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HEADING IN SOCCER

There is concern surrounding the potential long-term consequences of subcutaneous, concussive repetitive head impacts sustained in sports, including "headers" in soccer. As serum plasma tau and serum neurofilament light (NF-L) protein have been found to be promising candidates for biomarkers for central nervous system damage, this study examined how these levels are affected by soccer heading.

Subjects were 11 male, highly competitive soccer players with a mean age of 23.7 years and with at least five years of experience. The subjects were tested under three conditions, including heading, sham and control. For the heading condition, participants were positioned 25 m from a JUGS machine which launched regulation soccer balls at 77.4 km/h, (the velocity that had been previously estimated from corner kicks in collegiate and professional soccer matches). During the heading condition, players performed 40 headers within 20 minutes, with 30 seconds separating each trial. In the sham condition, contact with the ball was made with the hands, chest or thigh. No balls were launched during the control condition. Serum samples were collected, with plasma tau and NF-L calculated before and one hour after each testing condition, and again at three week follow-up. Symptoms were assessed using the Standardized Concussion Assessment Tool— 3rd edition (SCAT3).

While serum levels remained unchanged following the sham condition, at one hour following the heading condition, NF-L levels rose an average of 26%. Of the seven players who returned at 22 days, these levels were elevated at 311% above baseline (p=0.04). Tau levels remained unchanged in all conditions. Both the total number of concussion symptoms and symptom severity scores were increased compared with pre-heading values (p=0.01 and p=0.03, respectively).

Conclusion: This study demonstrated that serum neurofilament light protein was increased at one hour and at 22 days following an episode of 40 headers at speeds mimicking professional play.

Wallace, C., et al. Heading in Soccer Increases Serum Neurofilament Light Protein and SCAT3 Symptom Metrics. **BMJ Open Sport Exer Med**. 2018; 4(1): E000433.

LOW INTENSITY EXERCISE REDUCES CONTRALATERAL MUSCLE INJURY

Previous studies have shown that low intensity eccentric contractions can reduce the magnitude of muscle damage induced by maximal eccentric contractions. This study assessed whether those contractions can provide a protective effect to the contralateral limb.

Sedentary young men with no musculoskeletal injuries of the upper extremities were randomized into one of six groups, including one control group. The experimental groups underwent one bout of low intensity eccentric contractions of the elbow flexors (EF) at 10% of maximal eccentric contractions (MaxEC). The exercise was performed with one arm on either one, two, seven, 14 or 21 days prior to a bout of MaxEC, applied to the contralateral arm. The maximal eccentric contraction bouts consisted of five sets of six MaxECs. The control group only performed MaxEC of the non-dominant arm. Blood samples were taken to assess muscle damage, with muscle soreness assessed using a visual analog pain score.

Immediately after exercise, the maximal voluntary concentric contraction torque (MVC-CON) decreased by 40% for all groups. Compared to the control group, recovery was faster for the one, two- and seven-day groups. Recovery was also faster for the one-day and two-day groups, as compared to the two- and three-week groups, respectively. The magnitude of creatinine kinase activity after MaxEC was smaller for all experimental groups than the control group with the one-day and two-day muscle soreness found to be lower than in the two-week and the three-week groups.

Conclusion: This study found that performing 10% eccentric contractions in one arm conveys protection against exercise related muscle damage and soreness in the contralateral arm up to three weeks later.

Chen, T., et al. Low Intensity Elbow Flexion Eccentric Contractions-Attenuate Maximal Eccentric Exercise Induced Muscle Damage of the Contralateral Arm. **J Sci Med Sport**. 2018, October; 21(10): 1068-1072.

MEDITERRANEAN DIET AND OSTEOARTHRITIS

Osteoarthritis (OA) is the most common cause of musculoskeletal disability in the elderly. While many studies have investigated the factors affecting joints, few have investigated the effect of diet on OA. This study investigated the association between the Mediterranean diet and morphologic parameters of the joint cartilage.

Data for this study were gathered from the Osteoarthritis Initiative database, containing information from participants residing in four cities in the United States. All had symptomatic knee OA or were at high risk for developing OA. Dietary patterns were analyzed, with adherence to the Mediterranean diet (aMED) evaluated using the Mediterranean Diet Score. Magnetic resonance imaging was completed, with those findings compared with scores on the aMED.

Subjects were 703 adults with a mean age of 62.3 years. Stricter adherence to the Mediterranean diet corresponded to better MRI findings, including a significant increase in the central medial femoral cartilage volume (p<0.0001), the mean central medial femoral cartilage thickness

(p<0.001), the mean cartilage thickness of the central medial tibiofemoral compartment (p<0.0001) and the cartilage volume of the medial tibiofemoral compartment (p<0.001).

Conclusion: This study found that higher adherence to the Mediterranean diet was associated with significantly better knee cartilage scores, as assessed by magnetic resonance imaging, even after adjusting for confounding factors.

Veronese, N., et al. The Association between the Mediterranean Diet and Magnetic Resonance Parameters for Knee Osteoarthritis: Data from the Osteoarthritis Initiative. **Clin Rheum**. 2018, August; 37(8): 2187-2193.

MRI-GUIDED THROMBOLYSIS FOR STROKE

This study, the Efficacy and Safety of MRI-Based Thrombolysis in Wake-Up Stroke (WAKE-UP) trial was designed to determine whether treatment with alteplase improves functional outcomes among patients with unknown time of stroke onset and a mismatch between diffusion-weighted imaging and FLAIR findings on magnetic resonance imaging (MRI).

Subjects were 18 to 80 years of age, all of whom could not report the timing of the onset of stroke symptoms, but was thought to be more than 4.5 hours. Patients were eligible who had an admission MRI revealing a mismatch between the presence of an abnormal signal on MRI diffusion-weighted imaging and no visible signal change on FLAIR in the region of the acute stroke.

Those randomized to the treatment group received 0.9 mg of alteplase per kilogram of body weight or a placebo. Clinical assessments were completed at baseline, and up to 90 days after randomization. The primary efficacy endpoint was a "favorable" clinical outcome, defined as a modified Rankin scale (MRS) score at 90 days of zero to one. The primary safety endpoints were death and a composite outcome of death or dependence, defined as an MRS of four to six at 90 days.

At 90 days, favorable outcomes were noted in 53.3% of the treatment group and 41.8% of the placebo group (p=0.02). The median scores on the MRS at 90 days were one in the alteplase group and two in the placebo group (p=0.003). Death or inability to live independently occurred in 13.5% of the alteplase group and in 18.3% of the placebo group (p=0.17). Symptomatic intracranial hemorrhage was found in two percent of the treatment group and in 0.4% in the placebo group (p=0.15).

Conclusion: This study of patients with acute stroke with an unknown time of onset found that intravenous alteplase, guided by a mismatch between diffusion-weighted imaging and FLAIR in the region of ischemia, resulted in significantly better functional outcome at 90 days.

Thomalla, G., et al. MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset. **N Engl J Med.** 2018, August 16; 379(7): 611-622.

ASPIRIN FOR PRIMARY PREVENTION OF STROKE AMONG DIABETICS

In 2009, the Antithrombotic Trialists Collaborations meta-analysis concluded that aspirin use can result in a 12% lower risk of serious vascular events. This study, ASCEND (A Study of Cardiovascular Events in Diabetes) was designed to determine whether aspirin can also affect the risk of cardiovascular disease among diabetics.

This randomized trial included 15,480 participants, all at least 40 years of age, with a diagnosis of diabetes mellitus. The subjects were randomized to receive either a placebo or 100 mg of aspirin once per day. Participants were also assigned to receive capsules of omega three fatty acid daily or a matching placebo. At baseline and every six months thereafter, questionnaires were sent regarding serious vascular events (myocardial infarction, stroke, transient ischemic attack, or death from any vascular cause, excluding any confirmed intracranial hemorrhage), adherence to the trial regimen and use of non-trial antiplatelet anticoagulant therapy.

At a mean follow-up of 7.4 years, the primary efficacy outcome occurred in 8.5% of the aspirin group and 9.6% of the placebo group (p=0.01). Major bleeding occurred in 4.1% of the aspirin and 3.2% of the placebo group (p=0.003). Of these 41.3% bleeds were gastrointestinal (GI), of which 62.3% were upper GI and 32.9% were lower GI.

Conclusion: This study of patients with diabetes and without cardiovascular disease found that aspirin at a dose of 100 mg per day produced a 12% reduction in the risk of serious vascular events, although at an increased risk of major

bleeding.

The ASCEND Study Collaborative Group. Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus. **N Engl J Med.** 2018, August 26. DOI: 10.1056/ NEJMoa1804988

BOTULINUM TOXIN AND MOTOR AXON REGENERATION

Peripheral axon regeneration has been found to improve when the nerve lesion has recently been preceded by another nerve injury. This study tested whether preconditioning chemodenervation with botulinum toxin-A (BoNT-A) prior to nerve repair would enhance motor axonal regeneration.

In a mouse model, an experimental nerve lesion was delivered, followed by four doses of BoNT-A, prepared in 50 µL of normal saline (0, 0.1, 0.25 or 0.5 units), and injected into the triceps sura muscle. One or four weeks after the injections, a second surgery was performed to assess the neuron neurite outgrowth immunohistochemistry and morphometric analysis. In a separate human preclinical model human embryonic stem cells were plated with BoNT-A applied two weeks after plating.

The BoNT-A preconditioning resulted in an 89% increase in the number of myelinated axons ($p=0.004$) and a 39% increase in the number of motor neurons ($p=0.02$) that reinnervated the distal nerve. In human cell cultures, BoNT-A increased the number ($p<0.01$) and length ($p<0.001$) of the neurons, as compared to the sham treatment group.

Conclusion: This study, including animal and human peripheral nerves, found that pre-conditioning with BoNT -A may enhance motor axonal regeneration.

Franz, C., et al. Botulinum Toxin Conditioning Enhances Motor Axonal Regeneration in Mouse and Human Preclinical Models. **Neurorehab Neural Repair**. 2018, August; 32(8): 735-745.

RISK FACTORS FOR RECURRENT NEUROTRAUMA

Previous studies have demonstrated an increased risk for additional injury, and greater injury severity, among those who have sustained a previous traumatic brain injury (TBI). This study was designed to better understand the socioeconomic factors associated with recurrent neurotrauma.

Data were obtained from the Agency for Health Research and Quality Health Care Cost and Utilization Project, with the data retrieved from the Michigan State Input Database for the years 2006 through 2014. Data were available for 50,744 hospital admissions, with each admission coded as having a neurotrauma diagnosis or not. The mechanism of neurotrauma and patient specific variables were reviewed for patterns of association.

Of patients with admissions for more than one neurotrauma, most were admitted with a different mechanism on each occasion. The most common repeated mechanism was falling. Those with multiple neurotrauma admissions were somewhat more likely to be male ($p<0.001$) and black ($p<0.001$), and to be diagnosed with depression (38%), psychosis (22%) and neurologic disorders (58%). Factors associated with being *less* likely to be admitted for additional neurotrauma included alcohol abuse (39% less likely) and other substance abuse (15% less likely).

Conclusion: This study of patients seen in the emergency rooms in Michigan found that, among those hospitalized for neurotrauma, the risk of repeat neurotrauma admission was decreased among those with substance abuse, and increased among those with depression, psychosis and neurologic disorders.

Hayward, D., et al. Risk Factors for Recurrent Neurotrauma: A Population Based Study in Southeastern Michigan. **Brain Inj.** 2018, September 19; 32(11): 1373-1376.

TRANSCRANIAL DIRECT CURRENT STIMULATION FOR POSTSTROKE APHASIA

As several pilot studies have indicated a potential role of transcranial direct current stimulation (tDCS) for the treatment of aphasia, this study was designed to better understand the utility of this intervention in patients with stroke.

Eligible participants were between the ages of 25 and 80 years, all with a single event ischemic stroke resulting in aphasia, as confirmed using the Western Aphasia Battery-Revised (WAB-R). The subjects were randomized to receive either active tDCS or sham tDCS, coupled with computerized behavioral treatment of anomia. Sessions were 45 minutes each, totaling 15 sessions over three weeks. At one week post-treatment, the subjects were tested for the number of correctly named common objects.

At one week follow-up the mean change in scores on the naming task were 13.9 in the active group and 8.2 in the sham group, reflecting a 70% increase in correct naming in the active, as compared with the sham groups. No adverse events were associated with the active treatment.

Conclusion: This study of patients with post-stroke aphasia found that transcranial direct current stimulation can improve aphasia.

Fridriksson, J., et al. Transcranial Direct Current Stimulation versus Sham Stimulation to Treat Aphasia after Stroke: A Randomized, Clinical Trial. **JAMA Neurol.** Published online. August 20, 2018. doi:10.1001/ jamaneurol.2018.2287

SEX HORMONES IN MEN WITH MIGRAINE

Studies have shown that, during the fertile period, three times more women than men have active migraine. It is unknown, however, whether sex hormones might modulate migraine risk and activity in men. This study investigated the effect of sex hormones on migraines in men.

Subjects were 18 men between 18 and 74 years of age, all with episodic migraine without aura, and 22 matched controls. Blood samples were collected on a single day at 9:00 A.M., 12:00 P.M., 3:00 P.M. and 6:00 P.M. Those with migraine were measured three to four times daily until a migraine attack occurred. The baseline day was scheduled for at least three days after the last migraine attack, and within 10 days from the next expected attacked, based on the patient's historical frequency.

From blood samples, levels of 17B estradiol (E2), sex hormone binding globulin and free testosterone (T_f) were obtained. All subjects completed the Androgen Deficiency of Aging Men (ADAM) measure, which includes 10 items describing common symptoms occurring with age-related decline in androgens, as well as the Aging Males Symptoms (AMS) measure.

Men with migraine had a lower baseline ratio of T_f /E2 ($p=0.03$), primarily due to higher E2 levels ($p=0.001$). Post hoc analysis revealed

that preictal free testosterone (p=0.03) and E2 levels (p<0.001) were higher in those with migraine with premonition symptoms, as compared to those without. The mean AMS scores were higher in men with migraine (p=0.002), and were more often in the mild/severe range of AMS scores (p=0.006).

Conclusion: This study found that men with migraine had increased estrogen plasma levels, both in absolute levels and in levels relative to free testosterone. Those individuals further reported higher scores on the ADAM and AMS, suggesting clinical evidence of androgen deficiency.

Van Oosterhout, P.J., et al. Female Sex Hormones in Men with Migraine. **Neurol,** 2018, July 24; 91(4): E374-E381.

VAGUS NERVE STIMULATION FOR MIGRAINE

In a small, open label study, noninvasive vagus nerve stimulation (nVNS) was found to be effective for pain relief in patients with migraines. This study further assessed this treatment modality.

This multicenter, randomized trial included patients 18 to 75 years of age, diagnosed with migraine, with or without aura. The active nVNS group received 5 kHz sign wave blasts, lasting for 1 ms, repeated every 40 ms, with 24 V peak voltage and 60 mA output current. The sham device provided a low frequency biphasic signal, physically perceptive without stimulating the vagus nerve. Within 20 minutes from migraine onset, the participants self-administered bilateral stimulation to the right and left sides of the neck. Self-assessments were completed at 15, 30, 60 and 120 minutes, as well as 24 and 48 hours after the stimulation. They were allowed to repeat the stimulations if the pain had not improved at 15 minutes.

For the first treated migraine, the proportion of those who became pain-free was higher in the active group than in the sham group at 30 (p=0.012) and 60 (p=0.023), but not at 120, minutes. The mean percentage intensity reductions in pain for the first attack were significantly more pronounced in the active group than in the sham group, at 60 (p=0.033) and 120 (p=0.004) minutes.

Conclusion: This study of patients with migraine headaches found that noninvasive vagus nerve stimulation can effectively treat the pain of these headaches.

Tassorelli, C., et al. Noninvasive Vagus Nerve Stimulation as Acute Therapy for Migraine. The Randomized PRESTO Study. **Neurol**, 2018, July 24; 91 (4): e364-e373.

BOTULINUM TOXIN A FOR THE REPAIR OF DISTAL BICEPS TENDON RUPTURES

In patients with distal biceps tendon ruptures, surgical repair seems to be the optimal treatment. As botulinum toxin has been found to be an effective treatment option for a variety of orthopedic conditions, this study assessed the outcomes of patients who underwent distal biceps tendon repair, with the use of botulinum toxin A as an intramuscular adjunct.

During surgical repair of bicep tendons, botulinum toxin A, 100 units diluted in 10 mL of normal saline, was injected into the biceps tendon. Post-surgically, the patient was transitioned into a sling, with a five-pound weight restriction for lifting. At one month, activity was progressed to full active and passive range of motion, with the weight limit restriction removed.

Appropriate paralysis was determined in 14 of 15 patients. The average final postoperative follow-up occurred at 33.4 months. At final follow-up, 93.3% reported no pain, with DASH scores averaging 4.9. Two patients had wound infections requiring treatment, with one developing heterotopic ossification requiring surgical debridement at six months after the repair.

Conclusion: This study of patients with distal biceps tendon repair found that protective paralysis using botulinum toxin can be an effective adjunct to the surgical procedure.

Khalil, L., et al. The Utility of Botulinum Toxin A in Repair of Distal Biceps Tendon Ruptures. **Musculoskel Surg**. 2018, August; 102(2): 159-163.

REHABILITATION FOLLOWING LOWER LIMB MUSCLE INJURY

After a muscle injury, the risk of reinjury after return to play is elevated, particularly at the site of the original injury. This study was designed to determine the relationship between rehabilitation training loads and return to play time, as well as subsequent injury rate.

This investigation included participants in an Australian football club who had sustained a noncontact lower limb injury. Data were obtained for subsequent injuries within the same season. Rehabilitation was started on the day of injury and concluded on the day of the athlete's return to play. Rehabilitation periods included, stage I (characterized by absence of running loads), stage II (characterized by the beginning of running and non-football contacts) and stage III (resumption of group football training). Data collected included chronic training load, calculated by the average weekly load over four weeks, total load and average weekly load at each stage of rehabilitation.

Of the 85 athletes with muscle injuries, 70 underwent rehabilitation until return to play. Of these, 11.8% sustained a recurrent injury, with 31.4% having an injury at a new site. The risk of recurrent injury was reduced among those with greater time spent in stage I, and greater total rehabilitation accumulated load. Those who were allowed to return to play within four days of injury had a significantly higher risk of subsequent injuries, as compared to those with a longer delay.

Conclusion: This study of Australian football players found that, after a muscle injury to the lower extremity, higher rehabilitation training loads can delay return to play, but can protect against subsequent injury.

Stares, J., et al. How Much Is Enough in Rehabilitation? High Running Workloads following Lower Limb Muscle Injury Delay Return to Play but Protect against Subsequent Injury. **J Sci Med Sport**. 2018, October; 21 (10): 1019-1024.

TRIAMCINOLONE IN IDIOPATHIC CARPAL TUNNEL SYNDROME

Subsynovial connective tissue fibrosis and vascular proliferation have been reported as significant factors in the development of carpal tunnel syndrome (CTS). This fibrosis impedes the normal motion of the median nerve and may result in nerve compression between the flexor tendons and flexor retinaculum. This study examined the effect of steroid treatment on fibrosis development.

Subsynovial connective tissue samples were obtained from patients with CTS, as well as from fresh cadavers with no history of CTS. Collagen gels were prepared from

these cells, with these gels treated with either 10 M of triamcinolone acetonide (TA) or vehicle. Using a gel contraction model as a measure of fibroblast activation, the gels were photographed every four hours for three days, in order to calculate the contraction rate. The tissue was then harvested for analysis.

In all cases, cells treated with TA had significantly higher contraction rates ($p<0.001$), tensile strength ($p<0.001$) and stiffness ($p<0.001$) than did the untreated gels. When the control group was compared with the TA-supplementation group, nine genes in the human fibrosis array were up-regulated and 11 were down regulated. In the TA supplemented CTS cells, the addition of TA was found to modulate tumor growth factor beta signaling, with fibrotic genes and 6 ECM regulators down regulated. This finding suggests that TA may work in part by decreasing fibrotic gene expression.

Conclusion: This study demonstrates that steroids can affect cell regulation and gel structural integrity and regulate fibrotic gene expression, thus affecting carpal tunnel syndrome by modulating cellular function.

Yang, T., et al. Triamcinolone Acetonide Affects TGF-Beta Signaling Regulation of Fibrosis in Idiopathic Carpal Tunnel Syndrome. **BMC Musculoskel Dis.** 2018; 19: 342.

MIRROR ILLUSION FOR SENSORIMOTOR TRAINING IN STROKE

Mirror therapy (MT) has been shown to be very effective for the motor recovery of the upper limb among stroke survivors. This study was designed to determine the effect of MT on sensory and motor recovery.

Subjects were 30-60 years of age who had sustained a unilateral stroke with hemiparesis of at least six months prior to the study. The participants were randomized to a MT group or to a control group. The MT group received 30 sessions of 40 minutes' duration over six weeks, with control patients receiving only standard motor and sensory rehabilitation. In the MT group, the affected side was hidden beside the non-reflective side of the wall, with the subjects provided sensory stimuli on the less affected and the more affected hands simultaneously, in order to induce the mirror illusion for sensory perception. The primary outcome measures were the Semmes Weinstein Monofilament test, the Two-Point Discrimination Test and the Fugl-Meyer assessment.

The 31 participants' average age was 46 years, with a mean, post-stroke duration of 15 months. At follow-up, there was a 30% increase in positive touch response for the hand quadrants among those in the experimental group, as compared with 13.5% in the control group ($p<0.004$). The cutaneous thresholds of the less affected palm improved significantly among the mirror therapy subjects, as compared to controls ($p<0.04$).

Conclusion: This study of patients with ischemic stroke found that mirror therapy may be useful for the treatment of sensory deficits.

Arya, K., et al. Mirror Illusion for Sensori-Motor Training in Stroke: A Randomized, Controlled Trial. **J Stroke Cerebrovasc Dis.** 2018; https://doiorg.proxy.library.emory.edu/10.1016/j.jstrokecerebrovasdis.2018.07.012

ATRIAL FIBRILLATION AND NON-VITAMIN K ANTAGONISTS

Atrial fibrillation (AF) is a major risk factor for stroke, conveying a fivefold increased risk of stroke. This study investigated how clinical outcomes have changed since the introduction of recommendations for increased anticoagulant treatment for patients with AF.

This retrospective study included the Stockholm Healthcare Analysis Database, which incorporates data for all inhabitants within the region. From this database, two cohorts of patients with non-valvular AF were identified for follow-up, including the 2012 and 2017 cohorts. Patients treated with any oral anticoagulant (OAC) were identified, with the stroke risk of each subject estimated using the CHA2DS2-VASc. Bleeding risk was assessed with the HAS-BLED score. The primary efficacy outcome variable was ischemic stroke. The primary safety outcome variable was major bleed.

In 2012, 51.6% of the patients received treatment with any OAC, rising to 73.8% in 2017. The proportion of patients treated with an OAC increased in all age groups, with the largest increase in patients 80 years of age or older, increasing from 47% to 74.1%. The ischemic stroke IR decreased from 2.01 per 100 person-years in 2012 to 1.17 in 2017. No significant change was seen in major bleeding.

Conclusion: This population based, comparative, cohort study found that the use of oral anticoagulants markedly reduced ischemic strokes, without increasing the rate of bleeding.

Forslund, T., et al. Improved Stroke Prevention in Atrial Fibrillation after the Introduction of Non-Vitamin K Antagonist Oral Anticoagulatants: The Stockholm Experience. **Stroke;** 2018, September 49(9): 2122-2128.

METFORMIN, MYOTONIC DYSTROPHY AND MOBILITY

Myotonic dystrophy type I (DM1) is an autosomal dominant monogenic disease, which is the most common form of muscular dystrophy in adults. Previous research has found that the compound metformin can induce changes towards normalization in the ratios of protein isoforms, with an uncertain mode of action, in this disorder. This study assessed whether metformin can affect mobility in nondiabetic, adult patients with DM1.

This double-blind, placebo-controlled trial included adult patients with a diagnosis of DM1 confirmed by gene mutation, all of whom were ambulatory and able to perform the six-minute walk test. The subjects were randomized to receive either a placebo or treatment with metformin, at an escalating dose of up to 3,000mg/d. All subjects were assessed by clinical evaluation, and with the six-minute walk test at baseline and at weeks two, four, 16, 28, 40 and 42.

While the placebo group demonstrated stable performance between baseline and week 52, the metformin treatment group showed a trend towards increased performance, as compared to the control group, including improved distance in the six-minute walk test from baseline to weeks 16 ($p<0.019$) and 52 ($p=0.48$).

Conclusion: This study suggests that Metformin could help improve mobility and gait mobility among patients with myotonic dystrophy.

Bassez, G., et al. Improved Mobility with Metformin in Patients with Myotonic Dystrophy Type I: A Randomized, Controlled Trial. **Brain**, 2018, October; 141(10): 2855-2865.

GOUT AND THE RISK OF ATRIAL FIBRILLATION

Gout affects 3.9% of US adults.

Atrial fibrillation (a-fib) is the most common cardiac arrhythmia worldwide, and is thought to increase the risk for mortality and stroke. As chronic inflammation and oxidative stress are the hallmarks of gout, studies have shown that gout is associated with higher cardiovascular morbidity and mortality. This study was designed to determine whether gout is associated with higher risk of a-fib in people 65 years of age or older.

This retrospective, cohort study used data from a five percent random sample of Medicare claims obtained through the Centers for Medicare and Medicaid Services' chronic condition data warehouse. These data were reviewed for a diagnosis of gout and a new diagnosis of a-fib. From these results, the association between a diagnosis of gout and a new onset of a-fib was calculated.

Data were collected for 1,647,812 individuals with gout from 2006 to 2012. Of these, 9.8% developed incident a-fib. The crude incidence rates of persons with a-fib, with versus without gout were 43.4/1000 patient years and 16.3/1000 patient years, respectively. A multivariable analysis revealed that gout was associated with a higher hazard rate of incident a-fib (1.92).

Conclusion: This study of elderly Americans found that gout was independently associated with a 71% to 92% higher hazard/risk of incident atrial fibrillation in patients 65 years of age or older.

Singh, J., et al. Gout and the Risk of Incident Atrial Fibrillation in Older Adults: A Study of U.S. Medicare Data. **RMD Open** 2018, July; 4(2): e000712. doi:10.1136/rmdopen-2018-000712.

REDUNDANT NERVE ROOTS OF THE CAUDA EQUINE AND LUMBAR SPINE STENOSIS

Patients with degenerative lumbar spinal stenosis with neurogenic claudication symptoms often present with thickened, buckling, serpentine or loop-shaped, redundant nerve roots (RNRs). As little is known about the clinical significance of these nerve roots, this metanalysis was designed to better understand the association between redundant nerve roots and clinical outcomes of patients with lumbar spine stenosis.

A systematic electronic database search was conducted for cohort studies with group comparisons of patients with and those without evidence of RNRs. From that record review, seven studies were chosen, comprising 1,046 patients with lumbar spine stenosis, of whom 308 had evidence of RNR. The records were studied for preoperative clinical variables and postoperative clinical outcome.

The pooled postoperative clinical scores of patients with RNRs were significantly worse than were those without RNRs (p=0.0004). Compared to those without RNR, the post-operative clinical scores were lower in patients with RNRs (p=0.0004), recovery rates slower (p=0.0001), and the cross-sectional area of the spinal cord was smaller (p<0.001).

Conclusion: This study of patients undergoing surgical intervention for lumbar spine stenosis found that those with redundant nerve roots had worse post-operative clinical scores and lower recovery rates than did those without redundant nerve roots.

Marques, C., et al. The Clinical Significance of Redundant Nerve Roots of the Cauda Equine in Lumbar Spinal Stenosis Patients: A Systematic Literature Review and Meta-Analysis. **Clin Neurol Neurosurg.** 2018; 174: 40-47.

TRIMETHYLAMINE N-OXIDE AND FIRST STROKE AMONG HYPERTENSIVES

Recently, alterations in gut microbiota composition have been identified as contributing factors in cardiovascular disease. These include Trimethylamine N-Oxide (TMAO), a metabolite derived from dietary choline, phosphatidylcholine and L-carnitine through the action of gut microbiota. This is eventually oxidized to generate TMAO in the liver, which is thought to exacerbate atherosclerosis. This study examined the relationship between TMAO levels and the risk of stroke.

Data were derived from a randomized, double-blind, clinical trial, conducted from 2008 to 2013 in 32 communities in China. Participants were 45 to 75 years of age, all with a diagnosis of hypertension. The participants were randomly assigned to receive 10 mg of enalapril and either 0.8 mg of folic acid or a placebo. All subjects were followed every three months, with the primary outcome measures either a first nonfatal or fatal stroke. Using data from this study, a nested case-controlled study was conducted, including those with TMAO data, comparing 622 cases who developed stroke with 622 match controls.

After adjusting for important covariates, the risk of first stroke increased for each increment in TMAO, with an odds ratio of 1.22. Compared with the lowest tertile (1.79micromoles/L), the adjusted ratios for first stroke in the middle and highest tertiles of TMAO were 1.27 and 1.43, respectively. A significantly higher risk of first hemorrhagic stroke, and a higher trend of first ischemic stroke, were found in participants in tertiles two to three, as compared with those in tertile one.

Conclusion: This Chinese study of patients with hypertension demonstrated that higher levels of serum Trimethylamine N-Oxide are associated with an increased risk of a stroke.

Nie, J., et al. Serum Trimethylamine N-Oxide Concentration is Positively Associated with First Stroke in Hypertensive Patients. **Stroke.** 2018, September; 49(9): 2021-2028.

SERUM GFAP AND UCH-L1 PREDICT THE ABSENCE OF TRAUMATIC INTRACRANIAL INJURIES

Prior studies have shown the potential for blood-based brain injury biomarkers to predict the absence of intracranial injury after traumatic brain injury (TBI). No biomarkers are approved by the USFDA for clinical use. This study assessed the ability of a biomarker test combining two proteins, ubiquitin C-terminal hydrolase-L1 (UCH-L1) and glial fibrillary acidic protein (GFAP), to predict CT-detected traumatic intracranial injuries within 12 hours of injury.

This 22-site, international study included patients 18 years of age or older presenting to the emergency department with a suspected TBI. Venous blood was taken, with samples analyzed for UCH-L1 and GFAP. These results were combined into a single test result, with the test considered valid if it satisfied the "Boolean criteria" as either positive or negative. A head CT scan was completed for each individual, with these results compared with those of the serum analysis. The primary outcome variable was the negative predicted value and sensitivity of the test for intracranial injury visible on CT.

Data from 1,959 patients were reviewed. Of these, 125 (six percent) had CT detected intracranial hemorrhages, with eight requiring neurosurgical intervention. In three of the 1,959 patients, the CT scan was

positive when the serum test was negative. For detection of intracranial injury, the test had a sensitivity of 0.976 and a negative predictive value of 0.996.

Conclusion: This study of patients with a recent traumatic brain injury demonstrates the high sensitivity and negative predictive value of the combination of serum levels of UCH-L1 and GFAP testing, suggesting a clinical role for ruling out the need for CT scan.

Bazarian, J et al. Serum GFAP and UCH-L1 for Prediction of Absence of Intracranial Injuries on Head CT (ALERET-TBI): A Multicenter, Observational Study. **Lancet Neurol.** 2018, July 24; 17: 782-789.

PHYSICAL ACTIVITY VERSUS WEIGHT REDUCTION FOR IMPROVED FOOT FUNCTION

Foot disorders that impact foot function have been thought to affect 24% of those over 45 years of age and 42% of those over the age of 60. This study was designed to determine the effect of weight reduction and increased physical activity on foot structure and function in obese individuals.

Subjects were recruited with a body mass index of greater than 25 kg/m, each of whom performed less than 150 minutes of moderate to vigorous activity weekly and had no current or previous foot or ankle disorders. Those 51 participants were divided into a weight reduction group (WR) and increased physical activity group (PA).

Foot anthropometric data were measured with participants both sitting and standing, using a three-dimensional foot scanner. Those in the weight reduction group had energy intake restrictions of 1,680 kcal per day for males and 1,200 kcal per day for females. The activity group participated in a 90-minute session, three times per week for 12 weeks, titrated up to 60 to 70 percent of maximal heart rate for the final four weeks.

The mean weight changes were 2.8% in the weight reduction group and 0.9% in the exercise group. Significantly greater improvements in truncated foot length and on a decrease in the arch stiffness index were found in the physical activity group. A greater change was seen for the PA group than for the WR group in the increase in the dorsum height ($p=0.024$) and arch height index ($p=0.015$), and decrease in the truncated foot length ($p=0.02$).

Conclusion: This study demonstrated that both weight reduction and increased physical activity can influence foot structure and function, although a greater change was found in the increased physical activity group than in the weight reduction group.

Zhao, X., et al Increasing Physical Activity Might Be More Effective to Improve Foot Structure and Function than Weight Reduction in Obese Adults. **J Foot Ankle Surg.** 2018, Sept-Oct; 57(5): 876-879.

EFFECT OF VALPROIC ACID IN GLIOBLASTOMA

Glioblastoma (GBM) is a malignant disease with a median survival of 14 to 18 months. Up to 40% of those patients present with seizures, and are often managed with an antiepileptic drug (AED). This meta-analysis was designed to better understand the effect of valproic acid (VPA) on the clinical course of patients with GBM.

Data were reviewed for articles involving primary GBM patients, treated by elements of current conventional therapy, with patients who receive VPA compared to those who did not.

Of the 1,498 studies reviewed, 35 underwent full-text analysis. From these, seven retrospective, cohort studies were included for quantitative analysis. Pooling all studies yielded an overall survival hazard ratio of 0.71 for those who received VPA compared with those who did not. The pooled, mean difference in survival between the two groups was calculated to be 2.35 months ($p<0.01$).

Conclusion: This meta-analysis of studies involving patients with glioblastoma found that treatment with valproic acid was associated with a significantly increased time of survival.

Lu, V., et al. The Survival Effect of Valproic Acid in Glioblastoma and its Current Trend: A Systematic Review and Meta-Analysis. **Clin Neurol Neurosurg.** 2018, November; 174: 149-155.

THIRTY DAY ADVERSE EVENTS AFTER VERTEBROPLASTY

Vertebral compression fractures (VCFs) are a leading cause of morbidity among the elderly. This study was designed to better understand the incidence and risk factors for 30-day adverse outcomes among patients who undergo vertebroplasty or kyphoplasty.

Data were obtained from the American College of Surgeons' National Surgical Quality Improvement Program Database, collected from more than 400 North American medical centers. Postsurgical data were reviewed for 30-day outcome variables, with postoperative complications including wound complications, respiratory complications and cardiac complications.

Of the 2,433 patients included in the study, 242 underwent vertebroplasty and 2,191 underwent kyphoplasty. The overall, thirty-day readmission, reoperation and mortality rates were 10.6%, 3.6% and 2.0%, respectively. A greater risk of 30-day readmission was found among those who were 76 to 89 years of age ($p=0.013$), or 90 years of age or older ($p=0.001$). Comorbidities which increased the risk of readmission were COPD, (OR=1.77), disseminated cancer, (OR=2.98), chronic steroid use, (OR=2.21) and undergoing vertebroplasty as compared with kyphoplasty, (OR=1.65).

Conclusion: This retrospective study of patients with vertebral compression fractures revealed that the 30-day readmission rate after kyphoplasty and/or vertebroplasty was 10.6%.

Choo, S., et al. 30-day Adverse Outcomes, Re-admissions and Mortality following Vertebroplasty/ Kyphoplasty. **Clin Neurol Neurosurg.** 2018; 174, November: 129-133.

PLANTAR FASCIITIS: PREVALENCE AND TREATMENT

Plantar fasciitis (PF) is associated with heel pain, poor quality of life and disability. This study was designed to better understand the epidemiology of PF and to describe common treatments.

Data were obtained from the 2013 National Health and Wellness Survey, a self-administered, internet-based questionnaire completed by 75,000 subjects. Within the questionnaire, the participants were queried concerning diagnoses for pain, which included PF. All were then asked about interventions for pain, including medications, as well as demographics, pain characteristics and other health status characteristics.

Of the adults queried, 1.1%

(Continued from page 2)

reported a diagnosis of PF in the past year. Of those with PF, pain was reported as severe in 25.93%, moderate in 45.5% and mild in 20.6%. Most reported pain every day. Reports of PF were 2.5 times more prevalent in woman than in men, with the highest prevalence among those 45 to 64 years of age.

Those with a body mass index of 30 kg/mg or more were five times more likely to have PF than were those with a body mass index of less than 25 kg/mg. One third of the patients reported having been diagnosed at least five years previously. Approximate 70% used over-the-counter analgesics for pain management, with anti-inflammatory medications used by 50% and acetaminophen by 27%.

Conclusion: This large study suggests that plantar fasciitis has a prevalence of 1.1% in the general population, with the highest prevalence occurring among those 45 to 64 years of age.

Nahin, R., et al. Prevalence and Pharmaceutical Treatment of Plantar Fasciitis in United States Adults. **J Pain.** 2018, August; 19 (8): 858-896.

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