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Prevention and reversal of neuronal sensitization in the spinal cord by blocking spinal glial cell activation in an animal model of non-specific chronic low back pain

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Glia cells play important roles in long-term plasticity of the nociceptive system, but little is known about the influence of microglia and astrocytes on pain originating in low back muscles. The present study aimed at investigating the impact of spinal glial cells on latent sensitization of dorsal horn neurons in an animal model of non-specific low back pain.
In deeply anesthetized rats, recordings were made from dorsal horn neurons in the spinal segment L2. To induce hyperexcitability of the neurons, two injections of nerve growth factor (NGF) were made into the multifidus muscle at an interval of 5 days. To prevent the hyperexcitability, minocycline (a specific inhibitor of microglial activation) was continuously administrated intrathecally starting 1 day before the first NGF injection. To reverse the hyperexcitability, minocycline or fluorocitrate (an unspecific inhibitor of glial activation) were continuously administrated intrathecally starting 2 days after the first NGF injection. Separate animals with 2 NGF or phosphate-buffered saline injections were used for immunohistochemical staining to study the morphological changes of glial cells.
After 2 NGF injections, the proportions of dorsal horn neurons with input from deep tissues and neurons with convergent input increased significantly, indicating an NGF induced hyperexcitability of dorsal horn neurons. Minocycline given before the first NGF injection prevented the NGF-induced neuronal hyperexcitability. When minocycline or fluorocitrate were administrated during the state of latent sensitization (2 days after the first NGF injection), only fluorocitrate prevented the hyperexcitability of dorsal horn neurons, but minocycline did not. The immunohistochemical data showed that both microglia and astrocytes were activated by 2 NGF injections, but the astrocyte activation was weaker than the microglial activation.
These findings indicate that in the non-specific low back pain model used, both microglia and astrocytes were activated and contributed to latent sensitization and its transition to hyperexcitability. Spinal microglia presumably control the development of the neuronal hyperexcitability, while astrocytes are more involved in its maintenance.