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Volume 24 Number 5 | Published by Physicians In Physical Medicine and Rehabilitation | May 5, 2016

DRIED PLUM AND BONE DENSITY

It is estimated that nearly half of women over the age of 50 years will suffer an osteoporosis related fracture. In addition to medications and lifestyle factors, evidence suggests that some foods may improve bone growth and development, thus reducing diseases such as osteoporosis. Among the foods that have been found to have bone protective effects, dried plum has been shown to prevent and reverse bone loss in rat models of osteoporosis. This study was designed to determine the extent to which dried plum assists in the prevention of bone mineral density (BMD) loss and improves biomarkers in post-menopausal women.

This study included 48, osteopenic, postmenopausal women, 65 to 79 years of age, randomly assigned to one of three treatment groups; daily intake of 50 g of dried plum, 100 g of dried plum or a placebo (control group). BMD was evaluated at baseline and at six months using dual energy x-ray absorptiometry. In addition, venous blood samples were obtained for serum bone marker measurements at baseline, and at three and six months.

Both the 50 g and the 100 g per day groups experienced no change from baseline in total BMD, while the control group continued to lose bone ($p<0.05$). There was no significant difference between the two treatment groups. Laboratory tests revealed that a marker of bone resorption, tartrate-resistant acid phosphatase (TRAP-5b) decreased at three months, with that decrease sustained at six months in both treatment groups ($p<0.01$ and $p<0.04$ respectively). In addition, the bone-specific alkaline phosphatase (BAP)/ TRAP-5b ratio was greater in both treatment groups, with no change in the control group.

Conclusion: This study of elderly, postmenopausal women found that the daily consumption of 50 g of dried plum (approximately five prunes) may be effective in preventing bone loss, with no added benefits noted with higher doses.

Hooshmand, S., et al. The Effect of Two Doses of Dried Plum on Bone Density and Bone Biomarkers in Osteopenic Postmenopausal Women: A Randomized, Controlled Trial. **Osteoporosis Intern.** 16, February: DOI.10.1007/S0019 8–0 1 6–3 52 4–8.

CONCUSSION AND RISK OF LOWER EXTREMITY INJURY

After a single concussion, the probability of a second concussion increases by a factor of three. In addition a history of concussion has been shown to be associated with altered motor control and adoption of conservative gait strategies among clinically asymptomatic athletes. This study assessed the risk of musculoskeletal injuries within 90 days of return to sport post-concussion.

This retrospective study reviewed data for all men and women participating in National Collegiate Athletic Association Division I football, soccer, hockey, basketball, wrestling, volleyball and softball in the years 2011-2014. Injury records were obtained from the University's Sports Injury Monitoring System (SIMS) database, which identified 106 cases of concussion among 84 athletes. The data were reviewed for cases of musculoskeletal injuries in the 90 days after return to play, with these cases compared to up to three matched controls.

Concussed athletes returned to play at an average of 21 days post-injury. In the 90 days after return to play, the incidence of acute, noncontact, lower extremity, musculoskeletal injury was 17% in concussed athletes, as compared with nine percent in the controls ($p=0.04$).

Conclusion: This study found that, after returning to play, concussed athletes had a significantly increased risk of lower extremity injury.

Brooks, M., et al. Concussion Increases Odds of Sustaining a Lower Extremity Musculoskeletal Injury after Return to Play among Collegiate Athletes. **Am J Sport Med.** 2016, March; 44(3): 742-747.

ORAL CONTRACEPTIVES AND ANTERIOR CRUCIATE LIGAMENT INJURY

In a number of sports, women have higher injury rates of the anterior cruciate ligament (ACL) than do men. Some have postulated that estrogen may predispose women to ACL injuries. As progestins, the active compounds in oral contraceptives (OCs), disrupt the normal menstrual cycle, suppressing estrogen levels, this study assessed whether the use of oral contraceptives may be protective against ACL injury.

This case controlled study mined information from an insurance database collected from 2002 through 2012 concerning women ages 15 to 39 years. Subjects who underwent ACL reconstruction were compared to three matched controls. Cases had at least 90 days of OC use, with ACL injuries compared between those who did and those who did not use oral contraceptives.

Of the 26.7 million women enrolled in the database, 12,819 underwent ACL reconstruction. The age group 15 to 18 years had the highest incidence of ACL reconstruction. Of those who underwent ACL reconstruction,

23.39% were users of OCs, compared with 22.82% among controls ($p<0.0001$). Importantly however, those with ACL injury had significantly higher percentages of enrollees labeled as high risk, receiving steroid injections, prescribed inhaled or oral steroids or antibiotics and diagnosed with asthma. Overall the adjusted odds ratio did not differ significantly between groups. However, in the 15 to 19 year age range, subjects undergoing ACL repair were 18% less likely to use oral contraceptives than were matched controls ($p<0.0001$).

Conclusion: This population based study found that women 15 to 19 years of age who used oral contraceptives underwent 18% fewer ACL reconstructions than did matched non-users.

Gray, A., et al. Effects of Oral Contraceptive Use on Anterior Cruciate Ligament Injury Epidemiology. **Med Sci Sports Exer.** 2016, April; 48(4): 648-654.

CANNABIDIOL FOR TREATMENT RESISTANT EPILEPSY

While cannabis contains more than 80 phytocannibinoids, two compounds, tetrahydrocannabinol and cannabidiol, have received the most attention. Recent, anecdotal evidence has suggested that cannabidiol may be effective for the treatment of resistant epilepsy. This trial explored the efficacy of cannabidiol in children and young adults with highly treatment resistant epilepsy.

Between January of 2014 and January of 2015, patients were enrolled who had intractable childhood epilepsy receiving a stable dose of antiepileptic drugs. After a four-week baseline, the subjects were randomized to receive cannabidiol at a dose of two to five mg/kg per day, titrated to a maximum of 25 to 50 mg/kg per day. The primary endpoint was the safety and tolerability of cannabidiol, while the primary efficacy outcome was the median percentage change in the mean monthly frequency of motor seizures at 12 weeks.

The mean cannabidiol dose at 12 weeks was 22.9 mg/kg in the safety analysis group and 22.7 mg/kg in the efficacy analysis group. The median frequency of motor seizures was 30 at baseline and 15.8 over the 12 weeks of treatment, with a median reduction in monthly motor seizures of 36.5%. The greatest reduction was in those with focal seizures. Adverse events were reported in 79% of the patients, including somnolence, decreased appetite, diarrhea, fatigue and convulsions.

Conclusion: This study of patients with intractable seizures found that adding cannabidiol to a stable antiepileptic regimen resulted in a significant and clinically meaningful reduction in seizure activity, with only three percent of the patients discontinuing the study due to adverse events.

Devinsky, O., et al. Cannabidiol in Patients with Treatment Resistant Epilepsy: An Open Label, Interventional Trial. **Lancet Neurol**. 2016, March; 15(3): 270-278.

PROTON PUMP INHIBITORS AND THE RISK OF DEMENTIA

Proton pump inhibitors (PPIs) are among the most commonly used classes of medications, with many prescriptions thought to be inappropriate. Previous observational studies have suggested that PPIs may be associated with cognitive decline. This study used a large longitudinal database to better understand the influence of PPIs on the risk of incident dementia.

A longitudinal sample of elderly patients was obtained from the largest German statutory health insurer. Data retrieved included age, gender, inpatient and outpatient diagnoses and drug prescriptions. Data were aggregated into intervals, starting with a one-year baseline in 2004, followed by 18 month intervals. Subjects were 75 years of age or older with no dementia during the baseline interval. Exposure to PPIs was quantified, with these results compared to incident dementia. Confounding factors placed into the analysis as covariates included age, gender, polypharmacy and the comorbidities of stroke, depression, ischemic heart disease and diabetes.

Data were reviewed for 73,679 persons 75 years of age and older. Of these, 29,510 developed dementia during the study. The regular use of a PPI was observed for 2,950 persons and was associated with an

increased risk of dementia, with a hazard ratio (HR) of 1.44 ($p<0.01$). Of the potential confounding factors, depression (HR 1.28) and stroke (HR 1.37) showed the greatest risk increase of incident dementia. A lower risk ratio was found for occasional PPI use, as compared to greater use. The risk of incident dementia with the use of PPIs gradually decreased with age, with a HR of 1.69 for those 75-79 years of age, 1.49 for those 80-84 years and 1.32 for those 85 years or older.

Conclusion: This study found that the regular use of proton pump inhibitor medications is associated with a significant increase in dementia compared to nonuse of those medications.

Gomm, W., et al. Association of Proton Pump Inhibitors with Risk of Dementia. A Pharmacoepidemiological Claims Data Analysis. **JAMA Neurol**. 2016, April; 73(4): 410-416.

ANTIDEPRESSANT USE AND FALLS IN PARKINSON'S PATIENTS

Patients with Parkinson's disease (PD) have been found to have up to a 60% chance of falling, with these falls a major reason for hospitalization and changes in health related quality of life. Psychotropic medications have previously been found to be associated with increased morbidity, although drug-related fall risk has not been well studied. Thus, this cross-sectional, descriptive study was designed to determine the association between the risk of falls and the use of psychotropic drugs among patients with PD.

Data were obtained from two large PD research databases at the University of Florida Center for Movement Disorders and Neurorestoration. Subjects were patients clinically diagnosed with PD, with data collected from each patient once per year. From these databases, demographic and clinical variables, including the use of psychotropic drugs, were extracted. These data were compared to fall history.

Of the 647 patients included, 67% were taking at least one psychotropic medication, and 47% were taking a combination of drugs. Overall, 40% of the subjects sustained at least one fall during the study timeframe. Use of antidepressants alone, benzodiazepines alone and a combination of the two were found to be independent risk factors for falls (odds ratios 2.2, 2.2 and 4.1, respectively). The fall frequency was higher among patients taking antidepressants alone than among those not on psychotropic medications ($p<0.0001$), while benzodiazepine use alone did not increase the frequency of falls.

Conclusion: This study of patients with Parkinson's disease found that the use of antidepressants is associated with a higher frequency of falls.

Martinez-Ramirez, D., et al. Association between Antidepressants and Falls in Parkinson's Disease. **J Neurol.** 2016, January; 263(1): 76-82.

PSYCHIATRIC ILLNESS IN PATIENTS WITH ORTHOPEDIC POLYTRAUMA

Recent data have shown that patients with depression have worse outcomes after stroke, as well as after a number of surgical procedures. Recent orthopedic literature is deficient with regard to outcomes relevant to individuals with psychiatric illness. This study investigated the prevalence, management patterns and surgical outcomes of patients with psychiatric illnesses who sustain polytrauma.

Data of patients with trauma from a level-I trauma center were reviewed. All presented with femoral or axial skeletal fractures between October of 2010 and February of 2013. Records were reviewed to identify psychiatric disorders that were either already part of the record or were entered as part of the trauma intake. Complications in the postoperative period were then determined and compared between those with and those without a psychiatric diagnosis.

Data were reviewed of 332 patients with surgically treated orthopedic trauma. Of these, psychiatric disorders were present in 39.2%. Depression, identified in 22.3% and substance abuse in 16.9% were the most common. Of the sixty-six patients who experienced at least one post-operative complication, 42.4% had a pre-existing psychiatric illness, including 37.9% with a diagnosis of depression. Independent predictors of postoperative complications included male gender (OR 2.78), those with higher injury severity scores (OR 1.079) and patients with depression (OR 2.96).Of note, patients treated on the orthopaedic trauma service were less likely to have their home psychiatric medications restarted, as compared to those on the general trauma service.

Conclusion: This study of patients with orthopedic polytrauma found that psychiatric illness is common in these patients, and that those with depression have a higher likelihood of postoperative complications.

Weinberg, D., et al. Psychiatric Illness is Common among Patients with Orthopaedic Polytrauma and Is Linked with Poor Outcomes. **J Bone Joint Surg.** 2016, March 2; 98-A: 341-348.

BODY MASS INDEX IN ADOLESCENCE AND DEATH IN ADULTHOOD

Overweight and obesity in adolescence has increased substantially in recent decades, affecting one third of the adolescent populations in some developed countries. This study assessed the association between body mass index (BMI) in late adolescence and death from coronary heart disease, stroke and sudden death in adulthood.

Before mandatory military service, Israeli adolescents 17 years of age undergo a medical evaluation. Those evaluations which occurred between 1967 and 2010 were used to determine baseline BMI for the study. These individuals were followed for mortality outcomes and documentation of death through June 30, 2011. The primary outcome variable was death attributed to coronary heart disease, stroke, sudden death from an unknown cause or a combination of the three.

During follow-up, 2,918 deaths from cardiovascular causes were documented, with the mean age at the time of death of 47.4 years for coronary heart disease, 46 years for stroke and 41.3 years for sudden death. The rates of death per person-year were lowest in those with

a body mass index of 19.21–21.41 kg/m^2. After multi-variable adjustment, the risk of death from cardiovascular causes and all causes began to increase among those whose BMI in adolescence was 21.01 -23.62 kg/m^2, and was highest among those with a BMI of 28.44-47.54kg/ m^2.

Conclusion: This Israeli study found that body mass index of 21.01-23.62 kg/m^2, within the accepted normal range, was associated with increased cardiovascular and all-cause mortality during 40 years of follow-up.

Twig, G., et al. Body Mass Index in 2.3 Million Adolescents and Cardiovascular Death in Adulthood. **New Engl J Med**. 2016: 10.1056/ NEJM OA 1 5 03840

COMBINING PREGABALIN AND DULOXETINE FOR FIBROMYALGIA

Fibromyalgia (FM) is a clinical syndrome with chronic, widespread pain, frequently associated with sleep disturbance, depression, fatigue and cognitive dysfunction. Among the medications commonly used to treat this disorder are the anticonvulsant pregabalin and the antidepressant duloxetine. However, rigorous evidence for combining these medications is lacking. This study was designed to further understand the additional efficacy of combining these medications to treat patients with FM.

Subjects were patients 18 to 70 years of age, diagnosed with FM. The participants were randomized in a double-blind, crossover design to receive maximally tolerated doses of a placebo, pregabalin, duloxetine, or a pregabalin-duloxetine combination for six weeks. The primary outcome variable was the average pain intensity over the past 24 hours, with secondary outcomes including worst pain intensity over the past 24 hours, average nocturnal pain intensity during sleeping hours, global pain relief, the Fibromyalgia Impact Questionnaire, the SF–36 Survey, the Sleep Scale and the Beck Depression Inventory.

Pain in the combination group was lower than that in the placebo group ($p<0.001$) and that among those receiving pregabalin ($p<0.001$). Pain with duloxetine was lower than that in the placebo group ($p<0.001$) and the pregabalin group ($p=0.003$). The combination group had a greater reduction in the percent change in pain, as compared to the pregabalin and placebo groups. The portions of patients reporting at least moderate global pain relief at the maximum tolerated dose were 18.4% of those taking placebo, 38.5% of those taking pregabalin, 41.7% of those taking duloxetine and 67.7% of those taking the combination of medications.

Conclusion: This study of patients with fibromyalgia found that pregabalin/duloxetine combined provides better pain relief than pregabalin or duloxetine alone.

Gilron, I., et al. Combination of Pregabalin with Duloxetine for Fibromyalgia. **Pain.** 2016DOI: 10.1097/j.pain.0000000000000558

REPEATED BOTULINUM TOXIN INJECTIONS FOR NEUROPATHIC PAIN

Botulinum toxin type A has been used to inhibit synaptic exocytosis, reducing muscle tone. Several studies have demonstrated that this toxin may have analgesic activity, independent of its effect on muscle tone. This study assessed the efficacy of botulinum toxin A for the treatment of peripheral neuropathic pain.

This randomized, double-blind, placebo controlled, parallel group, clinical trial included patients with neuropathic pain scores of at least four out of 10, with daily pain for at least six months, attributable to a peripheral nerve lesion. One week after baseline assessment, patients were randomized to receive two, subcutaneous administrations of botulinum toxin A up to 300 units or an equal volume of placebo, 12 weeks apart. The primary outcome variable was the change in self-reported pain intensity after two successive injections, over the prior 24 hours, using the 11-point Brief Pain Inventory (BPI). All secondary endpoints were assessed at four, 12 and 24 weeks, including safety and tolerability and therapeutic gain.

Of the 66 adults included in the intent to treat analysis, the mean pain intensity was 6.5 at baseline and 4.6 at week 24 in the botulinum toxin group, and 6.4 at baseline and 5.8 at week 24 in the placebo group ($p<0.0001$). The difference in reduction in pain intensity between the groups was significant after the first administration, starting from week one, and increased between weeks 15 and 24. The proportion of those who responded with at least a 30% reduction in pain at week 24 was greater in the treatment group ($p=0.001$). This was not true of the proportion who responded with at least a 50% reduction in pain ($p=0.2$).

Conclusion: This study found that two administrations of botulinum toxin A resulted in a sustained analgesic effect against peripheral neuropathic pain.

Attal, N., et al. Safety and Efficacy of Repeated Injections of Botulinum Toxin A in Peripheral Neuropathic Pain (BOTNEP): A Randomized, Double-Blind, Placebo-Controlled Trial. **Lancet Neurol.** 2016, May; (15): 555-565.

COMPARING BOTULINUM TOXINS FOR CERVICAL DYSTONIA

Cervical dystonia (CD) is characterized by sustained contraction of agonist and antagonist neck muscles. As treatment for this condition includes injections of botulinum toxin, this meta-analysis compared the efficacy and safety of the different formulations of this toxin.

After a review of the literature, results from 11, randomized, controlled trials of botulinum toxin treatment of cervical dystonia were reviewed. A mixed treatment comparison (MTC) was conducted using a Bayesian hierarchical model, allowing indirect pairwise safety and efficacy comparisons of all toxins. The primary outcome measure was the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS).

Based on the MTC analysis, Dysport, Botox, Xeomin, Prosigne and Myobloc all demonstrated superiority over placebo in the treatment of CD, with similar ranges of efficacy. No significant differences were seen among the outcomes on the TWSTRS for severity, disability or pain. Further, adverse events did not differ significantly among the toxins, except in the case of Prosigne, as there were limited data to be drawn from a single study.

Conclusion: This literature review and meta-analysis of studies focusing on the treatment of cervical

dystonia with botulinum toxin found that Dysport, Botox, Xeomin, Prosigne and Myobloc are equal in efficacy.

Han, Y., et al. A Mixed Treatment Comparison to Compare the Efficacy and Safety of Botulinum Toxin Treatments for Cervical Dystonia. **J Neurol.** 2016, April; 263(4): 772-780.

AUTOLOGOUS PLATELET RICH PLASMA FOR KNEE OSTEOARTHRITIS

Some have estimated that 10% of men and 13% of women older than 60 years of age suffer from symptomatic knee osteoarthritis (OA). Recently, platelet rich plasma (PRP) injections have been suggested as an effective intervention, although there exists little high-level evidence evaluating the efficacy of this technique. This study was designed to better understand the efficacy of PRP for the treatment of knee OA.

This FDA sanctioned, prospective, randomized, double-blind, parallel group study involved patients with knee OA, randomized to receive either leukocyte-poor PRP autologous conditioned plasma (ACP) or saline for a series of three, weekly injections. The primary efficacy outcome measures were the change in pain, joint stiffness and physical function, as measured using the WOMAC at baseline, weeks one and two, and months two, three, six and 12.

Lower overall WOMAC scores were found in the treatment group as compared to the placebo group starting at two weeks, and remaining statistically significant throughout the duration of the study. In addition WOMAC subgroups for pain, stiffness and physical function were all significantly better in the treatment group than in the placebo group at 12 months.

Conclusion: This prospective study of patients with knee OA found that leukocyte-poor PRP autologous conditioned plasma could provide significant improvement in pain, stiffness and function, starting at two weeks and sustained for 12 months.

Smith, P., et al. Intra-Articular Autologous Conditioned Plasma Injections Provide Safe and Efficacious Treatment for Knee Osteoarthritis. An FDA-Sanctioned, Randomized, Double-Blind, Placebo-Controlled Clinical Trial. **Am J Sports Med.** 2016, April; 44(4): 884-891.

GAIT TRAINING AT SKILLED NURSING FACILITIES AFTER TOTAL JOINT ARTHROPLASTY

With an aging population, the demand for joint arthroplasties has resulted in a surge in the number of joint replacements performed annually. Numerous studies have suggested the need for early, rapid and continuous mobilization with weight bearing after surgery to ensure an optimal outcome. This study examined the ambulatory proficiency of patients discharged to a skilled nursing facility (SNF).

This retrospective study included patients undergoing total joint arthroplasty between November of 2012 and July of 2014. Records were reviewed of those discharged to a SNF, with extracted data including daily visual analog scale pain scores, distances ambulated, weight bearing status at discharge and total length of hospital stay.

Data concerning 68 patients from 31 sites were included in the final analysis. The average length of acute hospitalization for these patients was 2.9 days and that for SNF stay was 17.5 days. Of the patients studied, 29.4% began gait training on the day of acute hospital discharge, with 63.2% beginning on day one and 7.4% on day two. During the first four days of SNF admission, 35% of the patients had a single physical therapy session, 23.5% had two sessions, 38.2% had three sessions and 2.9% had four sessions. Those who walked on the day of admission (day zero) or the day after admission (day one) experienced a significant decline in distance ambulated (73% and 50% respectively) compared to the last acute hospital physical therapy session ($p<0.001$ for both comparisons).

Conclusion: This study of patients with total joint arthroplasties discharged to skilled nursing facilities found a significant decline in ambulation distance on the day of admission and the day after, relative to the last day of acute hospitalization.

Haghverdian, B., et al. Gait Training in Patients discharged to a Skilled Nursing Facility following Total Joint Arthroplasty. **Geriatric Ortho Surg Rehab**. 2016, March; 7(1): 33-38.

SINGLE INTRA-ARTICULAR INJECTION OF HYALURONIC ACID FOR HIP OSTEOARTHRITIS

Hip pain is reported by 19.2% of people 65 years of age or older. The optimal treatment requires a combination of nonpharmacologic and pharmacologic modalities. Intra-articular hyaluronic acid (HA) injections are widely used and are recommended in existing guidelines for patients with knee osteoarthritis (OA), with less evidence available concerning arthritis of the hip. This study evaluated the efficacy and safety of intra-articular injections of a single dose of high molecular weight HA for patients with hip OA.

Subjects were 207 patients with hip OA, with an average age of 67 years. The patients received a single injection of 2.5% high molecular weight (2800 kDa) HA, with the injections performed under fluoroscopic guidance. All participants were evaluated before injections and at three, six and 12 months, using the modified brief pain inventory (BPI), the Harris Hip Score (HHS) and a visual analog scale (VAS) of pain.

Pain, as measured by the BPI severity score, improved significantly between baseline and the three follow-up visits ($p<0.001$). Changes in pain between baseline and the first follow-up were significant for worst pain ($p=0.037$) and mean pain ($p=0.043$). Changes in worst pain remained stable from three to 12 months, although changes in average pain, slightest pain and pain during the visit were significantly improved at all intervals. Scores on the HHS and VAS improved from baseline to three months ($p<0.001$ and $p<0.001$), remaining stable thereafter.

Conclusion: This uncontrolled study of patients with hip osteoarthritis suggests that a single dose of high molecular weight hyaluronic acid can improve pain by three months, with results continuing for one year.

Rivera, F., et al. Single Intra-Articular Injection of High Molecular Weight Hyaluronic Acid for Hip Osteoarthritis.

J Orthopaed Traumatol. 2016, Mar; 17(1):21-26.

PHYSICAL ACTIVITY AND SYMPTOMS AFTER CONCUSSION

While some have argued that, acutely after a concussion, unrestricted physical activity may be detrimental to recovery, few studies have prospectively assessed the effect of behavior on patient outcome .This study was designed to better understand the association between physical activity and symptom recovery after an acute episode of concussion

This prospective study included all patients diagnosed with a concussion seen in a sports medicine clinic between October of 2009 and July of 2011. Patients were assessed by physical examinations, with symptoms determined using the Post-Concussion Symptom Scale (PCSS), a 22-symptom inventory. During the initial clinic visit, patients were asked whether they had continued their regular exercise from the time of injury. At follow-up, the participants described their average levels of physical and cognitive activity since the previous clinic visit.

A total of 364 patients were included in this study. The mean time to presentation after the injury was 11.8 days. Of those reporting a resolution of symptoms, the mean symptom duration was 48.9 days. While the initial PCSS scores and female gender were independently associated with symptom duration, physical activity after injury was not. For those ages 13 to 18 years, higher levels of physical activity after injury were associated with a shorter duration of symptoms.

Conclusion: This prospective study found that physical activity after a concussion is not associated with symptom duration.

Howell, D., et al. Physical Activity Level and Symptom Duration Are Not Associated after Concussion. **Am J Sports Med.** 2016, April; 44(4): 1040-1046.

LANGUAGE RECOVERY WITH M1 TRANSCRANIAL DIRECT CURRENT STIMULATION

Transcranial direct current stimulation (tDCS) has been found to improve naming ability in patients with post-stroke aphasia when coupled with therapeutic language rehabilitation. Previous studies have used functional imaging of nonviable cortical regions of the residual language function network and targeted specific domains for this stimulation. This study evaluated the effects of primary motor cortex, M1, stimulation on naming ability, among stroke patients, assessed immediately after and six months following stimulation.

This randomized, double-blind, clinical trial included 26 subjects with a post-stroke duration of over 12 months, with chronic aphasia and impaired naming ability. The subjects were matched by naming impairment severity. All underwent treatment with a language computer-assisted program, and were randomized to receive either anodal tDCS or sham tDCS. The primary outcome variable was the mean change in naming ability.

Naming ability for the trained items was significantly improved in both groups immediately and at six months' follow-up, with the effect trending larger for the tDCS group ($p=0.08$). The maintenance of effect at six months was greater for the tDCS group than the sham group ($p=0.01$). Generalization of treatment effects to untrained items were found in both groups immediately after the training but this effect was significantly larger in the tDCS group ($p= 0.0009$).

Conclusion: This study of patients with chronic stroke found that transcranial direct current stimulation, directed at M1, can augment language therapy outcomes, with intervention maintenance effects noted at six months.

Meinzer, M., et al. Electrical Stimulation of the Motor Cortex Enhances Treatment Outcome in Post-Stroke Aphasia. **Brain.** 2016, April; 139(4): 1152-1163.

ETORICOXIB VERSUS DICLOFENAC FOR HETEROTOPIC OSSIFICATION PREVENTION

Heterotopic ossification (HO) is thought to occur in 30 to 40% of patients undergoing primary total hip arthroplasty (THA). Prophylaxis often includes nonsteroidal anti-inflammatory and/or low-dose irradiation. As COX-II blockers have a lower rate of GI-complications than do non-selective NSAIDs, this study compared the efficacy of etoricoxib (ETO) and diclofenac (DIC) for the prevention of HO.

This prospective, double-blind, randomized trial included 100 patients scheduled for THA, with 50 randomized to receive etoricoxib, 90 mg/day, and 50 to receive diclofenac, 75mg/day for nine days post-surgery. During this time, only opioids and acetaminophen were permitted for pain control. The patients were evaluated at six months post-surgery, with radiographs of the pelvis obtained to evaluate for HO.

Eighty-nine patients were examined at six months, with HO found in 38.6% in the DIC group and 37.8% in the ETO group ($p=0.871$). While only Brooker grades 1 and 2 HO were found, there was a significant negative correlation between ossification and hip abduction and internal rotation. Two patients of each group complained of nausea, and one patient of the ETO group experienced elevated blood pressure.

Conclusion: This study of patients undergoing total hip arthroplasty found that heterotopic ossification prophylaxis with etoricoxib a Cox II blocker and diclofenac were equally effective.

Winkler, S., et al. Comparative Clinical Study of the Prophylaxis of Heterotopic Ossifications after Total Hip Arthroplasty Using Etoricoxib or Diclofenac. **Intern Ortho**. 2016, April; 40(4): 673-680.

ULTRASOUND GUIDANCE FOR SUBACROMIAL INJECTIONS

Subacromial impingement is a common cause of shoulder pain in adults, with corticosteroid injections a frequent management tool for this condition. Ultrasound (US) guidance has been recommended for these injections due to the increased accuracy provided by US use. This study compared the clinical effectiveness of US-guided subacromial injections to that of blind subacromial injections.

This prospective, double-blind, randomized, controlled trial included 51 patients diagnosed with subacromial impingement, with 28 shoulders undergoing US-guided

injections, and 28 receiving a landmark-guided injection. The main outcome measure was pain with overhead activity as measured by a 100 point visual analogue scale (VAS).

Both groups realized significant improvements in VAS scores for pain, decreasing from 59 before the injection to 33 at week six in the US group, and from 63 to 39 in the blind injection group, with no significant difference between the groups. Both groups showed significant improvement in the American Shoulder and Elbow Surgeons (ASES) score with no significant difference between the groups.

Conclusion: This study of patients with subacromial impingement syndrome found no significant difference in clinical outcomes between those injected using ultrasound guidance and those injected using landmark guidance.

Cole, B., et al. Ultrasound-Guided versus Blind Subacromial Corticosteroid Injections for Subacromial Impingement Syndrome. Randomized, Double-Blind, Clinical Trial. **Am J Sports Med**. 2016, March; 44(3): 702-707.

METABOLIC SYNDROME AND MILD COGNITIVE IMPAIRMENT

The Metabolic syndrome (MetS) is a cluster of cardiovascular risk factors that are known to be associated with an increased risk of cardiovascular disease and stroke. This study reviewed the association between the MetS and mild cognitive impairment (MCI) and its progression to dementia.

This population based study included subjects 55 years of age or older living in one of five districts in southeast Singapore. Baseline assessments were conducted from 2003 to 2004, with follow-ups conducted in 2005 to 2007 and 2007 to 2009. Subjects had no MCI or dementia at baseline. All subjects underwent detailed, structured interviews, clinical evaluations, blood sampling, neuropsychological evaluation and performance-based tests. Covariates included age, gender, education, APOE-ε4 genotype, smoking history and levels of physical, social and other productive activities.

At three-year follow-up, among the 1519 subjects, there were significantly more cases of incident MCI among those with MetS (13.5%) than among those without [8.1% ($p<0.001$)]. A significant increased risk of MCI was associated with MetS, as well as diabetes mellitus, central obesity, dyslipidemia, and three or more component cardiovascular risk factors (but not hypertension).

Conclusion: This study of cognitively normal persons 55 years of age or older found that the metabolic syndrome, diabetes mellitus, central obesity, dyslipidemia and the presence of three or more cardiovascular risk factors are associated with a higher risk of developing mild cognitive impairment and dementia.

NG, T., et al. Metabolic Syndrome and the Risk of Mild Cognitive Impairment and Progression to Dementia. Follow-Up of the Singapore Longitudinal Ageing Cohort. **JAMA Neurol.** 2016, April; 73(4): 456-463.

DIABETES MELLITUS AND GUILLAIN-BARRÉ

Chronic inflammatory demyelinating polyradiculopathy appears to be more common in patients with diabetes mellitus (DM) than in the general population. Diabetes may, therefore, predispose patients to the development or exacerbation of disimmunogenic peripheral neuropathies. This study explored the influence of underlying DM on the clinical and electrophysiologic features of Guillain -Barré syndrome (GBS).

Consecutive hospital admissions of patients with GBS were enrolled in this study. If available, subtypes were classified as acute demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN) or acute motor sensory axonal neuropathy (AMSAN) by using the results of anti-ganglioside antibody assays and serial nerve conduction study (NCS) findings. Diabetes mellitus was diagnosed using the criteria of the American Diabetes Association. Nerve conduction studies were performed with prolonged terminal latency and conduction block, used to identify AIDP. Functional outcomes of patients with GBS were determined at three months.

Subjects were 27 patients with GBS and DM (GBS+DM) and 58 patients with GBS without DM (GBS-DM). Ataxia as an initial symptom of GBS was more frequent in the GBS+DM group than in the GBS-DM group ($p= 0.02$). At three months after symptom onset, only about half of the GBS+DM patients could walk unaided, compared to 86% of the GBS-DM patients ($p=0.005$). A multivariate analysis found that a history of mechanical ventilation ($p=0.04$) and underlying DM ($p=0.003$) were independent risk factors for poor functional outcome at three months after symptom onset.

Conclusion: This study of patients hospitalized with Guillain-Barre' syndrome found that diabetes mellitus exacerbates both the clinical and the electrophysiologic features of this disorder and influences its related long-term disability.

Bae, J., et al. Diabetes Mellitus Exacerbates the Clinical and Electrophysiological Features of Guillain-Barré Syndrome. **J Euro Neurol.** 2016, March; 23(3): 439-446.

PIOGLITAZONE AFTER ISCHEMIC STROKE

As insulin resistance is present in more than 50% of patients without diabetes who have had an ischemic stroke or TIA, addressing this issue seems central to the treatment of these individuals. As one medication, pioglitazone, a peroxisome proliferator-activated receptor y agonist, has been found to reduce the risk of cardiovascular events in patients with type 2 diabetes, this study assessed the effect of this medication on the occurrence of stroke and myocardial infarction after ischemic stroke or transient ischemic attack (TIA).

Subjects were patients at least 40 years of age, with a stroke or TIA during the six months before randomization. Patients were included with insulin resistance, defined as a value of more than 3.0 on the homeostasis model assessment of insulin resistance (HOMA-IR) index. Subjects were randomized to receive either pioglitazone at 45 mg per day or a matching placebo. The participants

(Continued from page 2)

*Jennifer Soo Hoo, M.D.
Alicia Fuhrman, M.D.
University of Washington, Seattle, WA

*Bonnie Weigert, M.D.
David Schanbacher
Michael Suer, M.D.
University of Wisconsin, Madison, WI

*Olivier Rolin, M.D.
Christopher Beal, D.O.
Seth Haywood, M.D.
Rondy Michael Lazaro, M.D.
Heather Martin, M.D.
VCU, Richmond, VA

*Jeremy Hartman, M.D.
Sean E. Smith, M.D.
Washington University, St. Louis, MO

were contacted every four months, with the last scheduled contact before July of 2015. The primary outcome measure was the first fatal or nonfatal stroke or myocardial infarction.

A total of 3,895 patients were enrolled, with a median age of 63.5 years. During a median of 4.8 years follow-up, the primary outcome of stroke or myocardial infarction occurred in nine percent of the treatment group and 11.8% of the placebo group(p=0.007). The findings did not change after adjustment for covariates. Among secondary outcomes, the rate of progression to diabetes was lower in the treatment group than in the placebo group (p<0.001). Patients in the treatment group demonstrated more weight gain, edema, shortness of breath and bone fractures than did the placebo group.

Conclusion: This study of patients with a history of stroke or transient ischemic attack who were insulin resistant but not diabetic found that treatment with pioglitazone, an insulin sensitizing drug, reduced the risk of stroke or myocardial infarction, and was associated with a lower risk of developing diabetes.

Kernan, W., et al. Pioglitazone after Ischemic Stroke or Transient Ischemic Attack. **New Engl J Med.** 2016, April 7; 374(14): 1321-1330.

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ISSN # 1081-1303

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