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AEROBIC EXERCISE, THE HIPPOCAMPUS AND MILD COGNITIVE IMPAIRMENT

Mild cognitive impairment (MCI) is a recognized risk factor for dementia and may represent the prodromal stage of Alzheimer's disease (AD). This study explored the effects of resistance training (RT) and aerobic exercise on hippocampal volume among older women with probable MCI.

This 26-week, single blinded, randomized trial included women between the ages of 70 and 80 years, living independently with probable MCI. The women were randomized to twice-weekly RT, aerobic training (AT) or balance and tone training (BAT). The classes were 60 minutes in duration. To calculate hippocampal volume at baseline and at trial completion, the subjects underwent T1 weighted MRI. The patients were also assessed with the Rey Auditory Verbal Learning Test, wherein they were read a list of 15 words and asked to recall as many words as possible. The primary outcome measure was the change in hippocampal volume. At trial completion, the AT group had significantly increased total hippocampal volume compared with the BAT group ($p=0.01$). Both the left and right hippocampal volumes improved in the AT group as compared with the BAT group ($p=0.03$). Compared with the BAT group, the RT group did not demonstrate a significant increase in total hippocampal volume at trial completion.

Conclusion: This study of patients with MCI suggests that twice weekly aerobic training may be effective in maintaining hippocampal volume.

Brinke, L., et al. Aerobic Exercise

Increases Hippocampal Volume in Older Women with Probable Mild Cognitive Impairment: A Six-Month, Randomized, Controlled Trial. *Br J Sports Med.* 2015, February; 49(4): 248-254.

ASSESSMENT OF GOUT TREATMENT BY ULTRASOUND

Gout is a common arthritis, resulting from the deposition of monosodium urate crystals within the joints. This disorder affects one to two percent of adults in developed countries, and may be increasing in prevalence. Crystal deposition has traditionally been identified by using joint aspirants. Gout may also be diagnosed by ultrasound (US), based upon the presence of a "double contour sign". This study evaluated the ability of US to detect a decrease or disappearance of the US features of gout after the initiation of urate lowering therapy.

This prospective study included males with gout, averaging 61 years of age. Evaluations were made of the first metatarsophalangeal joints and knees at baseline and after six months of treatment. Medical intervention include either allopurinol, 100 mg per day, or febuxostat, 80 mg per day, both titrated to achieve target serum uric acid levels of less than 360 μmol per liter.

Features of gout had not disappeared in four patients who did not reach the target blood levels of serum uric acid. Among those who did achieve target levels, there was an excellent correlation with a decrease or disappearance of US features in all joints reviewed.

Conclusion: This study of patients with gout found that the disappearance of urate deposits by ultrasound analysis correlates well with the efficacy of urate lowering therapy drugs.

Ottaviani, S., et al. Ultrasound n Gout: A Useful Tool for Following Urate Lowering Therapy. *Joint Bone Spine.* 2015, January; 82: 42-44.

CALCITONIN AND NERVE REGENERATION

Calcium ions play an important role in normal neuronal function. Previous studies have shown that after nerve crush injury, functional recovery is correlated with calcium absorption and that accelerated calcium absorption can greatly improve nerve regeneration. This study tested the effect of an implantable mini-osmotic pump on the delivery of calcitonin to a damaged nerve.

This animal study included sixteen, healthy Sprague-Dawley rats, undergoing sciatic nerve transection followed by direct repair. The treatment group received an implantable mini osmotic pump with an attached catheter routed along the injured nerve. The pump delivered calcitonin at a constant, gradual rate to the injury site. A control group underwent the nerve transection repair without pump placement. The animals were evaluated at 12 weeks by electrophysiological and histologic studies, comparing the results between the two groups.

At follow-up, the relative fluorescent units (the calculated calcium intensity of the entire nerve segment) was significantly better in the treatment than in the control group ($p<0.001$). The treatment group had significantly more improved compound muscle action potentials ($p<0.001$), tetanic muscle force ($p<0.001$) and nerve fiber counts ($p<0.001$) compared to the control group.

Conclusion: This animal study of surgically resected nerves found that calcitonin, applied by a pump directly to the healing nerve, improves nerve regeneration and functional recovery. Yan, J., Calcitonin Pump Improves

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Nerve Regeneration after Transaction Injury and Repair. **Muscle Nerve.** 2015, February; 51(2): 229-234.

CANNABINOID NASAL SPRAY FOR NEUROPATHIC PAIN

Neuropathic pain is a chronic and potentially debilitating condition. Despite the availability of multiple treatment options, many produce only partial relief. As previous studies have demonstrated analgesic effects of the endocannabinoids, this study was designed to determine whether a nasal spray containing delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) could impact neuropathic pain.

This study included 380 patients with peripheral neuropathic pain associated with diabetes, or allodynia. The subjects were randomized to a control group or a treatment group. The treatment group received 2.7 mg of THC and 2.5 mg of CBD, administered at a maximum of 24 times every 24 hours. The outcome was measured by change in pain severity on a numerical rating scale (NRS). Secondary outcome measures included scores on a neuropathic pain scale, sleep quality, intoxication, subjective global impressions of change and quality of life.

All patients improved on the NRS pain scale over the initial weeks of treatment. The mean numeric rating scale score decreased from 6.9 at baseline to 4.2 at the end of the

study. Improvements in the neuropathic pain scores were observed after four weeks of treatment, and were maintained over the nine months of the study, without an associated increase in the daily dose of the spray. After nine months, the majority of patients reported 30% or more improvement in pain scores compared to baseline. In addition, improvements in the secondary outcome measures of neuropathic pain scale scores, quality of life and sleep quality were positive and were maintained throughout the duration of the study. **Conclusion:** This open label study found that patients with neuropathic pain can respond well, and over a long period of time, to a delta-9-tetrahydrocannabinol/cannabidiol oral mucosal spray.

Hoggart, B., et al. A Multicentre, Open Label, Follow-up Study to Assess the Long-Term Maintenance of Effect, Tolerance and Safety of THC/CBD Oral Mucosal Spray in the Management of Neuropathic Pain. **J Neurol.** 2015, January; 262: 27-40.

CHONDROPROTECTION AND PREVENTION OF OSTEOARTHRITIS PROGRESSION

Osteoarthritis (OA) is a major cause of musculoskeletal pain and disability worldwide. Most treatment focuses on reducing symptoms, rather than modifying the disease process itself. This systematic literature review was designed to better understand the evidence for the routine use of agents to modify the progression of the OA disease process.

An initial literature search identified 12 treatment agents, each recognized as possessing potential chondroprotective properties of the joint. The authors then identified randomized, controlled trials with a minimum of 12 months' follow-up, evaluating the efficacy of each of those agents. Measures included joint space width, distance between the femoral condyle and the tibial plateau and joint space narrowing or changes in cartilage volume. Of the articles reviewed, 13 fulfilled the criteria.

The data revealed that the long-term use of both oral glucosamine and chondroitin sulfate may have a small, but significant, effect on slowing disease progression in patients with OA of the knee. No conclusions were possible for

treatment using intra-articular injections of these agents. Oral vitamins, including D and E, as well as nonsteroidal anti-inflammatory drugs, did not significantly affect the progression of the joint disease.

Conclusion: This literature review supports the use of both oral glucosamine and chondroitin sulfate as structure modifying, chondroprotective drugs in patients with osteoarthritis of the knee.

Gallagher, B., et al. Chondroprotection and the Prevention of Osteoarthritis Progression of the Knee: A Systematic Review of Treatment Agents. **Am J Sports Med.** 2015, March; 43(3): 734-744.

CIRCULATING C-REACTIVE PROTEIN IN OSTEOARTHRITIS

While osteoarthritis (OA) is generally perceived as a noninflammatory disease, recent studies suggest that local inflammation may play a prominent role in its pathogenesis. This meta-analysis reviewed literature concerning the association between C-reactive protein and OA.

Literature was reviewed for the years 1992 through 2012 from multiple databases. The authors identified studies which involved patients with OA, and included serum high sensitivity C-reactive protein (hsCRP). The data were reviewed to determine the relationship between circulating levels of CRP and OA phenotypes.

The literature review produced 32 studies, including 10 case controlled, cross-sectional, four longitudinal and three clinical trials. Overall, hsCRP was modestly elevated in the population with OA ($p < 0.001$) as compared to controls. In addition, serum hsCRP was associated with symptoms of OA, including pain ($p < 0.001$) and loss of physical function ($p < 0.001$). Serum hsCRP was not, however, significantly associated with joint space narrowing nor Kellgren Lawrence scores. The findings revealed no evidence of a predictive value of hsCRP for the progression of OA.

Conclusion: This literature review and meta-analysis found that low-grade systemic inflammation may play a role in symptoms related to OA, but not radiographic changes associated with OA.

Jin, X et al Circulating C Reactive Protein in Osteoarthritis: A Systematic Review and Meta- Analysis. **Ann Rheum Dis.** 2015, March; 74 (4): 703-710.

EFFECTIVENESS OF SURGERY FOR SPONDYLOLISTHESIS AND LUMBAR STENOSIS IN OCTOGENARIANS

While the surgical treatment of lumbar stenosis and degenerative spondylolisthesis has been found to have substantial and lasting benefits, data are sparse concerning the effect of age on this outcome. This study assessed the clinical outcomes of this surgical intervention for patients at least 80 years of age.

The Spine Patient Outcomes Research Trial (SPORT) included patients with neurogenic claudication or radicular leg pain with associated neurological signs, spinal stenosis on cross-sectional imaging and symptoms persisting for at least 12 weeks. The subjects were randomized to receive either surgical or nonsurgical treatment. The primary outcome measure was the American Academy of Orthopedic Surgeons Musculoskeletal Outcomes Data Evaluation And Management System Version of the Oswestry Disability Index (ODI), as well as the Physical Function and Bodily Pain domains of the SF-36. Secondary outcomes included the Stenosis Bothersome Index, the Low Back Pain Bothersome Scale, patient satisfaction and patient self-reported improvement.

Of the patients with lumbar stenosis, 105 were at least 80 years of age and 1,130 were younger. For patients at least 80 years of age, improvement in all primary outcome measures from baseline was significantly greater in the surgical group, including the SF-36 Bodily Pain score, the SF-36 Physical Function score and the ODI ($p < 0.05$). The surgical treatment effect as measured by the SF-36 Bodily Pain score was significantly better in the younger patients ($p < 0.01$). In the older group improvement in all secondary outcome measures from baseline was significantly greater in the surgically treated group ($p < 0.05$).

Conclusion: This prospective study of octogenarian patients with spondylolisthesis and lumbar stenosis found that surgery offers a significant benefit as compared to nonsurgical

intervention.

Rihn, J., et al. Effectiveness of Surgery for Lumbar Stenosis and Degenerative Spondylolisthesis in the Octogenarian Population. Analysis of the Spine Patient Outcomes Research Trial SPORT Data. **J Bone Joint Surg.** 2015, February 4; 97(3): 177-185.

ENDOGENOUS ADENOSINE A₃ RECEPTOR ACTIVATION AND PAIN

The most successful approaches to the treatment of chronic pain rely on engagement of endogenous circuits involving opioid, adrenergic and calcium channel mechanisms. While adenosine has been found to provide potent and long-lasting pain suppression in both animal and humans studies, targeting this endogenous pathway for pain management has not yet been achieved. This animal study explored the analgesic effects of increasing endogenous adenosine through the use of a selective A₃AR agonist.

Male Sprague Dawley rats and female mice were studied. Persistent neuropathic pain models were produced through chronic constriction injury (CCI), spared nerve injury, spinal nerve ligation, chemotherapy induced peripheral neuropathy (CIPN) and cancer induced bone pain. The animals then received intrathecal injections of a selective non-nucleoside adenosine kinase inhibitor, ABT-702. Mechano- allodynia was assessed using calibrated von Frey filaments. Neurologic function and motor coordination were evaluated by a Rotarod motor test. Nociception was assessed by tail flick and hotplate latency tests. Spontaneous and affective aspects of spinal nerve ligation-induced pain were assessed using conditioned place preference.

Administration of ABT-702 at peak CCI-induced pain reversed mechano- allodynia. These effects were partially attenuated by pretreatment with selective A₃AR antagonists. In addition, in the model of CIPN, ABT-702 reversed mechano- allodynia and mechano- hyperalgesia. ABT-702 did not alter paw withdrawal thresholds in the unaffected contralateral paws.

Conclusion: This animal study found that an A₃AR agonist can be effective in treating several types of persistent pain.

Little, J., et al. Endogenous Adenosine

A₃ Receptor Activation Selectively Alleviates Persistent Pain States. **Brain.** 2015, January; 138(1): 28-35.

EXERCISE FOR WHIPLASH ASSOCIATED DISORDER

Data suggest that, one year after injury, 50% of people with whiplash associated disorder (WAD) still report neck pain. Despite clinical recommendations, there remains no clinical evidence of benefit for many conservative methods of management of chronic WAD, including neck specific exercise. As chronic neck disorders may have symptoms with both physical and psychosocial contributing factors, this study assessed the effects of incorporating a behavioral approach to neck specific exercises.

Subjects were 216 individuals with chronic WAD, with a mean age of 40.5 years. The subjects were randomized to receive either physiotherapist led neck specific exercise (NSE), twice-weekly, aimed at facilitating activity of the deep cervical muscle layers, or similar exercise combined with behavioral intervention. The behavioral treatment included education concerning pain, as well as activities aimed at pain management and problem solving (NSEB). A third group was prescribed physical activity, to be completed outside of the healthcare system (PPA). The primary outcome measure was the Neck Disability Index (NDI). Other outcome variables included self - reported general health, measured with the Euroqol 5-D instrument, and activity level, measured with the International Physical Activity Questionnaire. Pain was recorded with a pain visual analog scale (VAS). At three months, disability levels were found to have significantly improved in both the NSE ($p < 0.01$) and the NSEB ($p < 0.001$) groups, with no improvement observed in the PPA group. At six months, the proportions of responders, as indicated by changes in scores on the NDI, were 21% in the PPA group, 28% in the NSE group and 54% in the NSEB group. Pain bothersomeness was significantly reduced over time in all three groups. Self-efficacy improved only in the NSE group.

Conclusion: This study of patients with whiplash associated disorder found that supervised, neck specific

exercise may have better clinical benefits than a prescription for home exercise, with additional benefits found when combined with a behavioral approach.

Ludvigsson, M., et al. Effect of Neck Specific Exercise with or without a Behavioral Approach on Pain, Disability and Self-Efficacy in Chronic Whiplash Associated Disorder: A Randomized Clinical Trial. *Clin J Pain*. 2015, April;31(4):294-303.

HIP FLEXION STRENGTH FOLLOWING ANTERIOR CRUCIATE LIGAMENT REPAIR

Few studies have evaluated the biomechanics of the hip after anterior cruciate ligament (ACL) reconstruction. This study evaluated hip flexion muscle strength in ACL reconstructed patients with patellar or hamstring tendon graft use, comparing them with healthy controls. This randomized, controlled trial included ACL deficient patients undergoing reconstruction. The subjects were randomized to receive ACL reconstruction with patella tendon or hamstring tendon grafts. In addition, 64 healthy, male athletes participated as controls. The patients were progressed to resistance and endurance training the 13th to 24th weeks post-surgery. All patients underwent isokinetic hip muscle flexion strength testing the day before surgery and one year after surgery. Healthy controls were tested at baseline and at the end of the study.

Preoperatively, no significant difference was found in hip flexion strength between the patella tendon and hamstring groups. While hip flexion strength was increased one year after ACL reconstruction, it remained significantly reduced compared with healthy controls. In addition, hip flexion strength was significantly higher in the patella tendon group than in the hamstring group at one-year postoperatively ($p < 0.001$).

Conclusion: This study demonstrates that hip flexion strength of reconstructed anterior cruciate ligament deficient patients is decreased compared to that of controls at one year post-surgery.

Monzopouloa G., et al. Hip Flexion Strength Remains Decreased in Anterior Cruciate Ligament Reconstructed Patients at One-Year Follow-Up Compared to Healthy Controls. *Intern Orthoped*. 2015; Doi. 10.1007/S00264 – 014.

HOSPITAL STAY AFTER HIP FRACTURE AND RISK OF DEATH

One strategy for controlling health service expenditures involves reducing the length of hospital stay. This study investigated the impact of changes in length of stay after hip fracture in relation to the risk of death among Swedish citizens at least 50 years of age.

Using a closed nationwide cohort, the authors identified patients who had experienced a hip fracture between January 1, 2006, and December 31, 2012. Data were obtained from the Swedish National Patient Register, covering all inpatient care in Sweden. Using a national prescription database, medication use, including that of antidepressants and neuroleptics at the time of hip fracture, was determined. The date of death and underlying cause of death were obtained through the National Cause of Death Register.

During the study period, 116,111 patients sustained a hip fracture at a mean age of 82.2 years. The mean length of stay in 2006 was 14.2 days, decreasing to 11.6 days in 2012 ($p < 0.001$). Patients discharged within five days of admission had twice the risk of death within 30 days of discharge as compared to those with a length of stay of at least 15 days. In 2012, for patients with a length of stay of 10 days or less, each day's reduction in length of stay increased the risk of death within 30 days by 16% ($p < 0.007$).

Conclusion: This Swedish study found that, among the elderly, after hip fracture, a shorter length of hospitalization is associated with an increased risk of death after discharge.

Nordstrom, P., et al. Length of Hospital Stay after Hip Fracture and Short Term Risk of Death after Discharge: A Total Cohort Study in Sweden. *BMJ*. 2015; 350:h696 doi: 10.1136/bmj.

HOSPITAL READMISSION AFTER HIP FRACTURE

Hospital readmission following hip fracture is a frequent and serious event that may indicate a gap in care. National readmission rates following hip fracture have remained essentially unchanged from 2004 to 2009. This study examined the 30-day hospital readmission rate in a center that employs the Geriatric Fracture Center Model of care.

This retrospective study included patients 65 years of age or older, admitted between 2005 and 2010 with a unilateral low-energy hip fracture, requiring surgical correction. Readmissions were identified, with records reviewed to determine the primary cause for readmission.

Of the 1,081 patients reviewed, 129 were readmitted within 30 days of their initial discharge date. Of these, 18.6% were admitted for surgical reasons, including fixation failure, refracture, new fracture, dislocation, hematoma or wound complications. In addition, 81.4% were readmitted for medical reasons. The most common medical reason was pulmonary problems, at 27%. Of those readmitted, 18.6% died during that hospitalization. The one-year mortality rate for patients readmitted within 30 days was 56%, as compared to 21% for those not readmitted ($p < 0.0001$).

Conclusion: This retrospective study of patients undergoing surgical correction for hip fracture found that 11.9% were readmitted, with 18.6% of those readmitted dying during that hospitalization.

Kates, S., et al. Hospital Readmission after Hip Fracture. *Arch Orthopaed Trauma Surg*. 2015, March 3; 135 (3): 329 -337.

INTRA-ARTICULAR BIPHOSPHONATE FOR KNEE OSTEOARTHRITIS

Osteoarthritis (OA) of the knee is a major cause of disability, affecting 10% of people over the age of 55 years. A prior multicenter study found intra-articular clodronate, a bisphosphonate, to be as effective as hyaluronic acid, for the treatment of OA, with significant progression in

improvement of pain and functional outcomes. This study further assessed the tolerability and efficacy of intra-articular clodronate for patients with OA of the knee.

This randomized, double-blind, study included men and women between the ages of 50 and 75 years of age. All had knee OA with radiographic confirmation. The patients were randomly allocated to receive either weekly intra-articular injections of two mg of clodronate or a placebo saline solution for four weeks. The subjects were then followed for a total of 12 weeks. The primary outcome measure was pain relief, as rated on a 100mm Visual Analogue Scale (VAS) at eight weeks. Secondary outcomes included WOMAC scores, Lesquesne index scores and global knee OA (KOA) evaluations by patients and investigators.

Significant improvement was noted on all outcome measures at all time points in both groups. Patients in the clodronate group demonstrated greater improvement in VAS pain scores at eight weeks than did the saline group (by 27.4 mm). However, that difference was no longer evident at 12 weeks. The experimental group demonstrated greater improvement on the Lequesne index, global KOA evaluations of both patients and investigators and the WOMAC pain subscale.

Conclusion: This double-blind, single center, randomized, controlled trial found that intra-articular clodronate provides symptomatic and functional benefits for patients with osteoarthritis of the knee.

Rossini, M., et al. Effects of Intra-Articular Clodronate in the Treatment of Knee Osteoarthritis: Results of a Double-Blind, Randomized, Placebo-Controlled Trial. *Rheum Intern.* 2015, Feb; 35(2): 255-263.

LASTING IMPAIRMENT FOLLOWING HAMSTRING INJURY

Previous studies have shown that neuromuscular maladaptations associated with previous hamstring strain injuries may be related to an elevated risk of future injuries. This study assessed eccentric hamstring strength changes among athletes with a history of hamstring injury.

A cohort of 99 elite Australian footballers, 17 of whom had sustained unilateral hamstring

injuries in the prior 12 months, were recruited for this study. All injured had completed rehabilitation, ranging from 19 to 79 days, and had completed preseason exercise training from November through February. Hamstring eccentric strength was measured at the first and final weeks of each month of preseason training, using an instrumented Nordic hamstring device.

By averaging strength daily, it was discovered that previously injured athletes had a significantly reduced improvement in muscle strength over the course of preseason training, as compared to the uninjured athletes ($p < 0.001$). This diminished response was not confined to the previously injured limb, but was also observed in the contralateral uninjured limb.

Conclusion: This study of elite Australian footballers with hamstring injuries found that, despite completing rehabilitation, these athletes have a reduced response to eccentric strengthening, as compared to those without such an injury history.

Opar, D., et al. The Effect of Previous Hamstring Strain Injuries on the Change in Eccentric Hamstring Strength during Preseason Training in Elite Australian Footballers. *Am J Sport Med.* 2015, February; 43(2): 377-384

MEMANTINE FOR FIBROMYALGIA

Pain is the most common and disabling symptom of fibromyalgia (FM). Glutamate, a central nervous system excitatory neurotransmitter, has been thought to play a role in the pathophysiology of FM. Given the glutamate blocking role of memantine, this study was designed to determine the efficacy of this medication for the treatment of FM.

This controlled, double-blind, randomized trial involved 63 patients diagnosed with FM, randomized to one of two groups. A treatment group received memantine, titrated to 20 mg per day, while a control group received a similar appearing placebo. The main outcome measure was the change in pain threshold and pain perception, evaluated using the Pain Visual Analogue Scale (PVAS), with assessments at baseline, and then at three and six

months' follow-up.

Compared with placebo, patients treated with memantine showed significant improvements in PVAS scores at one, three and six months follow-up ($p = 0.001$ for all comparisons). For secondary outcomes, at six months, significant improvements in favor of the memantine group were found in assessments of global function ($p = 0.000$), clinical global impression ($p = 0.000$), quality-of-life ($p = 0.001$), cognitive function ($p = 0.001$) and depression ($p = 0.002$).

Conclusion: This study of patients with fibromyalgia found treatment with memantine to be effective for the treatment of pain and improvement in quality-of-life.

Oliván-Blázquez, B., et al. Efficacy of Memantine in the Treatment of Fibromyalgia: A Double-Blind, Randomized, Controlled Trial with Six-Month Follow-Up. *Pain.* 2014, December; 155(12): 2517-2525.

NSAIDS: EFFECTS ON OSTEOARTHRITIS SYMPTOMS AND DISEASE PROGRESSION

An estimated 27 million people in the United States have osteoarthritis (OA). Clinical guidelines for the management of this disease include both pharmacologic and nonpharmacologic therapies. This study was designed to estimate the extent to which prescription nonsteroidal anti-inflammatory drugs (NSAIDs), taken over the long-term, affect the symptoms and disease progression of OA.

Between 2004 and 2006, the Osteoarthritis Initiative (OAI) collected baseline data from four study sites, including a total of 4,796 patients with established OA, or who were at high risk for developing OA of the knee, and were not taking an NSAID at study onset, and who began use during the study period. The participants were evaluated for four years with annual follow-up assessments. All were assessed for changes in the Western Ontario and McMaster University Osteoarthritis Index (WOMAC), as well as for radiographic progression over four years. These outcomes were compared between NSAID users and nonusers.

Among nonusers at baseline, six

percent initiated treatment by one year, with 52% reporting regular use. Any prescription NSAID reported on the most recent assessment was not associated with scores for pain, stiffness or physical function on the WOMAC or with the joint space width. However, among those reporting use of prescription NSAIDs at all three of the yearly assessments, improvements were noted in patient reports of stiffness and function, with delayed joint space width progression.

Conclusion: This study found that long-term, but not short-term, use of NSAIDs is associated with important changes in stiffness, physical function and joint space width among patients with osteoarthritis of the knee.

Lapane, K., et al. Effects of Prescription Nonsteroidal Anti-Inflammatory Drugs on Symptoms and Disease Progression among Patients with Knee Osteoarthritis. *Arthritis Rheumatol.* 2015, March; 67(3): 724-732.

NUTRITIONAL SUPPLEMENTS FOR PRESSURE ULCER HEALING

Malnutrition is known to be prevalent among patients with pressure ulcers, and is considered a factor contributing to the development of, as well as inhibiting the healing of these ulcers. As previous studies have demonstrated that supplementation with nutritional formulas enriched with arginine, zinc and antioxidants may have a healing effect, this study further investigated whether an oral nutritional supplement enriched with those substances can assist in healing pressure ulcers.

Subjects were long-term care residents or homecare patients with stage II through stage IV pressure ulcers, all demonstrating malnourishment, defined as a low body mass index, recent unintentional weight loss, low serum albumin levels and reduced food intake. The subjects were randomized to receive a control formula or an experimental formula enriched with arginine, zinc, and vitamins E and C. All patients received optimal wound care. Pressure ulcer areas were documented at baseline, and four

and eight weeks.

Of the screened patients, 200 were randomized. Both groups realized improved wound healing. Compared to baseline, pressure ulcer areas were decreased by an average of 60.9% in the treatment group and 45.2% in the control group ($p=0.017$). In the treatment group, 16.9% experienced complete healing, as compared with 9.7% in the control group ($p=0.097$). Withdrawals from the study included two in the experimental group and three in the control group, with gastrointestinal intolerance as the primary cause of withdrawal.

Conclusion: This study found that, when added to optimal wound care and proper nutrition, a formula with arginine, zinc and antioxidants seems to accelerate pressure ulcer wound healing.

Cereda, E., et al. A Nutritional Formula Enriched with Arginine, Zinc and Antioxidants for the Healing of Pressure Ulcers. *Ann Intern Med.* 2015, February 3; 162(3): 167-174.

OCCUPATIONS ASSOCIATED WITH NECK PAIN

Research concerning the occupational patterns of neck pain has found that certain occupational groups have a higher prevalence of neck pain. This study further analyzed the associations among occupation, work hours and neck pain, as well as demographic factors which impact this pain.

Data were obtained from the National Health Interview Survey, a series of cross-sectional surveys of the health of the United States civilian, noninstitutionalized adults. This study reviewed 63,629 subjects ages 18 to 64, all of whom were employed at the time of the survey. Neck pain was defined as nonspecific neck pain within the past three months. Data collected included occupation classification, hours of work, demographic characteristics, socioeconomic status, leisure time physical activity and psychological distress. The odds ratios for neck pain were calculated using univariate and multivariate logistic regression.

The top five occupations for increased risk of neck pain were: 1) military specific; 2) health care support; 3) arts, design,

entertainment, sports, and media; 4) community and social services; and 5) personal care and services. Compared to those who worked 40 hours per week, those working higher and lower amounts had increased rates of neck pain.

Conclusion: This study suggests that certain demographics, occupations and work hours are related to a higher incidence of neck pain.

Yang, H., et al. Work Related Risk Factors for Neck Pain in the U.S. Working Population. *Spine.* 2015, February 1; 40(3): 184-192.

ORAL HYALURONIC ACID FOR KNEE OSTEOARTHRITIS IN OBESE PATIENTS

Osteoarthritis (OA) is a major cause of pain, disability and loss of function. Obesity is a known risk factor for OA, with hyaluronic acid (HA) plus glucosaminoglycan concentrations decreased in end-stage OA. This randomized, double-blind, placebo-controlled trial assessed the effect of an oral preparation for patients with OA and obesity.

Subjects were 51 patients, 50 to 75 years of age with knee pain of at least 50 mm as assessed with a 100 mm visual analogue scale. All had an effusion requiring joint aspiration or injection. The participants were randomized to receive either 80 mg of Oralvisc or a similar appearing placebo. Outcome measures included pain, function, and inflammatory markers in the serum synovial fluid. $^2\text{H}_2\text{O}$ analysis was completed to evaluate hyaluronic acid turnover and metabolic scores.

At three months, the HA group demonstrated greater improvements in pain and function ($p<0.005$), with decreased concentrations of inflammatory cytokines ($p<0.05$), bradykinin ($p<0.05$), leptin ($p<0.05$) and mean rate of HA decline in synovial fluid ($p=0.046$).

Conclusion: This study suggests that oral preparations containing hyaluronic acid and glucosaminoglycan can effectively treat pain and dysfunction in obese patients with osteoarthritis and active knee effusion.

Nelson, F., et al. Effects Of An Oral Preparation Containing Hyaluronic

Acid on Obese Knee Osteoarthritis Patients Determined by Pain, Function, Bradykinin, Leptin, Inflammatory Cytokines and Heavy Water Analysis. **Rheum Intern.** 2015, January; 35(1): 43-50.

SATELLITE CELL DIFFERENTIATION AND ELECTRICAL STIMULATION

Muscle satellite cells act as reserve cells, able to proliferate in response to injury and give rise to regenerated muscles. As electrical stimulation has positive effects on maintaining muscle contractile function and preventing muscle atrophy, this study reviewed the effects of electrical stimulation on satellite cell population after a nerve crush injury.

Subjects were 72 adult male Sprague-Dawley rats, randomly divided into three groups: Sham, sciatic nerve crush injury and sciatic nerve crush injury plus daily electrical stimulation. The animals in the electrical stimulation group received 30 minutes daily of electrical stimulation over the gastrocnemius muscle. Animals from each group were chosen randomly at two, four and six weeks post-injury for muscle harvest and analysis of muscle force production, Pax7 (measure of satellite cell nuclei), MyoD (measure of total nuclei) and embryonic myosin heavy chain assessment.

At follow-up, muscle mass was greatest in the sham group and least in the injury without stimulation group. In the injury group, the percentage of Pax7/MyoD was higher than in the sham group. Embryonic myosin heavy chain expression was elevated in stimulated muscles with this found to correlate with enhanced force production.

Conclusion: This animal study of crush injury to the sciatic nerve found that satellite cell differentiation is improved by electrical stimulation resulting in increased fiber regeneration and restoration of muscle function.

Xing, H., et al. Electrical Stimulation Influences Satellite Cell Differentiation after Sciatic Nerve Crush Injury in Rats. **Muscle Nerve.** 2015; 51(3), March: 400-411.

SINGLE SPORT SPECIALIZATION AND ADOLESCENT INJURY

Both the American Academy of Pediatrics and The American Medical Society for Sports Medicine have discouraged single sport specialization in youth. However, this recommendation has been made with limited data concerning the relationship between such specialization and the risk of injury. This study sought to clarify the relative impact of sports specialization on adolescent injury.

This case control study included athletes seven to 18 years of age seen in primary care sports medicine clinics. All participants completed surveys at enrollment, including demographics and current sports specialization, as well as self-assessment of pubertal maturation. Sports specialization was defined as year-round, intensive training in a single sport at the exclusion of other sports. Using this definition, sports specialization was categorized as low, moderate or high. Injuries were classified by clinical diagnoses obtained from medical records, characterized as acute or overuse.

Of the injuries noted, 67.4% were overuse, with patellofemoral pain the most common. Independent and dose dependent risks for injury, and for serious overuse injury were found for sports specialized training, after accounting for age and time spent in sports activity ($p < 0.01$ for all). There was no difference in the growth rate between the two groups.

Conclusion: This study found that sports specialization in young athletes increases the risk of acute and overuse injury.

Jayanthi, N., et al. Sports-Specialized Intensive Training and the Risk of Injury in Young Athletes. A Clinical Case Control Study. **Am J Sports Med.** 2015, February. doi:10.1177/0363546514567298

ULTRASOUND ASSESSMENT OF STEROID INJECTIONS TO THE KNEE

Osteoarthritis (OA) is a common form of arthritis, affecting up to 10% of the North American elderly

population. In addition, the prevalence of radiographically established OA in the United States is estimated to be 33% among individuals over 63 years of age. This study was designed to determine whether ultrasound (US) can be effective in demonstrating a response to intra-articular corticosteroid injections to the knee.

Subjects included 35, consecutive subjects who met the American College of Rheumatology's radiologic criteria for OA. All subjects completed a symptom assessment and US examination at baseline, and returned for follow-up at 14 weeks. Of those, 19 participants were determined to be in need of a corticosteroid injection, and received 80 mg of methylprednisolone mixed with 2 mL of lidocaine one percent. The remaining subjects underwent no therapeutic intervention. All participants were asked to rate their knee pain on a visual analogue scale, and to complete the Western Ontario McMaster Universities Osteoarthritis Index (WOMAC). The knee joints were assessed with US at baseline and at four weeks.

At follow-up US, synovial thickness was noted to have decreased in 16 of the 19 patients in the treatment group, and in two of the 14 patients in the control group ($p = 0.012$). A reduction in synovial thickness was associated with a reduction in pain greater than or equal to the predetermined minimally clinically important improvement level (> 20 mm on the VAS). With both groups combined, no substantial association was seen between changes in synovial thickness and changes in pain.

Conclusion: This pilot study suggests that US may be useful in detecting early changes in synovial pathology in response to intra-articular anti-inflammatory therapy.

Keen, H., et al. Ultrasound Assessment of Response to Intra-Articular Therapy in Osteoarthritis of the Knee. **Rheum.** 2015 DOI: 10.1093/rheumatology/keu529.

TRANSCRANIAL DIRECT CURRENT STIMULATION IN LUKOARAIOSIS

Lukoaraiosis involves hyperintensities in the cerebral

subcortical white matter, with associated gait and balance dysfunction. There are no proven treatments for gait disorder and balance dysfunction in these patients. This study evaluated the use of transcranial direct current stimulation (tDCS) to augment the effects of physical therapy training in the treatment of patients with lukoaraiosis.

This double-blind study included nine patients with lukoaraiosis, all with gait and balance disturbances, and 18 healthy controls. The subjects were randomized to receive either tDCS or sham stimulation during physical therapy training. This process was repeated one week later, with the stimulation situation reversed, in a double-blind design. The stimulation included a 2 mA current delivered during exercise for 15 minutes. The patients were assessed for gait velocity, stride length, stride length variability, six meter walk test results and quantitative retropulsion test results.

Patients in the control group performed significantly worse on all tests than did the treatment group.

Significant improvements were noted in the treatment group in gait velocity ($p=0.008$), stride length ($p=0.05$), stride length variability ($p=0.02$), timed up and go duration ($p=0.042$), the six meter walk test ($p=0.03$) and the retropulsion test ($p=0.045$). *Post-hoc* analysis revealed no effect of physical therapy alone.

Conclusion: This randomized, controlled study of patients with lukoaraiosis found that the combination of transcranial direct current stimulation and locomotor training can improve clinically relevant locomotor performance.

Kaski, D., et al. Improving Gait and Balance in Patients with Lukoaraiosis Using Transcranial Direct Current Stimulation and Physical Therapy Training: Exploratory Study. *Neurorehab Neural Repair*. 2013, November/December; 27: 864-871.

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