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Editorial comment

Effective treatment of osteoarthritic pain, tackling the challenge with pets

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Pain in joints is a major clinical problem. Among diseases causing chronic joint pain, osteoarthritis (OA) is a more frequent cause of pain than inflammatory joint diseases, such as rheumatoid arthritis [1]. While OA is rarely observed in young people (prevalence < 0.1% in age group 25–34 years), its prevalence is about 30% in age group 65–74 years and women are more likely to have OA than men [2]. In addition to age, among main risk factors of OA are obesity, injury and congenital anomalies. Obesity increases mechanical stress on the weight-bearing joints, which may explain association of obesity with OA, although a contribution of atypical hormone or growth factor concentrations that affect the cartilage or bone has not yet been excluded. It has also been speculated that nutrients might play a role in OA, e.g. by influencing bone mineralization and cell differentiation in joints [2].

OA affects joint cartilage and subchondral bone. OA typically leads to loss of articular cartilage, new bone formation in the subchondral region, and formation of new cartilage and bone at the joint margins [2]. Characteristic symptoms of OA are pain, stiffness, functional limitations and reduced quality of life. OA usually involves one or a few joints, most frequently knees or hips, and the pain is typically worsened by exercise and relieved by rest. In physical examination, the OA patient may have deformations and signs of local inflammation, such as joint swelling, which may cause difficulties in differentiating OA from other inflammatory forms of arthritis [2]. While OA is associated with X-ray abnormalities in the joint, the radiological findings only poorly predict whether the OA patient has pain. However, the correlation of OA pain with structural abnormalities has been better when using high-resolution magnetic resonance imaging than traditional X-rays [2].

Genetic factors, mechanical stress and age are considered to be among key factors influencing development of OA [3,4]. At cellular and molecular levels, multiple mechanisms may contribute to the pathogenesis of OA as indicated by the finding that initial stages of OA involve increased cell proliferation and synthesis of matrix proteins, proteinases, growth factors, cytokines and various other inflammatory mediators [3]. Many of the compounds generated in OA are known to sensitize nociceptive nerve fibers innervating the joint [5]. It is still unclear which cellular and molecular mechanisms are critical for the development of OA in general or for the induction of OA pain in particular. The contribution of various molecular mechanisms may vary with the genetic background of the patient [4]. Additionally, pain at various stages of OA may be caused by partly different mechanisms that include e.g. sensitization of joint-innervating nerve fibers at one stage of the disease and muscle contracture around the joint at another stage of the disease [2]. Furthermore, sustained injury discharge from sensitized nociceptors innervating the arthritic joint may induce plastic changes in pain-mediating and pain-regulating central pathways that play a role in chronic OA pain [5]. Multifactorial pathogenesis of OA pain may contribute to the limited efficacy of pain therapy in OA patients.

Better understanding of the pathogenesis of OA is expected to help in developing more efficient mechanism-based treatments for OA patients. A number of experimental animal models have been developed to allow studying OA mechanisms in various animal species, including mice, rats, rabbits, dogs and sheep [3]. In earlier experimental animal models, surgical techniques were used to produce joint instability as in OA, while recent OA models include transgenic and knockout mice with defects in various molecular mechanisms that control e.g. cartilage development [3]. Although these experimental animal models exhibit a varying number defects associated with OA, so far, none has modeled all aspects of human OA in clinical patients. Thus, while the currently used experimental animal models provide valuable possibilities for developing and testing mechanism-based treatments against selected aspects of OA pathology and symptoms, there are still many gaps in translation of results from the experimental models to clinical conditions.

In this issue, Vainio [6] proposes that we should take advantage of naturally occurring OA in our pets when developing more efficient therapy for OA pain. Naturally occurring primary canine hip dysplasia, for example, resembles OA in humans and provides a possibility for pre-clinical drug testing in veterinary patients. As pointed out by Vainio [6], recent studies have shown that the assessment of dog behavior and locomotion by pet-owners and veterinarians may allow valid and reproducible measures for following treatment effects at home as well as at the doctor's office. Since development of more efficient chronic pain treatment using pets, as proposed by Vainio [6], would benefit not only human patients but also the veterinary patients, the mutual benefits for pets and humans are expected to provide a motivation and an acceptable

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ethical cause for recruiting pet-owners. It is to be hoped that studies in naturally occurring pathological conditions in our pets will help in improving translation of novel pain treatment methods to clinical practice in human as well as veterinary medicine.

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