EPD/25/51 - Rewiring Pain: Targeting Brain-Immune Crosstalk with Transcranial Magnetic Stimulation

The mind and body are in a constant dialogue, shaping our health and well-being. Increasing evidence shows that the brain can influence disease progression across a wide range of conditions. Stress, bereavement, and mental health problems worsen outcomes in cancer, cardiovascular disease, and inflammatory conditions. For example, in cancer, stress is associated with poorer survival and increased tumour growth, likely due to its effects on the immune system. In infections like COVID-19, individuals with high psychological distress had worse disease severity and slower recovery. Likewise, in inflammatory diseases, stress and depression have been shown to trigger psoriasis and arthritis flares, suggesting a key role of brain-immune interactions in disease regulation.

Despite these well-recognised links, how the brain influences immune function remains poorly understood. This is particularly important in individuals with chronic inflammatory conditions like psoriatic arthritis (PsA). Modern treatments effectively reduce inflammation, yet, pain remains a major unmet need, affecting many people with arthritis. This suggests that pain is not only caused by joint inflammation but also by changes in how the brain and immune system communicate. Understanding these mechanisms could unlock new strategies for treating pain in inflammatory diseases.

My research suggests that the inferior parietal lobule (IPL) is a key orchestrator of brain-immune interactions. The IPL processes inflammatory signals and modulates immune responses. When its activity is altered, it may perpetuate immune activation and pain, even when inflammation appears to be controlled by standard treatments. Targeting this brain-immune pathway could offer a new approach to pain relief beyond conventional medications.

Current treatments for PsA-related pain, including anti-inflammatories, opioids, and neuromodulatory drugs, often have limited efficacy and significant side effects. A promising alternative is transcranial magnetic stimulation (TMS), a non-invasive technique that uses magnetic pulses to target specific brain circuits involved in pain regulation. Already an NHS-approved treatment for depression, TMS has shown potential in chronic pain syndromes. Unlike conventional pain medications, TMS does not affect the entire nervous system and has minimal side effects, making it a safer, more targeted approach.

We recently conducted a feasibility study demonstrating that a single session of TMS targeting the IPL reduced pain and altered immune cell activity in people with inflammatory arthritis. Specifically, I observed changes in monocytes, key immune cells involved in the body's first line of defence and central to the development of inflammatory arthritis. However, this was a small study; while promising, the pain relief was modest, and the immune changes need to be validated in larger numbers.

To fully explore the therapeutic potential of TMS, we now need to assess whether multiple TMS sessions over several weeks (as used in depression) can provide greater pain relief and measurable changes in immune function in inflammatory diseases.

Focusing on PsA as a model of inflammatory disease, this study will:

1) deliver TMS sessions 3 times per week for 4 weeks, targeting the IPL.
2) monitor immune responses in the blood to see how TMS affects immune cell activity.
3) track pain and symptom changes to determine whether this approach provides meaningful relief.

This research will be the first to demonstrate that a non-invasive brain intervention can directly modify immune function in humans. If successful, it could lead to a drug-free, mechanistically driven treatment for persistent pain in arthritis and other inflammatory conditions. By understanding how the brain regulates immune responses, this study has the potential to reshape how we think about and treat pain, ultimately providing relief to people living with inflammatory arthritis.