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SIX MONTH RESEARCH REPORT RE: GRANT FUNDED BY PAIN RELIEF FOUNDATION

In the past six months my PhD project funded by the Pain Relief Foundation has grown to include three main projects and contributions to other research fellows' work. My primary focus is in the following project title:

1.) Defining Small Fibre Neuropathy and Neuropathic Pain in Idiopathic Small Fibre Neuropathy and Chemotherapy-Induced Peripheral Neuropathy

For the above title I have recruited four participants and performed the first set of quantitative sensory testing visits with neurological exam and questionnaires. These patients have been input into the 'EDGE' database. Further to this, to accelerate recruitment a separate clinic will be implemented in February/March exclusively for ISFN/CIPN patients. Also, Mr. Iftikhar Khan has begun contributing CIPN patients from his clinic to be screened and approached. Progress has been made as both of the recruited ISFN participants have attended appointments at St. Paul's eye hospital with Prof. Stephen Kaye and his research fellows for corneal confocal microscopy. The first skin biopsy was performed on a healthy volunteer and was successful. The samples have been processed and frozen in liquid nitrogen pending arrival of antibodies and detection reagents (pending delivery at the William Henry Duncan Building). I attended a three-day training course in preparing skin biopsy for immune-histochemical (IHC) intra-epidermal nerve fibre density (IENFD) assessment at Oxford John-Radcliffe Hospital under the supervision of Dr. Thomas Vale. As part of this work I have completed all of my safety risk assessments, standard operating procedures and control of substances hazardous to health (COSSH).

2.) Diagnostic Test Accuracy (DTA) "Corneal confocal microscopy for diagnosis of small fibre neuropathy"

Together with my supervisor we are finalising a written DTA protocol for peer-review by the Cochrane Neuromuscular disease group. This DTA aims to understand how accurate corneal confocal microscopy (CCM) is in diagnosing diabetic peripheral neuropathy (DPN) compared to a reference standard. This process so far has involved peer-review of search strings for representative data capture for which I attended the York Health Economics Consortium (YHEC) in September for specialist training in advanced search techniques for systematic reviews and meta-analyses. In September I attended NeuroDIAB (2019) in Barcelona which was valuable in identifying how researchers present systematic reviews and meta-analysis data as part of research presentations. In February I will be attending Cochrane Diagnostic Test Accuracy (DTA) workshops to develop skills on the software Review Manager and presenting my protocol to the Neuromuscular disease group. I am also arranging travel and accommodation for a DTA course in June which is the earliest opportunity to attend this course in English (Utrecht, the Netherlands).

3.) UK Biobank data to identify neurodegeneration markers using optical coherence tomography (OCT) and OCT angiography

I have accessed encrypted UK Biobank data which includes anonymised data for over 200000 patients. Some of these fields will encode patient information including MR brain images and ophthalmic pathology. These bulk images will be subject to analysis on an application called 'FreeSurfer' to give a range of detailed descriptions of brain structures including volumes of a patient's neuroanatomy. This data will be compared to ophthalmic pathology to identify a variance and linearity together with co-variates such as age, height, weight, BMI etc. This data was encrypted and required a high-performance cluster (HPC) virtual device input (VDI) to open. Due to this, the data has only recently (December 2019) been extracted for analysis. To avoid this problem in the future the data has been extracted via input commands through an application called 'MobaXTerm' into twenty '10000' data-point .csv files.

4.) Additional work undertaken

• I have been assisting Dr. Jonathan Lim on his study 'An eye on the diabetic foot' in order to improve my skills with patients such as questionnaires, neurological exams and QST.

- Further, a component of 'An eye on the diabetic foot' requires 10 patients and 40 control patients to be included in an additional MR brain imaging component. I have taken the lead in recruiting/screening patients, meeting them at the Liverpool MRI centre (LiMRIC) and analysing the images on 'FreeSurfer'.
- One of Dr. Uazman Alam's PhD students is performing a systematic review and meta-analysis on retinopathy in patients undergoing aggressive treatment regimens for diabetes for whom I am mirroring her searches and selecting papers for data extraction.
- I am one of the authors of a monograph titled 'Mirogabalin besylate in the treatment of neuropathic pain' together with, Saad Javed, Bernhard Frank, Rayaz A Malik, and Uazman Alam. This manuscript has passed peer review and is currently with the chief-editor of Clarivate Analytic's "Drugs of Today".
- A further ethical amendment will be applied for to include a current perception threshold to the QST testing limen
- I attended a phlebotomy training (one day course) and am working toward my competency so that I can take bloods for the ISFN: CIPN study.
- I have been working with bio-engineering to validate the DPN-Stat Check and neuroaesthesiometer for one of Uazman Alam's other PhD students' projects (Calibrate)