Targeting brain cells to alleviate neuropathic pain

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New research indicates that neuropathic pain could be alleviated if treated within a few days. Credit: Rutgers University

Neuropathic pain – which affects more than 1 million Americans – could be reduced or even eliminated by targeting brain cells that are supposed to provide immunity but, in some instances, do the opposite,

causing chronic pain that could last a lifetime.

"The general thought has been that these cells are supposed to be beneficial in the nervous system under normal conditions" said Long-Jun Wu, a professor of cell biology and neuroscience at Rutgers University. "But, in fact, in those with this neuropathic pain the cells, known as microglia, have proliferated and instead become toxic."

In new research, published in both *Nature Communications* and *Cell Reports*, Wu and his team discovered that chronic neuropathic pain – caused by nerve damage as a result of an injury, surgery or a debilitating disease like diabetes or cancer – could be greatly reduced in animals if the injury was treated by targeting microglia within a few days.

"If we can catch that window within one to five days to inhibit microglia after nerve injury, we can partially reverse the development of chronic pain," said Wu. "If we were able to deplete the microglia cells causing the condition before nerve injury occurs, we can permanently prevent it."

Neuropathy occurs when nerves are injured from trauma or disease and can also be the result of a surgical procedure. This type of pain, unlike physiological pain, persists even after the injured nerve has healed and is often resistant to pain relievers like acetaminophen and naproxen. While opiates are used to alleviate pain, they have side effects and are not always effective for neuropathic pain patients.

In laboratory studies on mice, Wu and his colleagues used chemotherapy drugs to prohibit the microglia brain immune cells from proliferating, similar to the treatment used by oncologists to prevent cancer cells from multiplying. The results from Wu's laboratory showed that this chemotherapy drug reduced the amount of pain the mice experienced after the injury occurred.

"What needs to be done is prevent the microglia cells from multiplying in the first place," said Wu. "It had been thought that these cells were beneficial in a normal brain, but our research discovered how these cells function under neuropathic pain condition and initiate the problem."

Although scientists have studied microglia cells in relationship to neuropathic pain for the past two decades, Rutgers is the first to pinpoint the exact role the cells have in the initiation and maintenance of the condition. Wu and his colleagues found that the proliferation of these types of cells is one of the major contributors of microglial pain. This discovery could lead to the development of more effective painkillers with fewer side effects, he said.

"Our research raises the intriguing possibility that minimizing microglial proliferation may be a novel approach for pain control," Wu said. "We hope this will eventually lead to more effective pain killers that will battle this devastating disease."

More information: Nan Gu et al. Spinal Microgliosis Due to Resident Microglial Proliferation Is Required for Pain Hypersensitivity after Peripheral Nerve Injury, *Cell Reports* (2016). DOI: 10.1016/j.celrep.2016.06.018

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