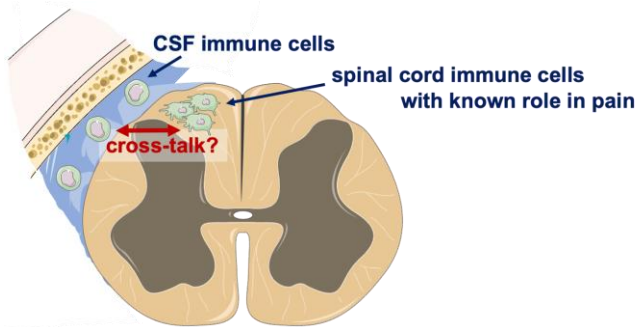


Cerebrospinal fluid- a window into how our central nervous system processes pain?

Background & Rationale: This study aims to find out whether we can use cerebrospinal fluid (which bathes our brain and spinal cord) to better understand chronic pain.



Research suggests that immune cells in the spinal cord play an important role in maintaining painful conditions, especially when they are caused by direct damage to nerves. Yet, for obvious reasons, studying these cells directly is impossible in people.

Our team set out to investigate whether we can instead assess the state of these cells by looking at the cerebrospinal fluid (CSF). It is known that substances released in spinal cord can leak into the fluid. Also, there are immune cells swimming about in the CSF – just across from spinal cord immune cells, and it is possible that these cell types are talking to each other.

To test whether this is the case, we are analysing CSF generously donated by individuals who are undergoing neuromodulation surgery to treat their pain. We look at the substances in the fluid, as well as the immune cells, with a technique called RNA sequencing.

Progress to date: The COVID19 pandemic naturally presented some challenges to our recruitment efforts. At present, we have obtained samples from 11 patients. Our original statistical plans indicated that we would require between 10 and 16 samples for the analyses we want to conduct. This means that we are making reasonable progress, but we still require more recruitment time to ensure that our results are replicable across individuals. We propose to extend the life-time of the grant by 6 months to give us time for additional sample collection.

Nevertheless, our current data already permit us to give preliminary answers to two of our proposal's questions:

1) *Can we use CSF as a way to measure spinal cord immune cell activation?*

In the past, research has observed that certain proteins are more prevalent in the CSF of chronic pain patients. These are proteins that could be released from the immune cells in the spinal cord or from those in the CSF itself. Our project shows that immune cells in the spinal cord, known as monocytes, are capable of making all the proteins also produced by spinal cord immune cells, known as microglia, including some usually assumed to be "microglial-specific". Our results to date therefore suggest that it will be tricky to distinguish whether a protein in the CSF came from an immune cell within the fluid or within the spinal cord.

2) *Can we detect any differences in CSF immune profiles that are related to the kind of pain someone experiences?*

Analyses are still ongoing, but our sample collection to date suggests that individuals with quite divergent chronic pain origins nevertheless have very similar immune cell numbers and populations in their CSF. The most striking differences to date have emerged as a result of spinal cord stimulation, after which we observed changes in immune cell numbers in two out of three individuals. More samples are required, particularly to gain confidence in the latter result.