The relationships between spinal abnormalities, neuronal plasticity and chronic low back pain in an animal model

Laura S. Stone

Faculty of Dentistry, Alan Edwards Centre for Research on Pain, McGill University

Persistent back pain is the most common form of chronic illness in Canadians aged 60 and under, affecting 15% of the population. Current diagnostic and therapeutic approaches to chronic back pain are limited by our narrow understanding of the underlying biological mechanisms.

Low back pain (**LBP**) is a continuum of painful conditions including both axial (confined to the spine and low back region) and non-axial (radiating to one or both legs) components. A major cause of chronic LBP is the breakdown of intervertebral discs (**IVD**), a condition called degenerative disc disease (**DDD**). The relationships between disc degeneration, axial LBP, and non-axial LBP, however, are not well understood, and a mismatch exists between the severity of disc degeneration and chronic pain. While it has been proposed that factors undetectable by imaging (i.e., biochemical changes in the discs or neuronal plasticity) are responsible for DDD-induced LBP, others suggest that IVD anatomy can be the source of LBP in many cases.

We have developed a mouse model of progressive, age-dependent LBP related to DDD and are building a complex data set measuring pain (including of axial and radiating LBP, motor impairment, anxiety and depression), disc degeneration (including anatomical data on IVD height and shape obtained by x-ray or MRI and histological data assessing the degree and type of disc degeneration post-mortem), and neuronal plasticity (sensory nerve density and plasticity around the lumbar discs and in their respective cell bodies, and markers for pain-sensing neurons) in mice as they age. In addition, we have data from interventional studies showing reversal of the behavioural phenotype with drugs used to treat LBP or exercise. While we have identified some relationships between anatomical and functional measures by simple correlation analysis, a predictive model that incorporates all the factors is needed. We propose a project where our anatomical, biological, and functional data are integrated into a predictive model that extracts potential causal relationships too complex to unravel with simple statistics.

Current treatment options for chronic LBP are inadequate. The pairing of a mathematical model with a pre-clinical in vivo model of this condition could generate new insights into the mechanisms underlying LBP and inform mechanism-based therapeutic approaches.

Background literature

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