

4 COLLAGEN ANTIBODY-INDUCED ARTHRITIS (CAIA) LEADS TO EVOKED AND ONGOING PERSISTENT PAIN-LIKE BEHAVIOR, BUT TRANSIENT JOINT INFLAMMATION

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Background and objectives Joint pain is one of the most common types of persistent pain, and it is frequently reported to be a bothersome symptom by rheumatoid arthritis (RA) patients. RA is a chronic autoimmune inflammatory disease characterised by joint swelling, stiffness, and cartilage and bone erosion. Currently there are few effective treatments for persistent pain conditions, thus, it is important to increase our understanding of chronic pain mechanisms. The collagen type II antibody-induced arthritis (CAIA) model is commonly used in the rheumatology field. This model is based on injection of monoclonal antibodies against CII, which induces arthritis-like symptoms and a joint pathology that resembles human RA. However, CAIA has not been evaluated as a model of arthritis-induced pain. Hence, our aim was to characterise CAIA from a pain perspective.

Materials and methods B10.RIII male mice were injected intravenously with collagen antibody cocktail (CAIA group) or saline on day 0 (control group). The CAIA group received lipopolysaccharide (LPS) and the control group saline intraperitoneally on day 5. Another group received intravenous saline followed by intraperitoneal LPS (LPS group). The degree of arthritis was assessed by visual scoring of the paws and evoked nociception by von Frey filament testing for 70 days. Ongoing pain-like behaviour (locomotion) was monitored for 48 h at two occasions and the antinociceptive effect on locomotion of the opioid buprenorphine (0.1 mg/kg intraperitoneal) was investigated. Spinal mRNA levels of inflammatory mediators were measured by real-time quantitative PCR.

Results CAIA mice displayed transient signs of arthritis, while mechanical hypersensitivity was observed prior to and outlasting reversal of joint inflammation. The LPS group showed reduced nociceptive thresholds only the day after LPS injection. Locomotion was reduced both during and after inflammation in the CAIA group, which was reversed by buprenorphine in both phases. Interestingly, the mRNA level of IL-1 β was elevated in the spinal cord during both phases, while other inflammatory mediators, such as tumour necrosis factor and high mobility group box 1 (HMGB1) were elevated only during the post-inflammatory phase.

Conclusions This study demonstrates that CAIA generates robust and highly reproducible hypersensitivity, making this model suitable for studies of joint pain driven by antibody-mediated inflammation, both during peak and remittent phases of RA. Our findings also indicate that peripheral joint inflammation drives time-dependent spinal cytokine synthesis.