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Volume 23 Number 2

Published by Physicians
In Physical Medicine and Rehabilitation

February 5, 2015

HYPERLIPIDEMIA, STATIN USE AND DEPRESSION

Recent studies have suggested an association between depressive disorders and circulating levels of inflammatory markers. As hyperlipidemia has been associated with elevated levels of systemic inflammatory markers, this study explored the relationship between statin use and depression.

The authors used the National Health Insurance Research Database (NHIRD), maintained by the National Health Research Institutes in Taiwan. From that database were identified 26,852 patients newly diagnosed with hyperlipidemia, without a history of depression. For a comparison group 107,408 patients were selected with no history of hyperlipidemia or depression. The two groups were followed from the index date to the date of insurance claim for diagnosis and treatment of depression, the end of 2008 or withdrawal from the program.

Compared with the non-hyperlipidemia group, the hyperlipidemia group had a significantly increased hazard ratio (HR) of depression (HR, 1.64). Compared with the non-hyperlipidemia group, the risk of depression in the hyperlipidemia patients with versus without statin use were 9.27 and 10.4, respectively. Hyperlipidemia patients receiving statins exhibited a significantly lower risk for depression than did those who did not receive statins (HR, 0.81).

Conclusion: This study found that hyperlipidemia increases the risk of depression, and that statin use is associated with a decreased risk of depression.

Chuang, C., et al. Hyperlipidemia, Statin Use and Risk of Developing Depression: A Nationwide, Retrospective, Cohort Study. **Gen**

Hosp Psychiat. 2014; 36(5): 497-501.

RADIOFREQUENCY STIMULATION FOR HEALING THE MENISCUS

Meniscal tears are among the most common injuries to the knee. Previous studies have demonstrated that radiofrequency, applied to hypovascular tissue, can stimulate vascularity and increase organizational fibroblastic cells. This study evaluated the effects of low temperature, bipolar radiofrequency stimulation, combined with suture repair, on the healing of tears at the avascular white-white zone of the meniscus.

This animal study included 54 New Zealand white rabbits with surgically induced meniscal tears in the white-white zone. Group 1 received no treatment, Group 2 received suture repair alone and Group 3 received suture repair plus radiofrequency stimulation. For all groups, the menisci were explanted at 28 and 84 days for gross and histologic analysis. For biochemical assessments, the menisci were examined at nine, 28 and 84 days.

With gross analysis, no healing occurred at 28 and 84 days in either the control group or the suture only group. In Group 3, 50% of menisci showed signs of healing, with one demonstrating complete healing, and 14 demonstrating incomplete healing. A 40% increase in cellular proliferation was noted in Group 3 as compared with controls ($p < 0.05$). Additionally, significant increases in mitogenic and angiogenic markers were noted in Group 3 at nine and 28 days ($p < 0.05$).

Conclusion: This animal study of meniscal injury suggests that radiofrequency stimulation, combined with suture repair, can enhance the healing response as compared to suture repair alone.

Lee, C., et al. Radiofrequency Stimulation for Potential Healing of Meniscal Injuries in the Avascular Zone. **Amer J Ortho.** 2014, December; 43(12): E292-E298.

FACTOR XI ANTISENSE OLIGONUCLEOTIDE FOR VENOUS THROMBOEMBOLISM

The risk of venous thromboembolism after joint replacement requires medical prophylaxis. Conventional therapies to address this risk include inhibitors of factor X_a or thrombin, which are effective, but associated with the risk of bleeding. Experimental data suggest that targeting factor XI, a key component of the intrinsic pathway of coagulation, attenuates thrombosis without affecting hemostasis. This study compared the efficacy of enoxaparin with a second-generation antisense oligonucleotide that reduces factor XI messenger RNA expression in the liver.

This randomized trial included patients 18 years of age or older, undergoing elective unilateral total knee arthroplasty. The subjects were randomized to receive one of three doses of FXI-ASO, a second-generation antisense oligonucleotide, or enoxaparin. Treatment with FXI-ASO was initiated 36 days before surgery (day one), with patients receiving additional doses on days eight, 15, 22, 29, 36 and 39. Enoxaparin 40 mg was administered subcutaneously beginning the day before surgery and continuing for eight days postoperatively. The primary efficacy outcome was the incidence of total venous thromboembolism or unexplained death for which pulmonary embolism could not be ruled out.

The primary efficacy outcome occurred in 27% patients in the 200 mg FXI-ASO group, in four percent in the 300 mg group and in 30% in the enoxaparin group. The 300 mg FXI-

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ASO group was superior to the enoxaparin group (p<0.001). Clinically relevant bleeding occurred in three percent of the 200 mg FXI-ASO group, 3% in the 300 mg FXI-ASO group and in 8% of the enoxaparin group.

Conclusion: This study found that a 300 mg dose of a factor XI inhibitor, FXI-ASO, is superior to the low molecular weight heparin, enoxaparin, for the prevention of venous thromboembolism, with a lower rate of bleeding.

Buller, H., et al. Factor XI Antisense Oligonucleotide for Prevention of Venous Thromboembolism. **N Engl J Med**, 2015, January 15(3); 372: 232-240.

EFFECT OF PHYSICAL AND COGNITIVE ACTIVITY ON SLEEP QUALITY

Poor sleep is reported by 50% of individuals 65 years of age or older. This study, a secondary analysis of the Mental Activity and Exercise Trial (MAX), compared the effects of different types of exercise and mental activity on self-reported sleep quality among older adults.

The MAX trial included 126 community residing adults, ages 65 years or older, with low activity levels as well as sleep and cognitive complaints. The subjects were randomized into four arms, including aerobic plus cognitive training, aerobic plus educational DVDs (with lectures on art, history and science), stretching plus cognitive training and stretching plus educational DVDs.

All interventions were provided for 60 minutes per day, three days per week, for 12 weeks. In the exercise groups, the target peak heart rate was 60% to 70% of maximum. The cognitive group performed computer tasks, designed to enhance the speed and accuracy in visual and auditory processing. The primary outcome measure was the Sleep Disorders Questionnaire on the 2005 to 2006 National Health and Nutrition Examination Survey (NHANES).

Based upon linear regression analysis, stretching was found to improve total sleep quality more than the aerobic training (p=0.002). The stretching plus educational DVD resulted in significantly greater improvement in overall sleep quality than did the other three arms

(p<0.05). Within this arm, individuals reported a 41% improvement in total sleep quality (p<0.001).

Conclusion: This study of elderly individuals reporting low physical activity and poor sleep found that sleep improvement was achieved to a greater extent by low intensity physical and mental activities than by moderate or high intensity activities.

Pa, J., et al. Effect of Exercise and Cognitive Activity on Self-Reported Sleep Quality in Community-Dwelling, Older Adults with Cognitive Complaints: A Randomized, Controlled Trial. **J Am Geriatrics Soc**. 2014, December; 62(12): 2319-2326.

DEMENTIA AFTER TRAUMATIC BRAIN INJURY VERSUS NON-BRAIN INJURY

Several studies and meta-analyses have failed to demonstrate an association between traumatic brain injury (TBI) and the risk of dementia. However, previous studies have had notable limitations in design. This study was designed to better understand the effect of a single, recent TBI on the risk of dementia.

Data were obtained from the State Inpatient Databases and State Emergency Department Databases for California, which are managed by the Healthcare Cost and Utilization Project (HCUP) and the Agency for Healthcare Research and Quality. Adults, 55 years of age or older, were included in the cohort if they were diagnosed as having a TBI or a non-TBI trauma (NTT) in 2005 or 2006. The primary outcome variable was a diagnosis of dementia, made during a subsequent emergency department visit or inpatient hospitalization.

After excluding patients with a dementia diagnosis less than one year after the initial trauma, the cohort included 164,661 trauma patients, of whom 51,799 had a TBI. Those with a TBI were more likely to be diagnosed with dementia, as compared to the NTT group (8.4% versus 5.9%, p<0.001). TBI remained significantly associated with a dementia diagnosis in the final model, adjusted for all covariates (p<0.001). The risk of dementia after more than one TBI was doubled (p<0.001). Moderate to severe TBI was associated with increased dementia

across all ages, whereas mild TBI became a more important predictor with increasing age.

Conclusion: This study found that mild traumatic brain injury (TBI), sustained at 65 years of age or older, or moderate to severe TBI sustained 55 years of age or older, may significantly increase the risk of developing dementia.

Gardner, R, et al. Dementia Risk after Traumatic Brain Injury vs. Non-Brain Injury. The Role of Age and Severity. **JAMA Neurol.** 2014, December; 71 (12): 1490-1497.

DOSE RESPONSE RELATIONSHIP BETWEEN EXERCISE DURATION AND COGNITION

Previous studies have demonstrated a positive effect of a single bout of exercise on cognitive performance. This study was designed to better understand the dose response relationship between exercise duration and cognitive function.

Subjects were 26 male adults between the ages of 20 and 22 years, attending one of two universities in Taiwan. At baseline, all subjects completed the International Physical Activity Questionnaire, and the Digit Span subtest of the Wechsler Adult Intelligence Scale. All participants underwent cardiovascular fitness testing, exercise intensity measurement and cognitive testing with the Stroop test.

Each participant came to the laboratory on four occasions, with at least three days separating these visits. On these days, the subjects received one of four treatments, including reading for 30 minutes or exercising for 10, 20 or 45 minutes. Then, each participant was instructed to perform practice trials on the Stroop test until at least 85% accuracy rate was achieved.

Response times were significantly shorter after the 20-minute exercise session, as compared with those after reading, 10 minutes of exercise or 45 minutes of exercise. Response times after reading and after 10 or 45 minutes of exercise did not differ significantly. Similar results were found in accuracy, with the 20-minute exercise condition resulting in the best performance.

Conclusion: This study suggests a curvilinear relationship between

exercise duration and cognitive performance, such that 20 minutes of moderate intensity exercise improves cognition, while shorter or longer durations have negligible effects.

Chang, Y., et al. Dose-Response Relation between Exercise Duration and Cognition. **Med Sci Sports Exer.** 2015, January; 47 (1): 159-165.

CELL PHONES AND THE CERVICAL SPINE

Previous studies have suggested that people spend an average of two to four hours per day with the head tilted over reading and texting on smart phones and electronic devices. With the ubiquitous use of cellular phones throughout the Western world, potential issues concerning chronic use have become apparent. Noting that the posture adopted by many to review information on the cellular phone screen involves forward cervical flexion, this study was designed to calculate the forces generated by this posture.

A model of the cervical spine was created, wherein the average weight of the head was determined to be 10 to 12 pounds. Calculations were then made of pressure at the spine, with the neck flexed at 0°, 15°, 30°, 45°, and 60°. The forces calculated at zero, 15°, 30°, 45°, and 60° of flexion were 10, 12, 27, 49, and 60 pounds, respectively.

Conclusion: This study, modeling pressures of the cervical spine, found that, as the cervical spine flexes, pressures increase significantly, with pressures nearly six times as high at 60° as when at neutral.

Hansraj, K., et al Assessment of Stresses in the Cervical Spine Caused by Posture and Position of the Head. **Surg Tech Intern.** 2014, November; 25: 277-279.

ANTIEPILEPTICS FOR MIGRAINE PROPHYLAXIS

The currently available prophylactics for migraines may, at best, lead to only an amelioration in the frequency of headache attacks. Evidence-based guidelines concerning the drug treatment of migraine have been developed and published by the European Federation of Neurological Societies.

These guidelines suggest that prophylactic therapy should be considered for patients with migraine when quality of life, business duties or school attendance are restricted. This paper reports on a Cochrane review of antiepileptic medications for migraine prophylaxis.

Multiple databases were searched, with information abstracted. Included studies were prospective, randomized, controlled trials of adults, 16 years of age or older. All of the studies had at least one arm with an antiepileptic drug. Data regarding headache frequency, quality of life and adverse events were obtained.

A total of 37 papers on antiepileptics were obtained for data analysis. The data revealed that both sodium valproate and topiramate significantly reduced the mean monthly headache frequency as compared to placebo. Patients taking divalproex or topiramate were more than twice as likely to have a 50% or greater reduction in headache frequency than were those taking a placebo. All target doses of topiramate significantly improved three or more domains of quality-of-life as compared to placebo. Data concerning other antiepileptics were insufficient.

Conclusion: This Cochrane review found that sodium valproate, topiramate and divalproex are all successful in the prophylaxis of migraine headaches.

Mulleners, W., et al. Antiepileptics in Migraine Prophylaxis: An Updated Cochrane Review. **Cephalalgia,** 2015, January; 35(1): 51-62.

FISH OIL FOR EPILEPSY

Drug-resistant epilepsy is a serious condition resulting in high morbidity. N-3 fatty acids cross the blood brain barrier and become incorporated into the cell membranes' lipid bi-layer, where they are believed to modify calcium and sodium channels, reducing membrane excitability in neurons. This study evaluated high-dose and low-dose n-3 containing fish oil in patients with drug-resistant epilepsy.

This 42-week, prospective, randomized, three-period, crossover, clinical trial evaluated high- and low-dose fish oil in 24 patients with drug resistant, partial onset seizures. The

three treatment periods consisted of six weeks of low-dose fish oil (1080 mg n-3 fatty acids per day), high-dose fish oil (2,160 mg n-3 fatty acids per day) or placebo. The primary endpoint was the percent change in total seizure frequency.

The average seizure frequency during low-dose treatment was 12.18 seizures per month, while that for high-dose treatment was 17.67 seizures per month, and that for placebo was 18.34 seizures per month. The difference between low-dose and placebo treatment was statistically significant ($p=0.02$). No significant difference was noted between high-dose treatment and placebo. Low-dose fish oil was associated with a 31% reduction in seizure frequency, as compared with high-dose ($p=0.05$)

Conclusion: This small, prospective study found a significant reduction in seizure frequency with low-dose fish oil as compared with placebo.

DiGiorgio, C., et al. Fish Oil (N-3 Fatty Acids) in Drug-Resistant Epilepsy: A Randomized, Placebo-Controlled, Crossover Study. *J Neurol Neurosurg Psych.* 2015, January; 86(1): 65-70.

DOES SPINAL MANIPULATION IMPROVE LEG PAIN

Patients with back related leg pain (BRLP) have been found to have greater pain severity and health-related costs than do those with uncomplicated low back pain. Among conservative treatments, spinal manipulative therapy (SMT), exercise and education are recommended as low risk strategies. This study tested the hypothesis that the addition of SMT to home exercise and advice (HEA) is more effective than HEA alone.

Subjects were adults with BRLP of at least four weeks' duration. The subjects were randomized to 12 weeks of SMT plus HEA, or to HEA alone. As many as 20 SMT visits were allowed, each lasting 10 to 20 minutes. Those assigned to the combination group also attended four HEA visits. During those sessions, the patients were provided a group of exercises, as well as tools to manage existing pain, prevent pain recurrences and facilitate engagement in daily activities. The

primary outcome measure was patient rated BRLP at 12 and 52 weeks.

At 12-week follow-up, the combination group had lower patient rated leg pain than did the HEA group ($p=0.008$). However, that difference was not apparent at 52 weeks ($p=0.146$). At 12 weeks, 37% of patients in the combination group had a least a 75% reduction in pain, compared with 19% in the HEA only group. Of the secondary outcome measures, global improvements, satisfaction with care and medication use were all better in the combination group than in the HEA group.

Conclusion: This study of patients with back related leg pain found that adding spinal manipulative therapy to a program of home exercise with advice improves patients' short-term outcomes, as compared with the home program alone.

Bronfort, G., et al. Spinal Manipulation and Home Exercise with Advice for Subacute and Chronic, Back-Related Leg Pain: A Trial with Adaptive Allocation. *Ann Intern Med.* 2014, September; 161(6): 381-391.

ACUTE KIDNEY INJURY IN ULTRAMARATHON RUNNERS

Ultramarathon runners are at risk for disruption in fluid balance. Extremes of fluid balance are potentially life-threatening. This study was designed to determine the prevalence and characteristics of acute kidney injury among ultramarathon runners.

Registered participants in the 2011 Soochow University 100 km ultramarathon were invited to participate. Blood was collected before the race, immediately after and one day post-race, with analyses including blood count, chemistries, creatine kinase and osmolarity. Dehydration was measured by weight loss. Urine was collected for analysis and measure of output. The primary outcome variable was level of acute kidney injury (AKI), based upon creatinine levels, as determined by the Acute Kidney Injury Network (AKIN) criteria.

Of those enrolled, 26 individuals were available for data analysis. Of these, AKI was diagnosed in 85% of the subjects post-race, with 15% at stage zero, 69% at stage I and 15%

at stage II. Post-race AKI resolved by post-race day one. No significant relationship was found between AKI stage and degree of dehydration. Clinical characteristics post-race included moderate dehydration in 65%, muscle cramps in 23% and hematuria in 12%.

Conclusion: This study of 26 ultramarathon participants found that acute kidney injury is common, but self-limited.

Kao, W., et al. Effects of 100 Km Ultramarathon on Acute Kidney Injury. *Clin J Sports Med.* 2015, January; 25(1): 49-54.

HIGH VOLUME INJECTIONS FOR ACHILLES TENDINOPATHY

Chronic Achilles tendinopathy is a common condition generally plaguing active adults between the ages of 30 and 60 years. Recent data have suggested that, instead of an inflammatory process, the pathology is more akin to a failed healing process. Conservative treatment has included eccentric exercises, although this approach often produces an insufficient response. One therapeutic option for recalcitrant Achilles tendon symptoms is the use of high volume image guided injection (HVIGI), typically using local anesthetic in sterile saline, with or without corticosteroid. This study assessed the outcomes of patients undergoing HVIGI for Achilles tendinopathy.

Subjects were 14 patients with chronic Achilles tendinopathy who had failed conservative therapy. All were referred for HVIGI. All underwent an injection under direct ultrasound visualization deep to the tendon, on the anterior surface between the Achilles tendon and Kagers fat pad. A total of 10 mL of one percent lidocaine was injected, followed by 40 mL of sterile saline. The patients were followed at two to three weeks, and then at six weeks, three months and six months. All were asked to rate their pain on a 10-point visual analogue scale (VAS), as well as to complete a Victorian Institute of Sport Assessment-Achilles (VISA-A).

The mean time to final follow-up was 347 days. Of the 14 patients studied, 50% reported a VAS pain score of zero or one. The average improvement in the VAS pain scores

was one point and the average improvement in the VISA-A scores was 41%. Two patients underwent surgical intervention for ongoing symptoms.

Conclusion: This study of 14 patients with chronic Achilles tendinopathy suggests that high volume image-guided injections without corticosteroid may be an effective intervention.

Wheeler, P., et al. The Use of High Volume Image-Guided Injections (HVIGI) for Achilles Tendinopathy: A Case Series and Pilot Study. *Inter Musculoskel Med.* 2014; 36(3): 96-103.

TRENDS IN OPIOID ABUSE AND MORTALITY IN UNITED STATES

The number of deaths per year due to prescription opioid medications reached 16,651 in 2010. The United States Office of National Drug Control Policy has responded with numerous recommendations, including the need to evaluate current databases that measure the extent of prescription drug use, misuse and toxicity. This study used the Research Abuse, Diversion, and Addiction-Related Surveillance (RADARS) system to describe the diversion and abuse of prescription opioid analgesics between 2012 and 2013.

The authors used data from five, separate RADARS programs. Data were gathered concerning all marketed products and formulations of six prescription analgesics, oxycodone, hydrocodone, hydromorphone, fentanyl, morphine and tramadol. In addition, data were retrieved concerning heroin abuse. Quarterly event rates for each medication were determined.

In 2006, 47 million prescriptions of opioid analgesics were written, with prescription volume peaking in the fourth quarter of 2012 at 62 million prescriptions. Except for that quarter, the number of prescriptions trended downward from 2011 to 2013. The rate of opioid related deaths increased from 2002 to 2006, plateauing from 2006 to 2008, and decreasing slightly from 2009 to 2013. The rate of drug diversion for abuse, as measured by several different programs, increased before mid-2010, and has trended down since then. The rate of heroin related deaths was flat from 2002 to 2010,

and has increased each year since then through 2013.

Conclusion: This study found that diversion and abuse of prescription opioid medications increased from 2002 to 2010, but has slightly decreased from 2011 to 2013.

Dart, R., et al. Trends in Opioid Analgesic Use and Mortality in The United States. *N Engl J Med.* 2015, January 15; 372: 241-248.

STATIN USE AND FRACTURE RISK

Previous studies have suggested that statins may exert positive biological effect on bones, and that chronic inflammation affects bone loss. This study was designed to determine whether treatment with statins is associated with a lower risk of fractures, and whether higher baseline serum high sensitivity C-reactive protein (hs-CRP) levels are associated with an increased risk of fracture.

The Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin (JUNIPER) was a randomized, double-blind, placebo-controlled, multinational trial, including 1,315 centers in 26 countries. Men and women older than 50 and 60 years, respectively, all with hs-CRP levels of at least 2 mg/L and low-density lipoprotein cholesterol levels of less than 130 mg/dL, were recruited.

At baseline, a detailed medical history was taken and a screening physical examination completed. The physical examination included hs-CRP levels. Subjects were randomized to receive either rosuvastatin calcium, 20 mg daily or placebo. The participants were assessed at three-month intervals, and were queried for the occurrence of fractures and other adverse events.

Of the 17,802 participants, 38.2% were women, with a total group mean age of 66 years. The overall incidence of fracture in the treatment and placebo groups were 1.20 and 1.14 per 100 person years, respectively (adjusted HR, 1.16). Increasing tertiles of baseline hs-CRP level were not associated with the risk of fracture (adjusted HR for each unit increase in hs-CRP tertile=1.06).

Conclusion: This large, randomized trial did not find that

treatment with rosuvastatin reduces the risk of fracture, nor that elevated baseline hs-CRP levels are associated with the risk of fracture.

Pena, J., et al. Statin Therapy and Risk of Fracture: Results from the JUNIPER Randomized, Clinical Trial. *JAMA Intern Med.* doi:10.1001/jamainternmed.2014.6388

LONG-TERM OUTCOME OF TOTAL HIP ARTHROPLASTY IN PATIENTS UNDER THIRTY

Despite the fact that total hip arthroplasty (THA) was designed for elderly, low-demanding patients, the benefit of this procedure to younger populations has been less well documented. This study reports on the 10-year outcomes of patients undergoing THA when 30 years of age or younger.

This retrospective review included all patients seen in the Department of Orthopaedic Surgery of the University of Ioannina who were under 30 years of age at the time of the THA. The main indications for surgery were juvenile rheumatoid arthritis (42%), followed by osteonecrosis of the femoral head (24.4%) and congenital diseases (11%).

Thirty patients, for a total of 45 hips, were available for analysis at a mean follow-up of 116 months. Of those, 24% underwent revision, with all of the revisions due to aseptic loosening. The mean time to revision surgery was 139 months. The 10-year survival rate was 90.3%. The parameters associated with increased risk for revision surgery were age, gender, use of graft, use of cement, use of screws, head size and type.

Conclusion: This study of patients under 30 years of age at the time of total hip arthroplasty found the 10-year survival rate to be over 90%. Aseptic loosening was the only reason for revision.

Pakos, E., et al. Long-Term Outcomes of Total Hip Arthroplasty in Young Patients under 30. *Arch Bone Jt Surg.* 2014, September; 2(3): 157-162.

HIV AND LOWER RISK OF MULTIPLE SCLEROSIS

There exists only one case report of a patient with multiple sclerosis

(MS) and HIV treated with HIV retroviral therapies. In that case report, the patient's MS symptoms resolved after starting a combination antiretroviral therapy, and remained subsided for more than 12 years' follow-up. This study explored the hypothesis that HIV therapies may ameliorate MS, providing an explanation for the large observed protective effect of HIV on the development of MS.

This study used data from the English Hospital Episode Statistics (HES) that identified all people with HIV discharged from National Health Service hospitals between 1999 and 2011. All were followed for any subsequent record of MS. These patients were compared with controls, stratified by age, gender, year of first hospital admission, region of residence and socioeconomic status.

The median follow-up time for the 21,201 patients with HIV was 2,454 days, while the median follow-up for the 5,290,496 controls was 2,756 days. The relative risk of MS in patients with HIV, as compared to those without HIV, was 0.38. After restricting the outcome to those whose first record of MS was more than a year after the first record of HIV, the relative risk was found to be 0.25.

Conclusion: This large cohort study demonstrated that HIV infection (and/or its treatment) is associated with a significantly decreased risk of developing multiple sclerosis.

Gold, J., et al. HIV and Lower Risk of Multiple Sclerosis: Beginning to Unravel a Mystery Using a Record-Linked Database Study. *J Neurol Neurosurg Psychiatry*. 2015; 86: 19-12 doi:10.1136/jnnp-2014-307932

OCCIPITAL NERVE STIMULATION FOR CHRONIC MIGRAINE

For migraines, the main rationale for occipital nerve stimulation (ONS) is the convergence of cervical somatic trigeminal, dorsal trigeminovascular afferent neurons on second-order nociceptors in the trigeminocervical complex. This study tested the hypothesis that sub-threshold stimulation of the occipital nerve is less effective than supra-threshold stimulation.

Patients with migraine, treated with ONS, all 18 years of age or older, were studied. All participants

were cycled through all three treatment groups in random order. These treatments included "effective stimulation", "subthreshold stimulation", with the amplitude set to just below perception, and no stimulation, with the implantable pulse generator set to the lowest amplitude. Outcome measures included the visual analog scale (VAS), the McGill Pain Questionnaire (MPQ) and the Short-Form-36 (SF-36) questionnaire. The primary outcome was reduction in pain. The secondary outcome measure was increased quality of life.

Eight patients were included in the study. Headache pain improved substantially with "effective stimulation" in all patients, as measured by both the VAS and MPQ ($p < 0.0001$ for both). In addition, significant differences in were noted in favor of the "effective stimulation" group on the SF-36 ($p = 0.012$). Pain was significantly improved with "subthreshold stimulation" ($p = 0.0031$), although less than noted with "effective stimulation" ($p = 0.0003$).

Conclusion: This study found that occipital nerve stimulation can reduce migraine headaches with either subthreshold or suprathreshold stimulation, with the latter found to be more effective.

Slotty, P., et al. Occipital Nerve Stimulation for Chronic Migraine: A Randomized Trial on Sub-Threshold Stimulation. *Cephalalgia*. 2015, January; 35(1): 73-78.

PROTEIN INGESTION AFTER CONCURRENT EXERCISE

Consumption of high quality protein in close temporal proximity to resistance exercise enhances translation initiation signaling, maximally stimulates rates of muscle protein synthesis and augments hypertrophy and strength gains. In addition, protein feeding after endurance exercise can increase the transcriptional profile of mitochondrion related genes and increase rates of myofibrillar protein synthesis. This study explored whether protein ingestion enhances anabolic and metabolic signaling and subsequent protein synthesis during the early recovery period after exercise.

This randomized, double-blind, crossover study involved subjects

completing two bouts of concurrent resistance exercise and cycling. The subjects received either post-exercise placebo or protein ingestion. The arms of the study were separated by a three-week recovery period. Eight healthy subjects underwent resistance exercise of eight sessions of five leg extensions and 80% of 1RM followed by cycling of 30 minutes at 70% of VO_{2peak} . Subjects were then randomized to receive either placebo or 25 grams of whey protein, provided immediately after cessation of exercise. Muscle biopsies were obtained to determine the fractional synthetic rate of mitochondrial and myofibrillar protein synthesis.

Myofibrillar protein synthesis increased above rest between one and four hours after exercise in both groups. This increased rate was greater in the protein supplement group than in the placebo group ($p < 0.05$). In addition, protein ingestion attenuated post-exercise increases in genetic markers associated with muscle proteolysis. The rates of mitochondrial protein synthesis were unchanged during the acute post-exercise period.

Conclusion: This study demonstrated that protein ingestion after combined resistance and endurance exercise can enhance myofibrillar protein synthesis and attenuate markers of muscle catabolism.

Camera, D., et al. Protein Ingestion Increases Myofibrillar Protein Synthesis after Concurrent Exercise. *Med Sci Sports Exer*. 2015, January; 47(1): 82-91.

SERUM VITAMIN D AND SLEEP DURATION

Previous studies have suggested that low serum vitamin D levels are closely associated with a variety of diseases. Several studies have suggested that sleep patterns are linked to serum vitamin D levels. This study investigated whether self-reported sleep duration is associated with serum vitamin D levels among elderly Korean adults.

Data were obtained from the Korean National Health and Nutrition Examination Survey (KNHANES) - 2010, a cross-sectional survey designed to measure health and nutritional status of the non-

institutionalized population. Data collected included demographic and anthropometric information, serum vitamin D measurements, and self-reported sleep duration. Subjects were 60 to 80 years old and had no record of chronic kidney or liver disease. The mean age of the sample (n=1614) was 68.1 years, and the mean daily sleep duration 6.6 hours. After adjustment for age, gender, body mass index (BMI), alcohol consumption, smoking history and daily sun exposure, sleep duration was found to be significantly correlated with the serum vitamin D level.

Women had significantly lower vitamin D levels than did men. Those who consumed alcohol two to three times per week, or more than four times per week, had significantly higher vitamin D levels than those who consumed alcohol less than once per month. BMI was inversely correlated with serum vitamin D levels.

Conclusion: This study found that sleep duration is positively associated with serum vitamin D levels in elderly Korean adults.

Kim, J., et al. Association between Self-Reported Sleep Duration and Serum Vitamin D Level in Elderly Korean Adults. *J Amer Geriatrics Soc.* 2014, December; 62(12): 2327-2332.

VACCINES AND THE RISK OF MULTIPLE SCLEROSIS

The concern that vaccinations increase the risk of multiple sclerosis (MS) remains controversial. This study examined whether certain vaccines, specifically human papilloma virus and hepatitis B, increase the risk of MS or central nervous system acquired demyelinating syndromes (CNS ADS).

This case controlled study reviewed electronic medical records from a large health maintenance organization. Incident cases of CNS ADS and MS were identified. All incident cases were matched with five controls for age, gender and zip code. Vaccination records within three years of the index date were obtained. A conditional logistic regression formula was used to estimate the matched odds ratio for the association between the

demyelinating syndrome and vaccination.

At follow-up, 780 new cases of MS, clinically isolated syndrome (CIS) or acute disseminated encephalomyelitis (ADEM) were included in the study. The most common of these was MS, present in 54.7% of the cases. Most cases were diagnosed within 300 days of symptom onset. No significant associations were found between the hepatitis B vaccination (odds ratio 1.12), HPV vaccination (odds ratio 1.05) or any vaccination (odds ratio 1.03) and the risk of CNS ADS.

Conclusion: This study found no long-term association between vaccines and increased risk of MS and other central nervous system demyelinating syndromes.

Langer-Gould, A., et al. Vaccines and the Risk of Multiple Sclerosis and Other Central Nervous System Demyelinating Diseases. *JAMA Neurol.* 2014, December; 71(12): 1506-1513.

GLUCOCORTICOIDS AND ION-CHANNEL-MEDIATED TOXICITY

The cellular and molecular mechanisms underlying rotator cuff tendon degeneration have included both intrinsic tendon failure and extrinsic mechanical impingement. The neuronal changes in tendinopathy appear consistent with a failed healing response and an up-regulation in the excitatory, glutaminergic system. This study assessed the histological and immunohistochemical effects of glucocorticoid injections on rotator cuff tendon.

Supraspinatus tendon biopsies were taken from eight patients undergoing rotator cuff repair, and from 12 patients undergoing subacromial glucocorticoid injection for rotator cuff tendinopathy. In the glucocorticoid injection group biopsies were taken immediately prior to and 7 weeks following glucocorticoid injection. In the rotator cuff repair group, biopsies were taken at the time of surgery and 7 weeks following rotator cuff repair. The tissue samples were assessed for histology and immunohistochemistry.

A significant increase in nuclei count and vascularity was noted after rotator cuff repair (p=0.008 for both comparisons), although not after

glucocorticoid injection. In addition, hypoxia inducible factor 1 alpha and cell proliferation were increased after rotator cuff repair (p=0.03, and p=0.03, respectively), and not after glucocorticoid injection. Further, the N-methyl -D- aspartate receptor 1 glutamate receptor was increased after glucocorticoid injection and not after rotator cuff repair.

Conclusion: This study of patients with rotator cuff tears or rotator cuff tendinopathy found that, post-surgery, there are numerous signs of an ongoing proliferative healing response that are not present after steroid injections. An increase in the NMDA-1 receptors after steroid injection raises concern of potential excitotoxic damage.

Dean, B., et al. Glucocorticoids Induce Specific Ion-Channel-Mediated Toxicity in Human Rotator Cuff Tendon: A Mechanism Underpinning the Ultimate Deleterious Effect of Steroid Injection in Tendinopathy? *Br J Sports Med.* 2014, December; 48(22): 1620-1626.

AVOCADOS AND LIPOPROTEIN

The PREDIMED trial reported that a Mediterranean diet supplemented with monosaturated fatty acid (MUFA) rich foods that included either extra-virgin olive oil or mixed nuts could significantly reduce the incidence of major cardiovascular disease events. As avocados are a rich source of MUFA, this study examined the effects of avocados on traditional and novel lipid risk factors.

Healthy, overweight men and women were randomly assigned to a treatment sequence of three diets. Beginning with the average American diet (AAD), defined as 34% fat, 51% carbohydrate (CHO) and 16% protein [PRO], the diets were modified. A low fat (LF) diet replaced six to seven percent of energy from saturated fatty acids (SFA) with carbohydrate (CHO) (from grains that were incorporated in the diet in place of SFA) in the AAD. The avocado (AV) and moderate fat (MF) diets replaced six to seven percent of energy from SFA with MUFA, using either one Hass avocado per day (for the AV diet) or high oleic acid oils for the MF diet, as the main sources of MUFA. At the end of each diet period, fasting blood samples were collected on two consecutive days.

(Continued from page 2)

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Compared with the AAD, the LF and MF diets significantly reduced LDL-C and triglycerides. However, the reductions in LDL-C and TC by the AV diet were significantly greater than those of the LF and MF diets. In addition, the AV diet resulted in a greater reduction in non-HDL-C compared with the MF diet. TC/HDL-C and LDL-C/HDL-C significantly decreased after the AV diet, and were lower ($p=0.04$ and $p<0.0001$) than after the MF and LF diets. Further, only the AV diet significantly decreased LDL particle number ($p=0.0001$), small dense LDL ($p=0.04$) and the ratio of LDL/HDL ($p<0.0001$) from baseline.

Conclusion: This study demonstrates that a moderate fat diet low in saturated fatty acids and high in MUFA derived from a daily avocado can significantly decrease cardiovascular disease risk factors.

Wang, L., et al. Effect of a Moderate Fat Diet with and without Avocados on Lipoprotein Particle Number, Size and Subclasses in Overweight and Obese Adults: A Randomized, Controlled Trial. *J Amer Heart Assoc.* 2015; doi: 10.1161/JAHA.114.001355.

Rehab in Review (RIR) is produced monthly by physicians in the field of Physical Medicine and Rehabilitation (PM&R), with the cooperation and assistance of Emory University School of Medicine, Department of Rehabilitation Medicine. The summaries appearing in this publication are intended as an aid in reviewing the broad base of literature relevant to this field. These summaries are not intended for use as the sole basis for clinical treatment, or as a substitute for the reading of the original research.

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ISSN # 1081-1303
www.rehabinreview.com



REHAB IN REVIEW

Produced by the Department of
Rehabilitation Medicine, Emory
University School of Medicine



Department of
Rehabilitation
Medicine

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