Immune cell changes in neuropathic pain revealed by nanomedicine treatment in animal model

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Video Abstract

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Abstract

Pain is useful. It's a natural mechanism for protecting the body in humans and other animals. However, pain that is chronic and persists longer than it should is considered a disease. Research has revealed that pain is often the result of an important interplay between the immune system and the nervous system. When the body produces an inflammatory response to injury, or disease, inflammation can activate [pain circuits], sensitize them, and lead to increased and ongoing pain. Now, using nanosized particles of medicine that momentarily switch inflammation off, researchers have discovered new clues as to how chronic pain unfolds and how it might be relieved. The team began by inducing immune-based chronic pain in rats. They did so surgically by constricting the right sciatic nerve with loosely tied sutures, causing swelling and inflammation through the infiltration of white blood cells, immune cells including monocytes that become macrophages. Nanomedicine developed by a co-author of the study is designed to target these monocytes. The medicine is small enough to be engulfed by pathogen-seeking white blood cells, where it delivers the NSAID drug celecoxib as well as a fluorescent tag. That enabled the researchers to track the location of the drug and inflammation in the body. A single ultra-low dose, approximately 2000-fold lower than the typical oral dose, provided 6 days of pain relief. Experiments were designed to compare rats injected with a placebo control nanomedicine containing no drug with animals administered drug-loaded nanomedicine. The experiment looked at two time points: [when the treated rats experienced pain relief] and [when the rats returned to a state of chronic pain]. The researchers assessed inflammation at the injured nerve and at its associated dorsal root ganglia, neuronal cell bodies of the sciatic nerve fibers that cluster near the spinal cord. One key finding was a switch in macrophage polarity, from a pro-inflammatory type to an anti-inflammatory type involved in tissue repair. The researchers also found that another important immune cell involved in chronic pain, so-called mast cells, exhibited reduced degranulation — the release of proteins and compounds that can cause further inflammation. These insights into the biology of the injured nerve and its ganglia, as well as the improved understanding of the nanomedicine's function, offer a new paradigm for understanding the immune cell pathology of chronic pain and for findings ways to relieve it.