characteristic erosion, found especially in PIP, is the so-called "saw tooth" appearance.
Results: Although the diagnosis of EOA is based on radiographic erosions, some clinical features may lead to a suspicion of EOA. According to the definition of "inflammatory OA", abrupt onset of pain, swelling, redness, warmth and limited function of IP joints are common. Sometimes the same features may be observed in non-EOA cases, but usually at the disease onset, during the first year. Characteristic of EOA is the throbbing paresthesias of the fingertips. EOA may lead to joint deformities, some indistinguishable from those of non-EOA, such as lateral subluxations and Heberden's and Bouchard's nodes, while others are seen almost exclusively in EOA, such as instability and ankylosis of DIP and PIP and, rarely, opera-glass deformity.
Concerning laboratory investigations, ultrasensitive CRP has been proposed as marker of the disease activity. Some OA markers, such as the CTX I, were found to be increased in the serum and urine in EOA in comparison with nodal non-EOA. In another recent study, serum levels of myeloperoxydase (MPO) and, at lesser extent, Coll2−1NO2, were elevated in EOA in comparison with non-EOA.
Pattrick et al observed an increased frequency of the HLA-A1B8 and MZ a1-antitrypsin phenotypes in patients with nodal OA. Among these, patients with EOA had an increased frequency of the MZ a1-antitrypsin phenotype (30 versus 9%). We found that HLA DRB1*011 was associated with EOA, in comparison with non-EOA and reference populations. Stern et al reported an association between EOA and a genomic region containing the interleukin-1b (Il-1b) 5810 single nucleotide polymorphism, thus supporting a potential role for Il-1 in the pathogenesis of this severe phenotype of hand OA.
In comparison with nodal OA, clinical aspects of EOA may sometimes be indistinguishable, although EOA is characterized by more frequent inflammatory episodes involving several joints simultaneously and may persist for many years, while nodal generalized OA exhibits its flares mainly at onset of the involvement of each joint, in a 'stuttering' onset polyarthropathy of DIPs and PIPs which resembles a 'monoarthritis multiplex'. Furthermore, instability and ankylosis of IPs are seen almost exclusively in EOA.
Conclusions: According to the recent EULAR recommendations for the diagnosis of hand OA, EOA may be considered "as subset of hand OA, characterized by radiographic erosions targeting IP joints which may progress to marked bone and cartilage attrition, instability and bony ankylosis. Typically it has an abrupt onset; marked pain and functional impairment; inflammatory symptoms and signs (stiffness, soft tissue swelling, erythema, paraesthesiae); mildly elevated CRP; and a worse outcome than non-EOA".

I-33 EXPERIMENTAL MODEL SYSTEMS TO ASSESS JOINT PAIN

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Purpose: The majority of patients suffering from osteoarthritis (OA) desire effective and safe pain relief. Despite the growing number of OA patients worldwide and the pressing need for efficacious analgesics, surprisingly little is known about the source and mechanisms of OA pain (for review see McDougall, 2006. Arthritis Res. Ther. 8: 220–229). One of the puzzling aspects of OA pain is the apparent disconnect between disease severity and patient reported pain levels. Animal models of OA provide a unique opportunity to investigate joint pain in an objective and empirical manner.
Methods: We have examined nociception in two animal models of OA viz. the Dunkin Hartley guinea pig model of spontaneous OA and the sodium monoiodoacetate rat model of chemically-induced OA. In the guinea pig model, the effect of age and joint destruction on joint nociceptor activity was determined by comparing micro-CT and histomorphological markers of knee joint pathology with single unit electrophysiological recordings from articular primary afferents. Nerve recordings were also performed on monoiodoacetate-induced OA rats as well as pain behaviour responses using hindlimb weight bearing and von Frey hair algesiometry. Pharmacological interventions were carried out in the rat model to help identify the chemical mediators involved in OA pain production and to discover novel pain therapeutics.
Results: Both animal models demonstrated heightened nerve activity at rest (spontaneous firing) and in response to mechanical rotation of the knee in the normal working range (non-noxious mechanical stimuli) and during noxious hyper-rotation. Disease severity in Dunkin Hartley guinea pig knees became progressively worse with advancing age and correlated with increased body mass; however, OA severity did not correlate with any of the objective electrophysiological measures of nociceptor activity. Peripheral administration of the neuropeptide antagonist VIP6−28 to monoiodoacetate-treated rat knees, reduced joint afferent sensitization (Schuelert & McDougall, 2006. Osteoarthr. Cart. 14: 1155–1162) and inhibited pain behaviour (McDougall et al., 2006. Pain 123: 98–105). In other experiments, local administration of a cannabinoid agonist attenuated afferent firing rate indicative of an anti-nociceptive effect in OA joints (Schuelert & McDougall, 2008. Arthritis Rheum. 58: 145–153).
Conclusions: These studies show that OA leads to peripheral sensitization of knee joint sensory nerves and this heightened neural activity is the physiological basis of joint pain. The data also provide the first objective evidence that disease severity is a poor indicator of joint pain. Moreover, we have identified VIP6−28 and locally administered cannabinoids as potential treatments for OA pain. Future studies using these and other OA models are required to elucidate further the neurophysiological processes responsible for generating joint pain so that novel therapeutics may be developed allowing OA patients to lead a pain-free life.

I-34 BEHAVIORAL METHODS FOR ASSESSING OA AND PAIN IN MOUSE MODELS

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Purpose: Osteoarthritis (OA) is a major musculoskeletal disorder that manifests with functional limitation and pain. In the United States, the incidences of OA are projected to double by 2020 primarily due to increased obesity. Although clinicians have concentrated upon treating the symptoms of OA and, in some cases, by advising changes in diet, various behavioral abnormalities may accompany the disease. This presentation will describe some methods for examining abnormal behaviors in mouse models of OA.
Methods: Neuromuscular status can be evaluated through behavioral tests of reflexes, posture, grip-strength, pole-climbing/walking, gait, and sensorimotor skills. Pain sensitivities are examined by tests of mechanical and thermal sensitivities. Anxiety-like behaviors are analyzed by responses in the zero maze, light-dark box, open field, and novelty-suppressed feeding tests, whereas depressive-like behaviors are studied by forced swim, tail suspension, and anhedonia.
Results: In a genetic model of OA, *Col9a1* mice showed knee joint degeneration and were deficient in sensorimotor responses and displayed heightened mechanical sensitivities. In a diet-induced model of OA, C57BL/6 mice fed a high fat diet also had knee joint changes. These animals presented with some deficiencies in sensorimotor skills and they displayed anxiety-like behaviors in the zero maze, as well as analgesia in the hot plate but appeared normal in the tail flick test.
Conclusions: As anticipated, these mouse models of OA show alterations in sensorimotor responses and pain sensitivities. However, the animals also display additional behavioral abnormalities. Clinicians should be aware that OA patients may present with similar comorbidities and treatment of these behaviors should be considered part of the regimen for OA therapy.

I-35 THE IDENTIFICATION OF SUSCEPTIBILITY GENES FOR THE ONSET AND PROGRESSION OF OSTEOARTHRITIS

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Purpose: To identify new osteoarthritis susceptibility genes for the onset and progression of Osteoarthritis.
Methods: A genome-wide linkage scan and combined linkage association analysis was applied to 179 affected siblings and 4 trios with generalized osteoarthritis (The GARP study). We tested for confirmation by association in 3 additional independent OA populations.
Results: Suggested evidence for linkage in the GARP study was observed on chromosome 14q32.11 (LOD = 3.03, $P = 1.9\times10^{-4}$). Genotyping tagging SNPs covering three important candidate genes revealed a common coding variant (rs225014; Thr92Ala) in the iodothyronine-deiodinase enzyme type 2 (D2) gene (*DIO2* [MIM 601413]) which significantly explained the linkage signal ($P = 0.006$). Confirmation and replication by association in the additional osteoarthritis studies indicated a common *DIO2* haplotype, exclusively containing the minor allele of rs225014 and common allele of rs12885300, with a combined recessive odds ratio of 1.79, 95% confidence interval [CI] 1.37−2.34 with $P = 2.02\times10^{-5}$ in females cases with advanced/symptomatic hip osteoarthritis. The gene product of this DIO2 converts intracellular prohormone-3,3′,5,5′-tetraiodothyronine (T4) into the active thyroid hormone