TRAM (Train and Retain Academic Musculoskeletal clinicians)
MB-PhD Project Summary

PhD project Title
Real-time fMRI Neurofeedback: a novel therapy for rheumatoid arthritis fatigue?

PhD supervisors (please provide name, affiliation and email) *[At least two supervisors]*	
1. Neil Basu, Professor of Musculoskeletal Medicine & Vasculitis, neil.basu@glasgow.ac.uk	2. Salim Al-Wasity, Research Associate, salim.al-wasity@glasgow.ac.uk
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Background

Fatigue is a normal experience, but for patients with rheumatoid arthritis (RA) and other musculoskeletal conditions, its impact is profound. As many as 70% people with RA consider fatigue to be equal to pain in terms of burden and 75% cite fatigue to be the main barrier to their remaining in employment. Despite the recent revolution in anti-inflammatory therapeutics, most people with RA continue to experience life disabling fatigue and so discovering novel fatigue specific therapies represents a major patient priority.

With the help of magnetic resonance imaging (MRI) techniques, our group have been among the first to study the relationship between changes in brain signals and the fatigue levels which RA patients experience. We have evidenced that high levels of fatigue are associated with abnormal brain activity in a key region known as the prefrontal lobe. In particular, this region appears to be functionally hyperconnected with other areas of the brain.

In parallel, our group are leading the technical development and testing of a cutting-edge technology known as real-time fMRI neurofeedback (rtfMRI-NF). RtfMRI-NF is a close loop system where participants are trained to control the activation of a defined brain region(s) using mental strategies and visual feedback from their real-time functional MRI brain images. This aims to alter the behavioural functions of the targeted brain regions.

Combining these programmes of work could lead to the development of an urgently required fatigue specific therapy in RA.

Aims

1.To develop a rtfMRI-NF paradigm to alter the functional hyperconnectivity of the pre-frontal brain region in patients with RA
2.To evaluate the effect of this paradigm on reducing RA fatigue severity.
3.To explore the feasibility of maintaining the acquired neurofeedback skills and applying them to real life

Training and experience provided *[Include types of methodologies that will be employed]*

This studentship will provide the opportunity to:

- Develop experience in clinical research delivery, including governance, recruitment and data collection
- Gain proficiency in use of brain fMRI and real-time MRI techniques
- Train in imaging analyses, employing packages such as MATLAB and BrainVoyager
- Develop advanced statistical skills

Supported by a team with active grant income >£2M and supervision experience of >20 PhD students. The successful student will be embedded in a unique interdisciplinary group (n=20) of clinical musculoskeletal researchers and neuroscientists (https://www.gla.ac.uk/researchinstitutes/iii/staff/neilbasu/neuroinflammatoryphenotypesresearchgroup/) based at University of Glasgow's Imaging Centre of Excellence (https://www.gla.ac.uk/colleges/mvls/ice/).

Expected outcomes

The interface between the brain and the musculoskeletal system likely contributes to a large proportion of the current rheumatological patient burden and yet few musculoskeletal based researchers are adequately trained to face this challenge. This studentship will help address this generational shortfall.

Specifically, the studentship will develop a rtfMRI-NF paradigm to target the hyperconnectivity of the prefrontal lobe and then to evaluate any subsequent changes in fatigue. The results of this study will help us to better understand the mechanistic and the causal relationship between prefrontal brain activity and fatigue levels and will ultimately deliver knowledge that will facilitate developing novel fatigue relief strategies for patients with RA and beyond.

References

Basu N, Kaplan C, Ichesco E, Larkin T, Schrepf A, Murray AD, Clauw DJ, Waiter GD, Harris RE (2019). Functional and structural magnetic resonance imaging correlates of fatigue in patients with rheumatoid arthritis. Rheumatology, 58 (10), 1822–1830

Watanabe T, Sasaki Y, Shibata K, Kawato M (2017). Advances in fMRI Real-Time Neurofeedback. Trends in Cognitive Sciences, 21 (12), 997-1010