expression of all MMPs was greater in meniscus than AC. In general MMP expression in the outer meniscus was more responsive to TNFα. TIMP-1 and -3 were generally decreased in all tissues by IL-1α and TNFα. There was more pro and active MMP-2, and pro-MMP-13 in control cultures of outer meniscus than AC or inner meniscus. Unlike AC, both meniscal zones released active MMP-13 after IL-1α and TNFα treatment, and active MMP-2 after IL-1α (inner) or both cytokines (outer).
Conclusions: Aggrecan processing differed between outer versus inner meniscus, with the later being similar to AC. Aggrecan proteolysis in the outer meniscus rather than AC, may be responsible for MMP-generated neoepitopes detected in OA human knee synovial fluid. The meniscus was generally more responsive to TNFα than AC, particularly the outer zone. Expression of MMPs and ADAMTS was higher in meniscus than AC, and unlike AC active MMPs were released from meniscus. The meniscus may contribute significantly to metalloproteinase levels in the joint, and therefore to cartilage breakdown in OA. Differential regulation of MMPs and ADAMTS in the knee joint meniscus compared with AC, and between inner and outer meniscal zones has important implications in OA therapy.

033

EFFECTS OF FEEDING A HIGH OMEGA-3 FATTY ACID DIET ON THE PAIN-RELATED DISABILITY IN DOGS WITH NATURALLY OCCURRING OSTEOARTHRITIS

M. Moreau, É. Troncy, D. Gauvin, B. Lussier
Université de Montréal, St-Hyacinthe, QC, Canada

Purpose: Lameness associated with osteoarthritis (OA) is highly prevalent in dogs. Typically, OA dogs have a decrease in their limb function, demonstrate discomfort and disability with an unwillingness to perform daily life activities. To alleviate those clinical signs, management of OA based on diet enriched in polyunsaturated omega-3 fatty acids (omega-3 PUFAs) is broadly considered by clinicians despite the lack of published clinical trials supporting their efficacy. The aim of this study was to measure functional outcomes in lame client-owned dogs afflicted by naturally occurring OA before and after a 13 week period of feeding with either a control diet (CTR) or a veterinary therapeutic diet (VTD) containing high levels of omega-3 PUFAs. Hypothetically, the functional outcomes would be significantly improved from Baseline only in VTD-treated dogs. The magnitude of those changes would exceed CTR-treated dogs.
Methods: A randomized, double-blinded, placebo-controlled trial was performed in 45 lame client-owned dogs with OA. Dogs were included in the study when they had hind limb lameness observed by a veterinary surgeon, signs of OA upon orthopedic examination and low dynamic weight bearing (peak vertical force, PVF) recorded on force platform gait analysis. The presence of OA was confirmed on radiographs (hip and/or stifle). The initial condition (Baseline) of dogs was determined by the recording of PVF (primary study outcome) and by client-specific outcome measures (CSOM). Dogs were randomly allocated to 3 groups (15/group) and received a control diet (CTR1 or CTR2) or the therapeutic VTD diet. Assessment by CSOM was performed twice weekly by the owner, and PVF was repeated after 13 weeks of treatment. Statistical analyses were performed using nonparametric tests at $p<0.05$.
Results: Median PVF values increased significantly in VTD-treated dogs (+9.4%, $p=0.049$). Neither CTR1- (+2.4%,$p=0.582$) nor CTR2-treated (+2.6%, $p=0.187$) dogs revealed such significant improvement. In addition, at week 13, CSOM assessment denoted a significant decrease in score (meaning improvement) for VTD-treated dogs (-20%, $p=0.021$), but not for CTR1 (0%, $p=0.216$) or CTR2 (-5.8%, $p=0.267$). The magnitude of the changes of PVF and CSOM in VTD-treated dogs was not significantly different from CTR-treated dogs.
Conclusions: The use of a high quality diet and good nutritional habits may have prompted the monitoring of a trend toward a better function in CTR dogs, despite the absence of omega-3 PUFAs in these control diets. Nutrition-based OA management improved functional outcome and performance in daily life activities when dogs were fed with VTD over a short-term period. This veterinary diet containing omega-3 PUFAs should be considered as a therapeutic modality to alleviate the clinical signs in dogs afflicted by OA as a unique treatment or as part of a multimodal approach in the management of OA.

034

CENTRAL SENSITIZATION IN KNEE OA: PRELIMINARY RESULTS FROM THE MOST STUDY

T. Neogi[1], J. Niu[1], L. Arendt-Nielsen[2], J. Scholz[3], L. Frey-Law[4], C. Woolf[3], Y. Zhang[1], L. Bradley[5], M. Nevitt[6], D. Felson[1]
[1]BUSM, Boston, MA; [2]Univ. of Aalborg, Aalborg, Denmark; [3]Childrens Hosp., Boston, MA; [4]UIowa, Iowa City, MA; [5]UAB, Birmingham, AL; [6]UCSF, San Francisco, CA

Purpose: Mechanisms contributing to knee pain in osteoarthritis (OA) are not well understood. Mechanical and inflammatory stimuli in the joint may lead both to changes in the peripheral threshold of nociceptors (peripheral sensitization) and a central amplification of signals in the CNS (central sensitization), resulting in heightened pain sensitivity. We hypothesized that knee OA, particularly OA severity and duration, may be associated with central sensitization. We therefore examined whether knee OA was associated with temporal summation, an augmented pain response to repetitive mechanical stimuli that indicates the presence of central sensitization.
Methods: The Multicenter Osteoarthritis (MOST) Study is cohort study of persons with or at high risk of knee OA. Participants underwent knee radiography at baseline, 30, and 60 months. At 60 months we carried out an evaluation of temporal summation using a 60g monofilament at the wrist and separately over each patella. Temporal summation was defined as being present when, after touching the skin with the monofilament repeatedly at a frequency of 1Hz for 30 seconds, the subject reported new pain or increased pain at the site being tested. Persons were categorized by number of knees (0, 1 or 2) with OA at 60 months (OA defined on x-ray by KL≥2). Knees were categorized according to KL grade, OA presence and OA duration. We examined the relation between OA (presence, severity, duration) with temporal summation cross-sectionally using Poisson regression for person-based analyses and with GEE for knee based-analyses, adjusting for potential confounders. We also used a within-person knee-matched approach among persons with knees discordant for temporal summation to explore these relationships while eliminating between-person confounding using matched conditional logistic regression.
Results: To date, data on 920 participants' 60-month clinic visit are available (mean age 68.0, mean BMI 30.8, 67.3% female). The age- and sex-adjusted prevalences of temporal summation at the wrist among persons with 0, 1 and 2 knees with OA were 55%, 53%, 57%, and at either patella were 61%, 56%, 63%, respectively. Persons with 1 and 2 knees with OA were 0.85 and 1.09 times as likely to have temporal summation at the wrist (95% CI 0.59-1.22 and 0.78-1.54, respectively), and 0.74 and 1.04 times as likely to have temporal summation at either patella, respectively (95% CI 0.51-1.06 and 0.73-1.48, respectively), than persons with no knee OA. In knee-based analyses, OA presence, severity and duration were not associated with presence of temporal summation at the patella. For example, presence of knee OA was associated with 1.16 times higher prevalence of temporal summation compared with no OA (95% CI 0.91-1.49). However, in the within-person knee-matched analyses, knee OA was associated with 2.30 times higher prevalence of temporal summation than no OA (95% CI 1.10-4.83). Further, knees with KL grade ≥3 had 2.80 times higher prevalence of temporal summation than knees with KL grade 0 (95% CI 1.06-7.40). Even among knees with some degree of radiographic abnormality, those with KL grade ≥2 had a higher prevalence of temporal summation than those with KL grade 1 (prevalence ratio (PR) 1.59, 95% CI 1.01-2.52). Knees with a longer duration of OA also had higher prevalence of temporal summation than those without any OA (PR 2.56, 95% CI 1.03-6.37).
Conclusions: In these preliminary results from a large cohort, the presence, severity and duration of OA were associated with temporal summation when between-person confounding could be adequately controlled for. Such findings suggest that severity and chronicity of pathology are associated with central sensitization. Future work will include longitudinal evaluation of central sensitization and its manifestations in OA.