Aims: Recent research indicates that mechanisms affecting both the brain and the bodily nerves in fibromyalgia syndrome patients are likely to work together to shape the patient pain experience. This project aims to investigate whether these two mechanisms are related to each other. As a pilot study, this represents the first research to measure relevant brain and bodily nerve activity in the same group of fibromyalgia patients by using a deep analysis of patients. We consider brain structure and function and many clinical evaluations of nerves throughout the body. As it is the first time anyone has attempted this particular research, this was classed as a pilot feasibility study. This means that one of our primary interests is to check that it is even possible to collect this battery of exciting data from a patient. Our second goal is to perform a first evaluation of known brain and non-brain mechanisms in a single patient group, to see if they are related to each another.

What do we do: The project team is comprised of experts in both brain imaging and the peripheral nervous system. We have access to a group of 77 people with fibromyalgia syndrome who are participating in a project to investigate their peripheral nerve function. In our study, 18 of these patients attended an additional brain scanning session at the Liverpool Magnetic Resonance Imaging Centre (LiMRIC) in the University of Liverpool. During this session the patients undergo 5 MRI brain scan procedures which quantify important aspects of the brain, including anatomical structure. We are also recording scans that measure patients brain function. The first considers brain activity when the patients are at rest, and a 'task scan' which evaluates brain activity as the patients undergone some heat stimulation to their foot to cause them some mild pain experience so that we can observe how their brains process the pain. In total the patients are in the scanner for 1 hour. We talk to the patients frequently via an intercom to ensure they are comfortable and the heat pain intensity for the task is individually tailored so that it is acceptable to every patient.

Progress: We have completed data collection on the initially planned 18 patients. Analysis of this data is *in progress* and analyses of brain structure are complete. We have reported preliminary findings at an international conference (*Controversies in Fibromyalgia* – Vienna 2023). We are pleased to report that we also achieved additional funding (internal funding from University of Liverpool) to expand the pool of patients to achieve a total of 30. This should ensure that the data is fully suitable for publication in the near future.

Results: In line with our aim to assess feasibility of this research, patients generally found our approach to be acceptable. Only one patient who attended our scanning facility decided against going through with the study – this was due to claustrophobia which is a common cause of drop-out in brain scanning studies. Verbal feedback from all patients has been positive, with no major issues identified with the study approach.

In terms of considering the mechanisms of fibromyalgia, analysis of both brain structure and function imaging and peripheral nervous system measurements is now ongoing. We have recently reported initial findings of relationship between brain anatomy and measures of peripheral nerve fiber structure in the form a scientific poster. For this analysis, we compared the density of the brains grey matter with a measure of bodily nerve integrity which was measured using a non-invasive eye examination. The analysis indicated 2 clusters located in right hemisphere of the brain which demonstrated a link to nerve fiber measures (Figure 1). Interestingly, this highlights points to how simple eye-scans could be used to identify fibromyalgia patients who have a particular characteristic, or subtype, which could one day be used to choose treatment options.

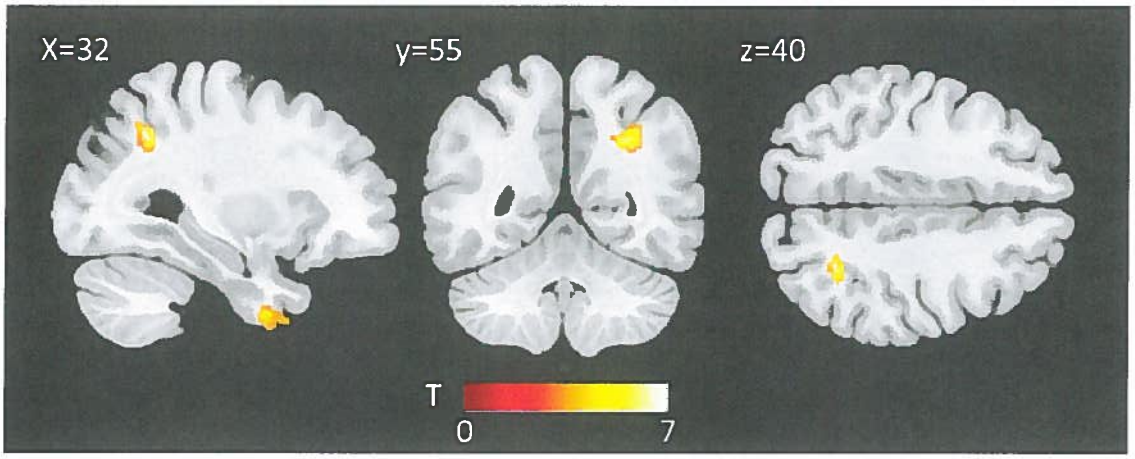

Figure 1. *Locations of significant clusters demonstrating positive relationships between grey matter density and nerve branching density*

As we have acquired additional funding, we will soon complete data collection with a sample size of 30 patients which will be sufficient to ensure this exciting data is published in a scientific journal and disseminated to clinical colleagues.

In coming months, we will analyse functional brain data with measures from peripheral nervous anatomy and activity from our patients, including skin biopsy results and nerve function tests. We will correlate these measures with the brain and behavioural results shown above in an attempt to further understand how different mechanisms may interact with one another.

Future outcomes: As described, a principle aim of this research is to consider the feasibility and acceptability of the approach for patients which has now been achieved. In future, we will now aim to secure funding to continue this exciting line of research at University of Liverpool with studies which will aim to consider how these mechanisms might interact to cause the development of fibromyalgia. Specifically, we are interested in research to understand the relationship of brain and bodily mechanisms in newly diagnosed patients compared to those who have had fibromyalgia for many years. We hope to contribute to knowledge that will aid the development of improved treatment approaches based on a better understanding of the multiple mechanisms contributing to each individual fibromyalgia experience.