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ACUPUNCTURE VERSUS IV MORPHINE FOR ACUTE PAIN

While acupuncture has been introduced to a number of health systems throughout the world, its use in the (ED) is rare. This study evaluated the efficacy and safety of acupuncture compared with that of morphine for adults presenting to the ED with acute pain.

This prospective, randomized, non-blinded trial included adult patients presenting to the ED of a university hospital in Tunisia with acute pain syndromes. All patients reported a pain intensity of at least 40 on a 100-point visual analogue scale (VAS). In the group randomized to receive acupuncture (n=150), protocols were selected from a pool of predetermined acupuncture points for each condition. Those randomized to the morphine group (n=150) received IV morphine, titrated from an initial dose of 0.1 mg per kilogram, adding a dose of 0.05 mg per kilogram every five minutes, until reaching sufficient pain relief, to a maximum of 15 mg. The primary outcome measure was pain severity at baseline and five, 10, 20, 30, 45, and 60 minutes.

Success, defined as a reduction of at least 50% in pain severity from baseline, was achieved in 92% of the acupuncture group and 78% of the morphine group ($p<0.01$). Pain resolution time averaged 16 minutes in the acupuncture group and 28 minutes in the morphine group ($p<0.01$). Minor adverse events were experienced by 56.6% of those in the morphine group and 2.6% in the acupuncture group.

Conclusion: This randomized trial of patients presenting with acute pain in the emergency department found that acupuncture could provide better and quicker relief than could IV morphine.

Grissa, M., et al. Acupuncture versus Intravenous Morphine in the Management of Acute Pain in the E.D. **Am J Emerg Med.** 2016, November; 34 (11): 2112-2116.

SHOCKWAVE THERAPY VERSUS BOTOX FOR PLANTAR FASCIITIS

Plantar fasciitis (PF) is very common in the general population, often persisting for many months. As extracorporeal shockwave therapy (ESWT) has been used in the management of tendinopathies and botulinum toxin A (BoNT-A) has been used to treat pain, this study compared the effects of those two interventions for the treatment of PF.

This open label, prospective, randomized study included patients with PF who had not responded to physiotherapy and electrotherapy. The participants were randomly assigned to receive either ESWT, focused at the area of maximum tenderness for 15 minutes per session, or 100 units of BoNT-A, with injections divided between the insertion of the plantar fascia in the calcaneus and the area of maximal tenderness. The subjects were assessed for pain in the affected foot on a 10-point visual analogue scale (VAS), when taking the first steps in the morning, during daily activity, and while performing exercises. Each patient was also assessed with the Quality of Life Health Status Questionnaire.

Data for 72 patients were included in the analysis. The median pain score when taking the first steps in the morning was significantly better in the ESWT group than in the BoNT-A group ($p=0.009$). Better improvement was also noted in the ESWT group than in the BoNT-A group on the Roles and Maudsley Scale of Pain between the first and second visit, as well as in the percentage of patients who noted improvement in pain on at least one of three modalities of VAS pain scores ($p=0.006$ and $p=0.029$, respectively). A regression analysis revealed that ESWT and low body weight were independently associated with improvement in pain.

Conclusion: This study of patients with recalcitrant plantar fasciitis found that shockwave therapy was superior to botulinum toxin A for reducing pain.

Roca, B., et al. Comparison of Extracorporeal Shockwave Therapy with Botulinum Toxin Type A in the Treatment of Plantar Fasciitis. **Disabil Rehab.** 2016, October. 38 (21); 2114-2121.

NEUROPATHIC CHANGES IN FORMER COLLEGE FOOTBALL PLAYERS

A recent National Collegiate Athletic Association report suggests that 11% of injuries in college football involve blows to the head, with players averaging more than 14 significant head impacts per game. This study compared MRI findings of the brain between those of former college football players who retired from participation after graduation, with those of former college athletes from noncontact sports.

Subjects were 25 former Division I players, under the age of 30, who were matched with 97, demographically similar, current and former track and field athletes from the same institution. The participants were queried about their history of concussions, with a diagnostic assessment performed using the Structured Clinical Interview for DSM-IV axis one disorders, and the National Adult Reading Test. All underwent MRI scanning, with diffusion tensor imaging (DTI).

Football athletes had significantly lower cortical thickness than did noncontact athletes, in portions of frontal and temporal cortex with significant differences in the left frontal pole ($p=0.03$), and the right superior frontal gyrus ($p=0.002$).

Cortical thickness in these two regions was inversely correlated with the number of concussions. In the DTI studies, fractional anisotropy did not differ between the groups.

Conclusion: This study found that former college football players had lower cortical thickness across the prefrontal and temporal regions involved in sustaining attention, memory and executive abilities, as compared to former track athletes.

Adler, C., et al. MRI Evidence of Neuropathic Changes in Former College Football Players. **Clin J Sport Med**. 2016; 0: 1-7.

CURCUMIN AND DIABETIC ATHEROSCLEROSIS

Curcumin, a compound existing in turmeric, has been widely used as an anti-inflammatory treatment in traditional Chinese and Ayurvedic medicines. This animal study assessed the efficacy of L3, an analog of curcumin, compared to probucol, a traditional lipid lowering drug, for the prevention and treatment of the cardiovascular complications of diabetes.

Using a mouse model of diabetes, 93 mice were divided into eight groups, with seven of those groups undergoing diabetes induction. The mice were randomized to receive one of two doses of curucmin, one of two doses of probucol, or one of three doses of L3, while receiving a high cholesterol/fat diet. The animals were studied for changes in lipid panel results and antioxidant status, as well as reactive oxygen species (ROS) generation in the pancreas. The subjects were sacrificed after 16 weeks.

After treatment with curcumin, plasma insulin levels returned to their normal levels. All three compounds were found to reduce blood lipids in a concentration dependent manner. All three compounds were also found to reduce the oxidative stress of liver and red blood cells. All treatment groups showed increased nitric oxide fluorescent intensities in the target tissues in a dose dependent manner. L3 was also found to decrease the production of ROS in the pancreas and lectin-like oxidized low-density lipoprotein receptor-1 expression in the aortic arch, as well as reduced fatty and atherosclerotic degeneration in the aortic arch, as compared with the control group.

Conclusion: This animal study of diabetes found that L3, an analog of curcumin, can, through a number of mechanisms, inhibit diabetic atherosclerosis.

Zheng, B., et al. Curcumin Analog L3 Alleviates Diabetic Atherosclerosis by Multiple Effects. **Eur J Pharmacol**. 2016. 775(15): 22-34.

TOOTH LOSS AND FUNCTIONAL CAPACITY

Many studies have reported on the relationship between oral health and general health. This study was designed to determine whether an association exists between dental health and a decline in higher-level functional capacity.

Data were derived from the Japan Gerontological Evaluation Study (JAGES), involving community dwelling adults, 65 years of age or older, who were cognitively independent. A baseline survey was conducted between August of 2010 and January of 2012, with a follow-up conducted between January of 2013 and December of 2013. Subjects were asked about the status of their dental health, including the number of natural teeth that they currently possessed. Higher-level functional capacity was assessed using the Tokyo Metropolitan Institute of Gerontology Index of Competence (TMIG-IC), with covariates including health, and health behavior variables that might be related to the TMIG-IC.

Of the respondents, 62,333 were included in the final analysis, with a median follow-up of 707 days. In the adjusted analysis, a multiple linear regression model found a dose response association between tooth loss and decline in TMIG-IC scores.

Conclusion: This large, population-based, prospective cohort study indicates a dose response association between tooth loss and a decline in higher-level functional capacity over two years.

Sato, Y., et al. Tooth Loss and Declining Functional Capacity: A Prospective Cohort Study from the Japan Gerontological Evaluation Study. **J Am Geriatr Soc**. 2016, November; 64(11): 2336-2342.

TURMERIC USE FOR GINGIVITIS

It is estimated that gingivitis effects 80% of the population. Chlorhexidine is a broad-spectrum antiseptic, considered the gold standard for preventing and treating gingivitis. Curcumin, a polyphenol found in turmeric, has been found to have anti-inflammatory, antioxidant, antibacterial, antiviral and antifungal properties. This literature review compared the efficacy of turmeric with that of chlorhexidine for the prevention of gingivitis.

Medical databases were reviewed for studies concerning gingivitis which compared curcumin or turmeric, with chlorhexidine for the treatment of gingivitis.

Data from five papers with a total of 290 participants were included in the analysis, with turmeric and chlorhexidine delivered as either a mouthwash or gel. The duration of all five studies was 21 days, with two studies including bacterial counts. All studies found that both turmeric and chlorhexidine improved scores on the gingival index (GI) and plaque index (PI). In two of the studies, chlorhexidine was found to be more effective in preventing plaque, with one of these finding that chlorhexidine was better at reducing inflammation.

Conclusion: This literature review, focusing on the treatment of gingivitis, found that, overall, compared to the gold standard chlorhexidine, treatment with turmeric was equally effective for preventing and treating gingivitis.

Stoyell, K., et al. Clinical Efficacy of Turmeric Use in Gingivitis: A Comprehensive Review. **Complement Ther Clin Pract.** 2016, November; 25: 13-17.

DIURETIC USE AND THE RISK OF VERTEBRAL FRACTURES

It has been estimated that 25% of postmenopausal women in the United States will sustain a vertebral fracture, with the prevalence increasing with advancing age. Among older adults in the United States, hydrochlorothiazide, a diuretic, is the second most commonly used prescription or over-the-counter drug. Thiazides have been shown to decrease urinary calcium excretion, improve calcium balance, but can also cause hyponatremia, a condition associated with an increased risk of fractures. Loop diuretics increase urinary calcium excretion and lower bone mineral density, but rarely cause hyponatremia. This prospective study compared the association between thiazide and loop diuretic use and vertebral fractures.

Data were obtained from the Nurses' Health Study, an ongoing, prospective, cohort study begun in 1976, and enrolling 121,700 female registered nurses, 30 to 55 years of age. Data from this study included 55,780 women who completed both the 2002 questionnaire including questions of diuretic use, and the 2012 questionnaire which included questions about vertebral fractures. Potential confounders for fracture risk were also recorded.

During 543,209 person-years of follow-up, there were 420 confirmed cases of incident vertebral fracture. In the multivariable-adjusted analysis, thiazide diuretic as well as loop diuretic use were both associated with a significantly increased risk of vertebral fracture (relative risk 1.47 and 1.59, respectively) compared to nonusers.

Conclusion: This study found that both thiazide diuretics and loop diuretics are independently associated with an increased risk of vertebral fracture in women.

Paik, J., et al. Diuretic Use and Risk of Vertebral Fracture in Women. **Am J Med.** 2016, December; 129(12): 1299-1306.

EPIDURAL STEROIDS AND BONE MINERAL DENSITY

Lumbar epidural steroid injections (ESI) are widely used to treat back pain. Previous studies have demonstrated that glucocorticoids have multiple side effects, including glucocorticoid-induced osteoporosis. This study assessed the relationship between ESIs and changes in bone mineral density (BMD) in postmenopausal women with low back pain (LBP).

This retrospective analysis included 126 postmenopausal patients who underwent ESI for the treatment of LBP, who had received dual-energy x-ray absorptiometry (DEXA) scans before and after treatment. Body mass index was calculated with BMD determined using DEXA. Of those included, group one comprised 74 patients who received injections with dexamethasone while taking an anti-osteoporotic medication, while group two comprised 52 patients who underwent these injections while not taking an anti-osteoporotic medication.

The mean changes between baseline and post-treatment BMD in group one were 1.25% in the lumbar spine and 0.45% in the femoral neck, 0.39% in the femoral trochanter and 0.21% in the total femoral region, with none reaching statistical significance. The mean changes in group two, were 0.69% in the lumbar spine, -1.48% in the femoral neck ($p=0.003$), -2.8% in the femoral trochanter ($p=0.008$) and -2.23% in the total femoral region ($p<0.001$).

Conclusion: This study of postmenopausal women undergoing epidural steroid injections found that these injections are associated with worsening osteoporosis, an effect that seems mitigated by the use of anti-osteoporotic medication.

Kim, Y., et al. Effect of Epidural Steroid Injection on Bone Mineral Density in Postmenopausal Women According to Anti-Osteoporotic Medication Use. **Pain Physician.** 2016, July/August; 19 (6): 389-396.

FRACTURE HEALING AND OSTEOPOROTIC DRUGS

The two major categories of pharmacologic treatment for osteoporosis are antiresorptive and bone anabolic medications. Teriperatide is the only currently approved anabolic medication for the treatment of osteoporosis. This study compared the effects of this medication with that of a bisphosphonate, risondronate, on the functional and radiographic outcomes after a hip fracture.

This multinational, randomized active controlled trial included patients with peritrochanteric hip fractures and bone mineral density T-scores of -2.0 or less, and 25-OH-vitamin D levels of 9.2 ng/mL or greater. The patients were randomized to receive teriperatide 20 µg per day subcutaneously, or risondronate 35 mg per week. At screening, both groups began oral supplements of calcium and vitamin

D and discontinued any ongoing osteoporotic drugs. Patients were assessed for functional mobility at six, 12, 18 and 26 weeks, with outcome measures including the SF – 36 survey, Timed up and Go (TUG) test, a visual analogue pain scale, the modified Charnley hip pain score, as well as the ability to walk.

Of the patients randomized, 171 contributed to the efficacy analysis. The time required to complete the TUG test was shorter in the teriperatide group compared with the risondronate group at six, 12, 18, and 26 weeks (p=0.021 for the overall between-treatment effect). The self-reported pain was reduced more in the teriperatide group than the risondronate group (p=0.032). There was no difference between groups in the domains of the SF – 36, radiographic healing, or the ability to walk at 26 weeks.

Conclusion: This prospective randomized trial of patients with peritrochanteric hip fractures found that teriperatide treatment after fracture is associated with better functional outcome compared with risondronate.

Aspenberg, P et al. Effects of Teriperatide Compared with Risondronate on Recovery after Peritrochanteric Hip Fracture: Results of a Randomized, Active Control, Double-Blind Clinical Trial at 26 Weeks. **J Bone Joint Surg Am.** 2016, Nov 16; 98 (22):1868 – 1878.

SUSTAINED HEAT TREATMENT FOR DELAYED-ONSET MUSCLE SORENESS

Muscle soreness after exercise is common, and can reduce the ability to perform in the days following. While cold is the most commonly recommended modality after exercise, both heat and cold have been prescribed. This study assessed the effect of sustained heat treatment on both objective and subjective measures of delayed-onset muscle soreness (DOMS).

The 20 subjects were randomized to one of three groups, including heat wraps applied immediately after exercise (group 1), heat wraps applied 24 hours after exercise (group 2) or a control. To provoke DOMS, subjects were engaged in squatting exercises for 15 minutes. Patients were assessed for muscle soreness with a visual analogue (VAS) scale, for strength and range of motion, and for changes in plasma biomarker measurements at baseline and 48 hours after exercise. Heat therapy was applied by placing a ThermaCare heat wrap on each leg over the quadriceps for eight hours.

At 24 hours post-exercise, the control group demonstrated a 23.8% loss of muscle strength as compared with baseline, with group 2 demonstrating similar results. In group 1, no significant reduction in strength was noted on any post-exercise day. An increase in pain was found after exercise for all three groups, peaking by post-exercise day two. Significantly less pain was noted by group 1 on the first and second days after exercise (p<0.001), but not day three. Greater pain-free passive range of motion was noted in group 1 than in the other two groups.

Conclusion: This study found that, after intense exercise, immediate, low level heat wraps applied for eight hours can reduce delayed-onset muscle soreness and post-exercise strength reductions.

Petrofsky, J., et al. The Efficacy of Sustained Heat Treatment on Delayed-Onset Muscle Soreness. **Clin J Sports Med.** 2016; DOI: 10.1097/JSM.0000000000000375.

CIGARETTE SMOKING AND CUBITAL TUNNEL SYNDROME

Studies have demonstrated that gender, age, body mass index and workers' compensation status contribute to the development of cubital tunnel syndrome (CubTS). As conflicting results have been found for the association between tobacco abuse and CubTS, this study was designed to better understand this relationship.

Subjects included 100 patients with CubTS who underwent surgical repair, compared with 100 individuals who underwent surgical correction for ulnar abutment syndrome (UAS). The latter were chosen, as the pathogenesis of UAS has not been shown to be associated with cigarette smoking. Smoking history was assessed by patient self-report, with subjects classified as current smokers, past smokers or never smokers.

A significantly greater proportion of the controls had never smoked cigarettes (p<0.001), while a significantly greater proportion of patients with CubTS were past smokers (p=0.001). There was no difference between groups in current smokers. There was a dose dependent association between pack years smoked and the odds ratio for CubTS, ranging from 2.9 among those with 1-15 pack years to 29.93 among those with more than 30 pack years.

Conclusion: This retrospective study suggests an association between cubital tunnel syndrome and a history of cigarette smoking.

Suzuki, T., et al. Cigarette Smoking Is Associated with Cubital Tunnel Syndrome. **Muscle Nerve.** 2016, December; 54(6): 1136-1138.

THE GUT MICROBIOME AND CHRONIC FATIGUE

Myalgic encephalomyelitis (ME), also known as chronic fatigue syndrome (CFS), is a debilitating illness with unclear etiology and no widely accepted therapy. Patients with ME/CFS often report gastrointestinal symptoms. As objective molecular markers for the diagnosis of CFS are lacking, this study examined plasma markers in the microbiota composition of patients with this diagnosis.

Subjects included 48 patients with CFS, and 39 controls who reported good health. For all subjects, fecal and blood samples were collected. From the samples, plasma levels of hsCRP, sCD14, lipopolysaccharade (LPS), LPS binding protein (LBP) and intestinal fatty acid binding protein (I-FABP), and stool for 16S ribosomal ribonucleic acid (rRNA) genes were derived. The levels of hsCRP, lipopolysaccharides (LPS) were measured, as a marker of microbial translocation (MT), and plasma intestinal fatty acid binding protein (I-FABP), as a marker of gastrointestinal damage.

ME/CFS patients had significantly higher plasma levels of LPS, LBP and sCD14 than did controls (p<0.0005), suggesting greater microbial translocation. Based upon data obtained from bacterial 16S rRNA markers, ME/CFS samples were found to have a significantly lower microbial diversity, with lower levels of the genus Faecalbacterium, Bifidobacterium, and the phylum

Firmicutes. In addition, increases in proinflammatory species and a reduction in anti-inflammatory species were found in the ME/CSF patients as compared with controls. With data obtained from 16S rRNA and inflammatory markers, individuals were classified correctly as ME/CFS with a cross-validation accuracy of 82.93 %.

Conclusion: This study of patients with chronic fatigue syndrome found evidence of ongoing damage to the gut mucosa, and differences between the gut microbiomes of healthy individuals and patients with ME/CFS in the relative abundance of specific genera.

Giloteaux, L., et al. Reduced Diversity and Altered Composition of the Gut Microbiota in Individuals with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. **Microbiome**. 2016; 4:30 DOI 10.1186/s40168-016-0171-4.

INTRANASAL KETAMINE FOR ACUTE TRAUMATIC PAIN

Opiates are the current mainstay of severe pain relief. Ketamine, an NMDA-antagonist, has been studied for its efficacy in analgesia and anesthesia. This study was designed to better understand the efficacy and safety of intranasal (IN) ketamine for use in the emergency department.

This single center, randomized, prospective, clinical trial recruited patients ages 18 to 70 years presenting to the ER with orthopaedic pain rated as $\geq$ 80/100 on a visual analogue scale (VAS). Eligible subjects were randomized to receive IN ketamine (1mg/kg), IM morphine (0.15 mg/kg IM) or IV morphine (0.1 mg/kg) in a 1:1:1 ratio. Vital signs and VAS measurements were recorded at five minute intervals. The primary outcome measure was the effectiveness of the drug in reducing pain intensity. The "time to onset" (TTO) was defined as the time until the patient reached a 15 mm VAS pain score reduction.

In the 90 patients recruited, the TTO for IN ketamine was 14.3 minutes, for IV morphine was 8.9 minutes (p=0.30) and for IM morphine was 26 minutes (p = 0.003). The maximal VAS pain score reduction was 56 mm, 59 mm and 48 mm pain for the IN ketamine, IV morphine and IM morphine groups, respectively (p = 0.3). The time to maximum pain reduction was 40.4 minutes for IN ketamine, 33.4 minutes for IV morphine, and 46.7 minutes for IM morphine (significant at p = 0.019 comparing IM and IV morphine). No significant difference was seen between groups in patient satisfaction.

Conclusion: This emergency room study of patients with moderate to severe orthopedic pain found that intranasal ketamine may have similar efficacy as IM or IV morphine.

Shimonovich, S., et al. Intranasal Ketamine for Acute Traumatic Pain in the Emergency Department: A Prospective, Randomized, Clinical Trial of Efficacy and Safety**. BMC Emerg Med.** 2016, November; 16: 43.

OCRELIZUMAB FOR PRIMARY PROGRESSIVE MULTIPLE SCLEROSIS

As B cells are thought to influence the pathogenesis of multiple sclerosis (MS), through antigen presentation, auto antibody production or cytokine secretion, a number of treatment options have focused on manipulating the function of B cells. This study explored the efficacy and safety of Ocrelizumab, a humanized monoclonal antibody that selectively depletes CD20-expressing B cells.

Subjects were 18 to 55 years of age with a diagnosis of primary, progressive MS. The patients were randomized to receive Ocrelizumab, 600 mg every 24 weeks, or a placebo for a minimum of five doses (120 weeks). All patients received IV methylprednisolone at 100 mg before infusion.

The primary endpoint was the percentage of patients with disability progression, using the Expanded Disability Status Scale (EDSS). Secondary endpoints included change from baseline to week 120 in performance on the timed 25-foot walk, change in the total volume of brain lesions on T_2-weighted MRI, change in the Physical Component Summary score of the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), Version 2, and change in brain volume from week 24 to week 120.

The percentages of patients with 24-week confirmed disability progression were 29.6% in the treatment group and 35.7% in the placebo group (p=0.04). Significant improvement was noted in the treatment group as compared with the placebo group on the timed 25 foot walk (p=0.04), with no difference between groups on the SF-36 Physical Component score (p=0.6). The total volume of hyperintense lesions on T_2-weighted images decreased in the treatment group and increased in the placebo group (p<0.001).

Conclusion: This study of patients with primary progressive multiple sclerosis found that Ocrelizumab is associated with lower rates of clinical and MRI progression.

Montalban, X., et al. Ocrelizumab versus Placebo in Primary Progressive Multiple Sclerosis. **N Engl J Med.** 2016. DOI: 10.1056/ NEJMoa1606468.

MEMORY DEFICITS IN MILD TRAUMATIC BRAIN INJURY

The detrimental consequences of mild traumatic brain injury (mTBI) are becoming more apparent in a number of different cognitive domains. This study reviewed the long-term effects of mTBI one year or more post-injury.

Undergraduate students were recruited from psychology classes at the University of Waterloo in Ontario, Canada, with older adults recruited from the Waterloo Research in Aging Participant Pool (WRAP). Of the 39 students recruited 20 reported a remote mTBI, and of the 42 older adults recruited, 20 reported a mTBI. Those with and those without remote mTBI were compared by performance on a series of neuropsychological tests.

As the mean intervening time since mTBI in the older adults was 38 years, the analysis was completed first with both groups combined, and then with only the younger group. Within the older group, no significant differences were observed based on mTBI status. In the younger group, those with a history of mTBI performed more poorly than did those without mTBI on free recall (p<0.05), as well as when recounting autobiographical memories (p<0.01).

Conclusion: This study of individuals with remote mTBI suggests that these individuals, despite having otherwise normal

cognitive test results, may have a specific pattern of cognitive deficits characterized by a decreased ability in free recall and reduced episodic detail when recounting autobiographical memories.

Wammes. J., et al. Autobiographical and Episodic Memory Deficits in Mild Traumatic Brain Injury. **Brain Cognition.** 2017, February; 111: 112-126.

PHYSICAL EXERCISE AND MYASTHENIA GRAVIS

Myasthenia gravis (MG) is a neuromuscular disease with weakness as a cardinal symptom. Little research exists concerning aerobic or muscular resistance training in patients with MG. This study examined the effects of exercise in this population.

This prospective study included patients diagnosed with chronic MG, recruited from three outpatient neurology clinics in Sweden. The participants underwent supervised exercise sessions lasting 75 minutes and consisting of aerobic, resistance and balance training two times per week for 12 weeks. The patients were assessed before and after training with nerve conduction studies, strength and performance measures and with blood tests of serum for serum specific microRNAs, interleukin-6, muscle enzymes, CRP, and creatinine, as well as the MG Composite Score, and peak expiratory flow.

Among the 10 participants, there was no evidence of increased disease activity during the study. In the nerve conduction studies, the CMAP amplitude increased significantly in the biceps and quadriceps ($p=0.002$ and $p=0.037$, respectively). Proximal muscle strength significantly improved in both arm and leg muscles. Performance on the Six-Minute Walk Test and 30-Second Walk Test improved significantly ($p=0.002$ and $p=0.0039$, respectively). While BMI did not significantly change, body composition did, with increased muscle mass and reduced fat mass ($p=0.02$). All patients scored much higher in physical activity after the study ($p=0.008$). The disease-specific microRNAs, miR150-5p ($p=0.048$) and miR21-5p ($p=0.0020$), were significantly reduced after the training period, while muscle enzymes remained normal.

Conclusion: This small study of patients with chronic myasthenia gravis found that exercise training, twice per week, increased aerobic capacity, improved body composition, improved motor action potential amplitudes, and improved disease specific biomarkers.

Westerberg, E., et al. Physical Exercise in Myasthenia Gravis Is Safe and Improves Neuromuscular Parameters and Physical Performance-Based Measures: A Pilot Study. **Muscle Nerve:** DOI: 10.1002/mus.25493.

PREVALENCE OF SUICIDAL BEHAVIOR FOLLOWING TRAUMATIC BRAIN INJURY

Several studies have suggested that, following a traumatic brain injury (TBI), the risk of developing major depressive disorder is elevated, as compared with that of the general population. Several smaller, isolated studies have suggested an increased risk of suicide as well. This study used the TBI Model Systems database (TBIMS) to better understand the rates of depression, suicidal ideation, suicide attempts and completed suicides among patients with moderate to severe TBI, who have undergone inpatient rehabilitation.

Data were collected from October of 2007 through September of 2013, including that of patients, ages 16-99, who completed the Patient Health Questionnaire (PHQ-9) assessment of depression at one or more assessment points. Suicidal ideation was assessed from the PHQ-9. Suicide attempts and completed suicide acts were also documented.

Of the 12,046 individuals enrolled, 21 completed suicides were recorded with a cumulative rate of 0.17%. The rate of suicide at years 1, 2, 2-5, 5-10, 10-15, and 15-20, was recorded at 0.03%, 0.05%, 0.06%, 0.02%, 0.02% and 0.0% respectively. During the 20 years of follow-up, rates of depression ranged from 25% to 28%, with 4.3% reporting one prior suicide attempt. Throughout the study, rates of suicidal ideation were two to three times higher than in the general population.

Conclusion: This study of patients with moderate to severe traumatic brain injury, who received inpatient rehabilitation, found higher rates of depression and suicidal ideation than in the general population.

Fisher, L., et al. Prevalence of Suicidal Behavior following Traumatic Brain Injury: Longitudinal Follow-Up Data from the NIDRR Traumatic Brain Injury Model Systems. **Brain Inj.** 2016; 30(11): 1311- 1318.

OCCIPITAL NERVE STIMULATION FOR CHRONIC MIGRAINE

Despite medical advances, it is estimated that five percent of patients with chronic migraine (CM) are refractory to treatment. As some have suggested the feasibility of occipital nerve stimulation (ONS) for the treatment of these headaches, this study examined the long-term outcomes of a single center cohort of patients with CM undergoing ONS.

Patients seen at a headache clinic in London with a diagnosis of CM were treated with implantation of bilateral ONS electrodes, and an implantable pulse generator (IPG). Remote controls were provided to the participants to adjust the stimulation amplitude. The subjects maintained headache diaries and were reviewed in clinic every three months for the first year and 12 months thereafter. The Migraine Disability Assessment Scores (MIDAS) and Headache Impact Test Six (HIT-6) scores were recorded before and after ONS to monitor headache-related disability. The primary outcome measure was improvement in mean monthly, moderate-to-severe headache days compared to baseline. A “responder” was defined as a patient who had a 30% or more reduction in headache days.

Of the 53 patients, the mean duration of CM was 11.77 years, with a mean follow-up of 42 months. At final follow up, 45.3% were “responders” including 34.3% of those with CM alone and 66.7% of those with multiple headache types. Monthly moderate-to-severe headache days fell by 8.51 days ($p<0.001$). While a significant improvement was noted in the HIT-6 scores, the reduction in MIDAS was not significant. Among responders, improvements in functional outcome related disability were noted.

Conclusion: This study of patients with chronic headaches, including migraine, found that

occipital nerve stimulation can significantly reduce the number of headache days, and, among responders, improve functional outcome and disability.

Miller, S., et al. Long-Term Outcomes of Occipital Nerve Stimulation for Chronic Migraine: A Cohort of 53 Patients. **J Headache Pain.** 2016, December; 17(1): 68.

SSRIs AND RISK OF SPONTANEOUS INTRACRANIAL HEMORRHAGE

While several studies have demonstrated that selective serotonin reuptake inhibitors (SSRIs) increase the risk for abnormal bleeding, the risk of intracranial hemorrhage (ICH) among those patients has not been clearly demonstrated. This study assessed the risk of spontaneous ICH associated with the use of SSRIs, as compared with tricyclic antidepressant drugs (TCAs).

Data were obtained from the United Kingdom's Clinical Practice Research Data Link (CPRD), with a search for individuals 18 years of age or older with a first prescription of antidepressant medications between 1995 and 2014. The patients were followed until the date of the first ICH outcome event, death, or the end of the study. Each case of first ICH was matched with up to 30 controls for age, gender, calendar time and duration of follow-up.

The cohort consisted of 1,363,990 users of antidepressants, with 56.7% using SSRIs and 39.2% using TCAs. Current use of SSRIs was associated with an increased risk of ICH relative to TCAs (relative risk, 1.44), with this risk highest in the first 30 days of use. The use of strong inhibitors of serotonin reuptake was associated with a 25% increased risk as compared with weak inhibitors.

Conclusion: This study of new users of antidepressants found that intracranial hemorrhage was elevated with the use of SSRIs, as compared with TCAs, with this risk highest in the first 30 days of use.

Renoux, C., et al. Association of Selective Serotonin Reuptake Inhibitors with the Risk for Spontaneous Intracranial Hemorrhage. **JAMA Neuro.** 2016 doi:10.1001/jamaneurol.2016.4529.

WIRELESS NERVE STIMULATORS TO ASSESS FUNCTIONAL RECOVERY

Peripheral nerve injuries are among the most common causes of sensory deficits, with great interest in surgical rehabilitative strategies to treat these injuries. This animal study assessed a wireless implantable stimulator to map the recovery of nerve and muscle function following a peripheral nerve injury.

Fifteen adult rats were divided into three groups. All groups underwent surgical exposure of the sciatic nerve, with group one undergoing no nerve injury, group two undergoing crush injury of the sciatic nerve and group three undergoing transection of the sciatic nerve with repair. All groups underwent implantation of a wireless nerve stimulator. Each week for 14 weeks, functional recovery was assessed by wireless stimulation of the sciatic nerve, with EMG recording at distal muscles. After the study, the animals were euthanized and distal muscles were harvested.

All implanted devices remained operational throughout the study. The EMG responses in muscles distal to the site of the injury demonstrated progressive recovery of function over six weeks. The change in EMG measured amplitude from week one to week 14 ranged from 6.4% to 69.1% measured in the plantaris of group three to 77.5% to 104.3% measured in the gluteal muscle of group two.

Conclusion: This animal study demonstrated that wireless nerve stimulators at the site of the injured nerve can be used to assess the course of recovery in both crush and transection injuries.

Gamble, T., et al. Serial Assessment of Functional Recovery following Nerve Injury Using Implantable Thin-Film Wireless Nerve Stimulators. **Muscle Nerve.** 2016, December; 54 (6):1114-1119.

HELMET USE AND THE RISK OF HEAD INJURY IN SNOWBOARDERS AND ALPINE SKIERS

Previous studies have suggested that helmet use can reduce the risk of head injury for Alpine skiers and snowboarders. According to the National Ski Areas Association National Demographics Study, helmet use has increased from 25% in 2003 to 70% in 2013. This study examined the effect of this change in behavior on the risk of head injury.

Six ski patrols at major Norwegian ski resorts registered injuries during the 2002, 2010 and 2011 seasons. Those with injuries to the head were compared to those with injuries to areas other than the head. The data were compared by year collected.

In 2002, 17.6% of the injuries among skiers were injuries to the head. In 2010, this percentage was 15.3%, while in 2011, it was 15.4%. During the same decade, helmet use increased among injured skiers and snowboarders, from 23.8% in 2002, to 68.1% in 2010, and 77.1% in 2011. Head injuries were less common among those wearing a helmet than among those who did not, with odds ratios of 0.57, in 2003, 0.82 in 2010 and 0.9 in 2011.

Conclusion: This study of injuries among skiers and snowboarders found that the use of helmets has increased dramatically over the past 10 years, with a significantly reduced risk of head injury among those wearing helmets.

Sulheim, S., et al. Helmet Use and the Risk of Head Injuries in Alpine Skiers and Snowboarders: Changes after an Interval of One Decade. **Br J Sports Med**. 2017, January; 51(1): 44-50.

PROGNOSTICATING RECOVERY AFTER MILD TBI IN OLDER ADULTS

In 2004, the World Health Organization highlighted the need to assess the effect of older age on recovery from mild traumatic brain injury (MTBI). This study was designed to determine whether, similar to younger adults, psychosocial markers would be identified as having prognostic value for older adults with MTBI.

Participants included adults, 65 years of age or older, presenting to the emergency room (ER) for MTBI within 72 hours of injury. The patients were contacted by phone within 10 days of the ER visit and asked to complete a computer-assisted telephone survey. The survey included sociodemographic, psychological and mental health factors, preinjury functional status and brain health, injury related factors and previous brain injuries. Six

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months after the ER visits, subjects were asked to complete several recovery outcome measures including post-concussion symptoms (PCSs), Glasgow Outcome Scale-Extended Version, the SF-12 and self-assessment of recovery.

Subjects were 97 adults with a mean age of 76.2 years. The only baseline factor independently associated with all measures of recovery was worse health in the one year prior to injury. At six months, those reporting fatigue at the initial follow-up were four times more likely to report a poor recovery. Poor self-prognosis and baseline depression were associated with poor recovery but did not reach statistical significance.

Conclusion: This study of elderly individuals with a mild traumatic brain injury, found that worse recovery at six months occurred among those reporting worse health one year before injury, poor self-expectations for recovery, depression and fatigue shortly after injury.

Kristman, V., et al. Prognostic Markers for Poor Recovery after Mild Traumatic Brain Injury in Older Adults: A Pilot Cohort Study. **J Head Trauma Rehab**. 2016; 31(6): E33-E43.

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