PHENOTYPIC CHANGES IN DORSAL ROOT GANGLION AND SPINAL CORD IN THE COLLAGEN ANTIBODY-INDUCED ARTHRITIS MODEL

Su J, Shi T J, Gao T L, Wiesenfeld-Hallin Z, Hökfelt T, Svensson C I. 1Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden; 2Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden

SJ and STJ contributed equally to this work.

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Background and objectives Rheumatoid arthritis (RA) is a chronic autoimmune disorder that affects approximately 1% of the adult population worldwide. Chronic or episodic pain is one of the most egregious symptoms reported by patients with RA. The authors are using the collagen antibody-induced arthritis (CAIA) model to investigate the molecular basis of alterations in nociceptive pathways induced by polyarthritis.

Materials and methods Male CBA mice were injected with five monoclonal collagen type II antibody cocktail on day 0, followed by 25 μg lipopolysaccharide on day 5. Mechanical hyperalgesia was measured using von Frey filaments and the ‘up-down’ method. Arthritic clinical score was assessed every third day. The CAIA mice displayed typical RA pathology characterised by joint swelling and redness (from day 6 to day 36) and reduced pain threshold monitored from the hind paws and starting on day 3 and still low at 43 days. Mice were killed 15 or 47 days after antibody injection, and dorsal root ganglia (DRGs) and spinal cord were collected. Expression of neuropeptides, ion channels and glia markers were assessed by immunohistochemistry.

Results A line of nociception-related biomarkers was studied in DRGs and spinal cord: SP, CGRP, NPY, SST2R, pERK, pAKT, pLCβ3 were expressed in equivalent amounts in all three groups. However, neuropeptide galanin and ATP-gated ion channel P2X3 were significantly increased in the CAIA DRGs as compared to controls, both at 15 days and 47 days after arthritis induction. GAP 43, a nerve injury marker, was increased in the CAIA DRGs on day 15 and lasted till day 47. In CAIA spinal dorsal horn, a significant increase in Iba-1 intensity was detected from day 15, while glial fibrillary acidic protein was upregulated on day 47.

Conclusions This data shows that RA induces selective phenotypic changes in DRG neurons. It is suggested that the upregulation of galanin and GAP 43 in DRGs in the CAIA mice...
reflected structural damage of peripheral branches of sensory neurons. In addition, the pattern of microglia and astrocyte activation detected in the dorsal horn indicates stage-dependent involvement of spinal mechanisms in the CAIA model. In conclusion, this data suggests that long-term joint inflammation leads to a pain state with a unique profile in neuropeptide expression and glial activation.