Excellence (NICE) guidance 173 recommended certain medications as initial treatments for PDPN. However, using these medications result in 50% reduction in pain in 33% of patients at best. These medications also have multiple significant side effects (such as weight gain, falls, urinary retention, constipation). Beyond these drugs, there are no NICE recommended treatments. As a result, many patients (43%) receive opioids, which have many unwanted side effects including addiction.

There is a clear need to identify a safe, well-tolerated, non-invasive, effective and cost- effective intervention in those who fail to respond to NICE recommended treatments. This could reduce medications and opioid use and improve QoL.

Aims and objectives

Efficacy objectives: 1. To evaluate the efficacy of FREMS using 11-point Likert numerical rating scale (NRS) 24-hour pain scores (0 to 10) averaged over the last 7 days (primary outcome). 2. Other outcomes: sleep, QoL and medication use amongst others. 3. To evaluate the cost effectiveness of FREMS in PDPN.

Safety objectives: To describe Adverse Events and Serious Adverse Events data (summarised both at patient level and event level).

Exploratory objectives: To investigate if patient phenotypes (demography, diabetes type, type of pain based on Neuropathic Pain Symptom Inventory [NPSI], mood, sleep) predict response to treatment.

Methods (please see flowchart in the uploads)

Design: A multi-centre 2-arm parallel group double blind RCT. The RCT will include an internal pilot with stop/go criteria.

Setting: Patients will be recruited from 10 NHS Trusts that have PDPN services and the aligned primary care and podiatry services, as well as social media and Diabetes UK local patient groups. The study device will be placed in the hospital.

Population: Adults with PDPN for ≥3 months with significant pain (a mean total pain NRS ≥4 for the week before randomisation) despite trying at least 2 classes of medications.

Intervention: FREMS+ standard care

Comparator: TENS (Transcutaneous Electrical Nerve Stimulation)+ standard care Outcome: As above. The primary outcome is at 3 months and study end at 6 months.

Timelines: Protocol, database & CRFs: months 1-8; HRA, REC, MHRA approvals: 5-9; Site set-up: 8-13; Recruitment: 10-29; Follow-up: 13-35, Data Cleaning: 35-38; Analysis & dissemination: 36-41; Health economic analysis: 36-41; Final report: 41

Anticipated impact: The trial is designed to address gaps identified by NICE multiple technology appraisal (MTA) of FREMS in 2017. Hence the trial is likely to lead to a NICE TA

Dissemination: Via peer-reviewed articles, national/international presentations, Diabetes UK patients groups and social media. The investigators will liaise with the manufacturer & NICE. Study participants will be informed of the findings.

Publication Success

Selina Johnson has had an exciting paper published titled "**Mechanistically informed non-invasive peripheral nerve stimulation for peripheral neuropathic pain: a randomised double-blind sham-controlled trial"**

This is available to read in the publication section of the PRI website

Patient & Public Involvement

PPI has always been important to us at PRI. We have been holding regular PPI groups for over 10 years and have even won a University award for our PPI involvements.

The most recent PPI initiatives have been

- Dr Nick Fallon and the relationship between psychological trauma and autoimmune mechanisms for developing chronic pain
- Dr Charlotte Krahe and Therapeutic Plasma Exchange' (TPE) can improve fibromyalgia syndrome (FMS).

On Friday 15th October we held **the 3rd Liverpool and North West Pain Research Institute research and publication day** and we would like to thank all who attended.

As expected it was a spectacular event with researchers from around the North-West presenting their studys, trials and findings.

The meeting gives researchers the opportunity to come together and discuss ideas and suggestions on the future research of pain.

We plan to hold this meeting approx every 18 months and information on the next PRI Research day will be available on the news section of the PRI website when a date has been confirmed

If you wish to sign up for this event then please contact Hayley.McCullough@liverpool.ac.uk

The Pain Relief Foundation are pleased to announce, that 2022 new round of grant applications is now open.

The Pain Relief Foundation provide grants to fund research on the mechanism and/or relief of human chronic pain and they are pleased to announce both small grants and a Prof John Miles Prize PhD Studentship are available.

The available grants have been publicised online with ResearchResearch.com, with the University of Liverpool and other University press newsletters.

The closing date for applications is 22nd February 2022, please contact Julie Williams on 0151 529 5820 or email julie.williams@painrelieffoundation.org.uk to request an application form

To add to the PRI newsletter then please contact Hayley.McCullough@Liverpool.ac.uk

Research Studies…. To name a few

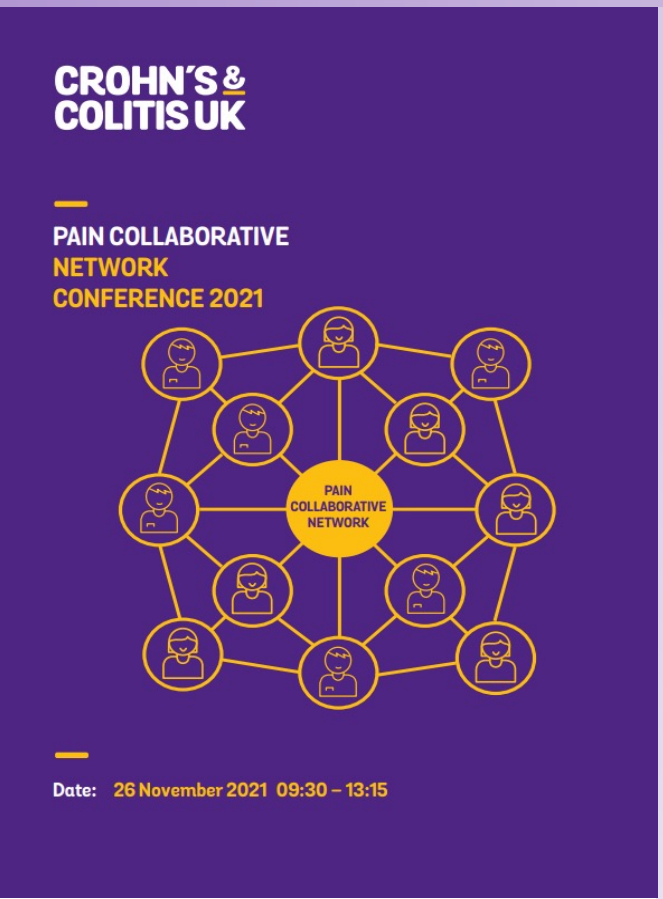
- Investigating Diabetic Neuropathy During Initiation of Intensive Glycaemic Control
- The Utility of Non-Invasive Ocular Imaging in Diabetic Foot Disease
- A Multicentre, double-blind, centre-stratified multi-period crossover trial to evaluate the efficiency of the Optimal Pathway for Treating neuropathic pain in Diabetes Mellitus (OPTION-DM)

- **Pain Relief Foundation Studentship-**A study looking into validity of confocal corneal microscopy in patients with painful chemotherapy induced and idiopathic small fibre neuropathy.

For more information on all of the above studies please contact the Principal Investigator on Ualam@Liverpool.ac.uk

- **Serum IgG autoantibodies in patients with Fibromyalgia-**We require 100 patients with a diagnoses of FMS (>1year), without other conditions, we will be collecting blood to be used in laboratory experiments. Principal investigator at **andreasgoebel@rocketmail.com**

- **Define-FMS- *77 patients – 28 of these for Microneurography and 1 year follow up.*** Main aim is to understand how nerve damage occurs in the nerves in the front of the eye and compare this to the nerves in the skin to determine if the eye examination is as good as skin biopsy. Contact anne.marshall@liverpool.ac.uk for more information
- **A qualitative study into the experience and outcomes of those attending a specialist facial pain management programme-**Three focus groups have been carried out exploring the experiences of services users attending a specialist facial pain management programme.
- **Doctorate Clinical Psychology trainee project-** How do people with fibromyalgia relate to their romantic partners? A qualitative study' Principal Investigator **Sean.Harris@thewaltoncentre.nhs.uk**
- A study for long term benefit of Spinal Cord Stimulator **–**Principal Investigator **Bernhard.frank@thewaltoncentre.nhs.uk**



Chrohns & Colitis UK Pain Collaborative network conference 2021

On 26 November 2021, Crohn's & Colitis UK will be hosting its second Pain Collaborative Network event. They plan to run three workshops on visceral pain – pain in or around internal organs with themes including: mechanisms of visceral pain and novel targets for treatment; clinical assessment of pain; and psychological treatments for pain For further details see https://www.crohnsandcolitis.org.uk/research/projects-pain-collaborative-research-network/pain-collaborative-network-conference-2021

LJMU have a new neuropsychology suite opening soon in the Life lab. In Collaboration with innovation lead Grahame Smith & David Tully of Scenegraph Ltd to provide virtual reality cognitive training as part of their on-going research to strengthen neural processes of impulse control. Once operational (likely end of Nov 21) they will invite staff & students interested to make a booking with the aim of strengthening their "will power"

The SPIRIT-iNeurostim and CONSORT-iNeurostim Working Group

Dear Colleague,

We would like to ask for your contribution in developing reporting guidelines for clinical trial protocols and reports of implantable neurostimulation devices: the **SPIRIT-iNeurostim** and **CONSORT-iNeurostim** extensions.

By taking part in our survey, you will help us to develop **guidelines for reporting clinical trials of implantable neurostimulation devices.** The survey will ask for your views on the most important items that should be reported by clinical trials of implantable neurostimulation devices.

We are particularly interested in the views of people who

have a condition that can be treated using an implantable neurostimulation device;

have experience of using an implantable neurostimulation device;

care for somebody who has a condition that can be treated using an implantable neurostimulation device or who is actively using an implantable neurostimulation device;

have expertise in implantable neurostimulation devices;

have expertise and are interested in trials reporting and methodology (e.g., journal editors, statisticians, methodologists);

are interested in the reporting of clinical trials of implantable neurostimulation devices (e.g., journal editors, representatives from pain and neurostimulation societies, companies who develop implantable neurostimulation devices).

You decide whether to take part. The survey does not ask for personal information. All data will be stored securely and deleted once the project reports have been published.

The Participant Information Sheet attached gives further information about the study and what would be involved if you choose to participate.

If you have any questions that you would like to ask, please contact:

Rui Duarte
Email rduarte@liverpool.ac.uk
Telephone +44 (0)151 794 5726
Rebecca Bresnahan
Email rebecca.bresnahan@liverpool.ac.uk
Telephone +44(0) 151 529 5949

Time to complete the survey will vary depending on how much you want to say. We anticipate it will take between 15 to 30 minutes. The survey will close on **Tuesday 30th November 2021**.

Please access the survey via the link below:

https://delphimanager.liv.ac.uk/ineurostim/Delphi

It is important that we capture a wide range of views and so **we encourage you to share the link widely with anyone you consider may have an interest in this project.**

We would like to congratulate 2 of our colleagues for their recent promotions

Dr David Moore is now a Reader in Pain Psychology at LJMU working in the Somaffect group

Helen Poole is now a Professor of Applied Health Psychology at LJMU

Well done to you both

The PRF would like to thank everyone who attended and supported their fundraising night in October. This fantastic night was thanks to friends and family donating raffle prizes and to the amazing businesses for their grand donations and support. They raised £1323.90 on the night and are forever grateful

The next edition of this newsletter will be in February 2022 if you would like to share anything then please email Hayley.McCullough@liverpool.ac.uk