BLOCKING ARTEMIN SIGNALING REVERSES OSTEOARTHRITIS ASSOSCIATED PAIN AT EARLY AND LATE TIME POINTS

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Osteoarthritis (OA) is a leading cause of disability, with ~100 million US adults suffering from chronic joint pain, widespread sensitization, and decreased mobility. Clinically efficacious and safe therapeutics for OA-pain are limited. *Thus, there is an urgent need to develop novel, clinically relevant analgesics for OA-pain*. We have linked synovial fluid concentrations of a neurotrophic factor, artemin, to naturally occurring joint pain in dogs. Further, expression of GDNF family receptor alpha 3 (GFRα3, artemin's receptor) was increased in dog sensory neurons serving OA joints compared to controls. Despite our compelling data, no studies have elucidated the role of artemin/GFRα3 signaling in the development and maintenance of OA-pain. This study explores the functional role of artemin/GFRα3 signaling in OA-pain. We used the monoiodoacetate (MIA)-induced model of stifle OA-pain to evaluate sensitivity to mechanical, hot, and cold stimuli and limb use at early inflammatory (day 7) and late OA (day 28) time points. At both time points, we assessed MIA-induced hypersensitivity and limb disuse at 2-, 5-, and 24-hrs. post-anti-artemin monoclonal antibody or isotype control administration. MIA-injected mice developed hypersensitivity to mechanical and thermal stimuli and had decreased limb use compared to the saline-injected controls. Artemin sequestration reversed MIA-induced hypersensitivity and limb disuse at early inflammatory and late OA-pain time points. This is the first evidence investigating the functional role of artemin/GFRα3 signaling in MIA-induced OA-pain at multiple disease time points. Our ongoing work elucidates the role of artemin/GFRα3 signaling in OA-pain and defines putative targets for developing safe and effective treatments.

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