and Signs Pain Scale (S-LANSS); and, 3. factors associated with NP symptoms as measured by the mPD-Q.

Methods: Eligible participants were members of an established population-based OA cohort with chronic symptomatic knee OA. A standardized questionnaire was mailed to 426 cohort members to assess NP symptoms (mPD-Q, S-LANSS); osteoarthritis status (WOMAC, Von Korff Chronic Pain Grade); psychological factors including depression (Center for Epidemiological Studies Depression Scale), anxiety (Hospital Anxiety and Depression scale) pain catastrophizing (Pain Catastrophizing Scale), and sleepiness (Epworth Daytime Sleepiness scale); co-morbid medical conditions; possible confounding neurological conditions; and medication use. The cut-point score (≥19) identified in other chronic pain populations was used to identify NP symptoms (‘NP range’ scores) in this study. The proportion of knee OA participants with mPD-Q scores in the NP range was calculated using a 95% confidence interval (CI). Spearman’s correlation between continuous mPD-Q and S-LANSS scores was examined. Potential correlates of NP symptoms were first assessed using bivariate analysis, followed by logistic regression modeling.

Results: Out of 426 cohort members who were sent a study questionnaire, 259 were deemed eligible to participate. The response rate among eligible cohort members was 66% (171/259). The proportion (95% CI) of participants with mPD-Q scores in the NP range was 0.28 (0.21-0.35). After removal of participants with neurological conditions, 0.19 (0.12-0.29) still had scores in the NP range. Continuous mPD-Q scores were highly correlated with continuous S-LANSS scores. NP range scores were strongly associated with OA severity, depressive and anxious symptoms, pain catastrophizing, and a higher frequency of neurological conditions, and chronic back or hip pain with radiation down either leg (‘pain radiation’). On multivariable analysis, pain intensity, ‘pain radiation’, and neurological conditions were independently related to NP range scores.

Conclusions: A substantial proportion of older adults with chronic symptomatic knee OA had symptoms of NP on the mPD-Q suggesting neuropathic mechanisms may be contributing to their pain experience. This subgroup of people may benefit from further evaluation for NP and consideration of NP medications. Validation work is ongoing on the mPD-Q, which may serve as a clinically feasible tool to aid the identification of NP in people with OA.

038
PERIPHERAL EFFECTS OF ENDOGENOUS LIGANDS IN THE RAT INFLAMED JOINT MODEL

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Purpose: Selective activation of peripheral receptors has the important advantage of providing effective analgesia without side effects typically associated with centrally acting drugs. Several data suggest that both opioid and NMDA receptors are localized at peripheral level, and drugs acting on these receptors may produce antinociception after topical administration, however, the antinociceptive effect of endogenous ligands at these receptors is poorly clarified. It is also well known that the organism can express very effective antinociception in different circumstances by releasing of various endogenous ligands. The goal of this study was to determine the antinociceptive potency of the endogenous opioid peptide, endorphin-1, and the endogenous NMDA receptor antagonist, kynurenic acid and their interaction at peripheral level in the rat inflamed joint model.

Methods: Mechanical hypersensitivity was produced by injection of carrageenan (300μg/20μl) into the tibiotarsal joint of the right hind leg. The mechanical pain threshold, the withdrawal from mechanical stimulation to the plantar aspect of the hindpaws, was assessed by logarithmic series of calibrated von Frey monofilaments (0.064-10 g). Endomorphin-1 (30, 100 and 200 μg), kynurenic acid (30, 100, 200 and 400 μg) and their combinations in a fixed-dose ratio: (1:1) were given into the inflamed joint 3 hours after the induction of inflammation, and the pain threshold was determined repeatedly for 75 min after the drug administrations. To determine the changes in the size of the inflamed joint, the cross section area of ankle joint was also calculated.

Results: None of the treatments influenced the degree of edema. Neither endomorphin-1 nor kynurenic acid administered to the inflamed joint influenced the pain threshold at the non-inflamed side. Both ligands produced dose-dependent anti-hyperalgesia, and the highest doses caused prolonged effect. Endomorphin-1 had higher potency (ED50 value was 112 μg [CI: 80-146]) compared to kynurenic acid (ED50 value was 204 μg [CI: 160-251]). The coadministration of endorphin-1 with kynurenic acid caused potentiated and/or prolonged antinociceptive effect. The ED50 value of the combination was 141 μg [CI: 83-182], which did not differ significantly from the theoretically additive value (ED50 145 μg [CI: 68-237]), thus the interaction between these ligands is additive. None of the treatments caused any sign of side-effects.

Conclusions: This study has shown that the intra-articularly administered endogenous μ-opioid receptor agonist EM1 and the NMDA receptor antagonist KYNA dose-dependently decreased the mechanical allodynia without signs of systemic side effects. The coadministration of these ligands produced additive interaction, thus a decreased dose of each drug can lead to effective antinociception. Furthermore, we did not find any changes on the normal side. Therefore, we may exclude systemic antinociceptive effects of these ligands. These results suggest an important direction for the development of pain strategies that focus on the coadministration of different endogenous ligands at peripheral level.

This work was supported by a grant of the National Research and Development Office, Hungary (OMFB-0066/2005/DNT) and the Hungarian Research Grant (OTKA, K60278).

039
VALIDITY OF PAIN ASSESSMENT METHODS IN THE EXPERIMENTAL DOG POND-NUKI MODEL

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Purpose: To evaluate the construct validation of behavioural and physiologic tools to measure orthopaedic pain induced in an experimental canine osteoarthrits (OA) model. We hypothesized that these methods will present different validity and reliability between placebo-controlled and anti-resorptive (tiludronate)-treated dogs. This drug was chosen for its potential as pain-killer without sedative activity.

Methods: This prospective randomized blinded study was performed on healthy adult dogs divided into two groups: Group 1, eight control dogs, and Group 2, eight tiludronate-treated dogs. This drug was chosen for its potential as pain-killer without sedative activity.

Conclusions: None of the treatments influenced the degree of edema. Neither endomorphin-1 nor kynurenic acid administered to the inflamed joint influenced the pain threshold at the non-inflamed side. Both ligands produced dose-dependent anti-hyperalgesia, and the highest doses caused prolonged effect. Endomorphin-1 had higher potency (ED50 value was 112 μg [CI: 80-146]) compared to kynurenic acid (ED50 value was 204 μg [CI: 160-251]). The coadministration of endorphin-1 with kynurenic acid caused potentiated and/or prolonged antinociceptive effect. The ED50 value of the combination was 141 μg [CI: 83-182], which did not differ significantly from the theoretically additive value (ED50 145 μg [CI: 68-237]), thus the interaction between these ligands is additive. None of the treatments caused any sign of side-effects.

Conclusions: This study has shown that the intra-articularly administered endogenous μ-opioid receptor agonist EM1 and the NMDA receptor antagonist KYNA dose-dependently decreased the mechanical allodynia without signs of systemic side effects. The coadministration of these ligands produced additive interaction, thus a decreased dose of each drug can lead to effective antinociception. Furthermore, we did not find any changes on the normal side. Therefore, we may exclude systemic antinociceptive effects of these ligands. These results suggest an important direction for the development of pain strategies that focus on the coadministration of different endogenous ligands at peripheral level.

This work was supported by a grant of the National Research and Development Office, Hungary (OMFB-0066/2005/DNT) and the Hungarian Research Grant (OTKA, K60278).
ing, quantification of behavioural change using automated video-analysis, and electrodermal activity (EDA) used as an indirect quantification of pain. Evaluations were performed at baseline, D28, and D56. General linear model for repeated measures was performed for the analysis of rating scores, PVF, locomotor activity and EDA. Logistic regression for repeated measurements was applied to ordinal and video-analysis data.

**Results:** VAS scores increased from D0 to D28 and remained stable from D28 to D56 for both observers. The overall scores of STAPS and SVAPS increased over time but no difference between groups was observed. The component “Willingness to hold up contra-lateral limb” in SVAPS was lower (p<0.0495), and PVF higher (p<0.05), in Group 2 compared to Group 1 at D56. The criteria “Lameness when walking”, “Lameness when trotting”, and “Reaction to palpation” increased over time in both groups (p<0.01). Intra-observer reliability was good to excellent for Observer 1 (rho = 0.95-0.73) and Observer 2 (rho = 0.91-0.72) over time. Locomotor activity was higher for Group 2 when compared with Group 1 from D0 to D28 (p<0.03), and the difference remained up to D56 without reaching statistical significance. On video-analysis, the occurrence of “Standing with full weight bearing” was 7.7 times more present in Group 2 as compared to Group 1 at D56 (p<0.03). The occurrence of “Walking/Trotting with no lameness” was respectively 5.5 and 6.5 times higher in Group 2 as compared to Group 1 at D56 (p<0.01). The EDA had a trend to be lower in Group 2 when compared to Group 1 at D24 (P=0.059), and without statistical significance at D56.

**Conclusions:** Behavioural methods of pain assessment in dogs indicated different levels of activity and discomfort in relation to treatment (tiludronate or placebo). Despite idiosyncratic compartment, similar conclusions can be drawn on behaviour video-analysis and locomotor activity. Lameness and orthopaedic manipulation were indicators of discomfort on rating pain scales. Tiludronate improved one component of SVAPS without affecting the dog attitude (no sedative effect). Objective methods were more sensitive and specific to detect the functional outcomes on tiludronate-treated dogs.

### 040

**INJECTION OF ALLOGENEIC IMMUNOSELECTED STRO-3+ MESENCHYMAL PRECURSOR STEM CELLS INTO LUMBAR INTERVERTEBRAL DISCS ATTENUATES DEGENERATION AND PROMOTES THE RESTORATION OF THE DISC EXTRACELLULAR MATRIX. AN EXPERIMENTAL STUDY IN AN OVINE MODEL OF DISC DEGENERATION**

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**Purpose:** Disc degeneration is a major cause of morbidity worldwide but non-surgical treatments are presently inadequate. In this study we examined the potential of allogeneic immunoselected STRO-3+ mesenchymal precursor stem cells (MPC), administered intra-discally (ID), to restore matrix integrity in an ovine model of disc degeneration.

**Methods:** Three adjacent lumbar discs (L3-L4, L4-L5, and L5-L6) of thirty-six age-matched adult male wethers were injected ID with 1.0 IU Chondroitinase ABC (cABC) to depolymerise their proteoglycans (PGs) and initiate disc degeneration. The remaining lumbar discs (L1-L2 and L2-L3) were non-injected and were used as normal controls. Fifteen weeks (+3 weeks) after cABC injection, L3-L4 discs were injected with Hyaluronan (HA) mixed with either a high dose (HD-MPC) (4 million)(N=6) or low dose (LD-MPC) (0.5 million)(N=6) cells. L4-L5 discs were untreated (cABC alone)(N=6) and L5-L6 discs were injected with HA alone (cABC+HA)(N=6). Animals were necropsied at 3 months (N=3) or 6 months (N=6) after treatments. Radiographs and MRIs were taken prior to cABC (Baseline), after cABC injection and immediately prior to treatments, and at necropy. Serial sagittal MRI slices of the whole discs were assessed by a blinded observer to grade disc degeneration using an ovine disc MRI scoring system. From the radiographs the disc height index (DHI) scores were calculated using a published method. At necropsy disc tissues, together with a segment of the vertebral bodies, were removed, processed and stained with Alcian Blue and H&E. Sections were scored by a blinded observer for degenerative changes using a published scoring system. Aliquots of the dried fixed disc tissues were analysed biochemically for PG glycosaminoglycans (GAGs) and hydroxy proline for collagen content.

**Results:** Fifteen weeks (+3 weeks) after injection of cABC, DHI decreased by ca 50%, confirming a substantial loss of disc PGs. The DHI results were confirmed by MRI degeneration scores. There was minimal change in DHI during the subsequent 3 months post treatments. However by 6 months all treatments showed an increase in DHI but significance was only observed for the low dose MPC injected discs (p<0.02, ANOVA). Histopathological scores 3 months post treatments showed that discs injected with HD-MPC were significantly improved (p<0.01) but this difference was lost by 6 months. In contrast, the 6 months LD-MPC injected disc histopathology scores were statistically different from the cABC alone and cABC+HA injected discs (p<0.01) but not from the non-injected normal control discs (L2-L3). This pattern of temporal response to the different treatments was consistent with the MRI aggregate disc degeneration scores at 6 months for LD-MPC injected discs confirming that the low dose MPC effect was more sustained than for the high dose MPC. Biochemical analysis revealed that the GAG content of the nucleus pulposus of the cABC and cABC+HA injected discs at 6 months were significantly different to controls (p<0.05) but the LD-MPC injected discs were not.

**Conclusions:** Collectively these data support the conclusion that injection of half a million MPC into degenerate discs accelerated the reconstitution of a new extracellular matrix and improved disc height.

### 041

**CARTILAGE RESTORATION AFTER HIGH TIBIAL OSTEOTOMY**

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**Purpose:** High tibial osteotomy (HTO) has established as an effective method for treatment of unicondylar knee osteoarthritis (kneeOA). The operation often includes an arthroscopic knee evaluation for an exact grading of kneeOA and arthroscopy for treatment of intraarticular pathologies (meniscectomy, extraction of loose bodies, synovectomy and others). The impact of cartilage treatments (debridement, bone marrow stimulation, cartilage transplantation) is still under controversial discussion.

This arthroscopic study was aimed to evaluate the effect of different kinds of treatment (simple joint lavage, mechanical shaving, thermochondroplasty, microfracturing) in combination with an HTO.

**Methods:** A total of 228 patients (118 male, 110 female; age 47.8 [36 to 67] years) had undergone implant removal (Angle-stable HTO [high tibial osteotomy]-plate, Königsee Implantate Germany) and simultaneous control arthroscopy after medial opening wedge HTO.