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NON-SUGAR SWEETENERS AND HEALTH

With an increased consumer interest in reducing energy intake, food products containing non-sugar sweeteners (NSS) have become increasingly popular. Studies of the health effects of these sweeteners have often produced inconsistent results. This study was designed to better understand the health effects of NSS.

This systematic review and meta-analysis included studies of healthy children or adults, which compared groups based on level of NSS intake, with outcomes including body mass index, glycemic control, oral health, eating behavior, preference for sweet taste, cancer, cardiovascular disease, kidney disease, mood, behavior, cognition, and adverse effects.

Data from 48 studies, including 17 randomized trials, were included in the analysis. No significant association was found between NSS intake and the risk of bladder or lower urinary tract cancer, non-Hodgkin's lymphoma subtypes or non-lymphoid leukemia, depression, kidney disease, or brain tumors. No significant health benefits were noted with increased NSS intake, including weight loss. Similar findings were found in studies of children.

Conclusion: This large data review and meta-analysis found no strong evidence of adverse health effects of non-sugar sweeteners.

Toews, I., et al. Association between Intake of Non-Sugar Sweeteners and Health Outcomes: Systematic Review and Meta-Analysis of Randomized and Non-Randomized Controlled Trials and Observational Studies. **BMJ.** 2019; 364: K4718.

SYSTEMIC INFLAMMATION DURING MIDLIFE AND COGNITIVE CHANGE

A growing body of evidence has implicated immune function in the pathophysiology of Alzheimer's disease (AD) and related dementia. In addition, a number of studies have associated cognitive decline with levels of circulating inflammatory markers. This study assessed the long-term effects of midlife systemic inflammation on progressive cognitive decline.

The atherosclerosis risk in communities (ARIC) study enrolled 15,792 adults, 45 to 65 years of age, between 1987 and 1989. Inflammatory biomarkers were measured in blood samples collected at visits one and two, including fibrinogen, von Willebrand factor, factor VIII, and white blood cell count. The inflammatory markers were converted to standardized Z scores. In addition, C-reactive protein (CRP) levels were also collected in 2011 to 2013 at visit two. Cognition was measured at visits two, four and five using standardized neuropsychological measures.

After adjusting for demographic and cardiovascular risk factors, those with a higher inflammation composite score at visit one had steeper twenty-year declines in cognitive scores. Compared to the lowest quartile, those with inflammation composite scores in the second, third and fourth quartiles had cognitive declines that were 7.5%, 7.7% and 8.9% steeper, respectively. Elevated CRP was associated with a steeper cognitive decline after adjusting for demographic and cardiovascular risk factors. Compared to a CRP in the top quartile (lowest level of inflammation), a CRP in the second, third and fourth quartiles was associated with a 9.7%, 8.5% and 12.3% steeper cognitive decline, respectively, as compared to the first quartile.

Conclusion: This study found that elevated inflammatory markers in the blood are associated with a decline in cognitive status.

Walker, K., et al. Systemic Inflammation during Midlife and Cognitive Change over 20 Years. The ARIC Study. **Neurol**: 2019, March; 92 (11): e1256-e1267.

SUPRASCAPULAR NERVE BLOCK VERSUS SUBACROMIAL INJECTION FOR ROTATOR CUFF TEAR

Rotator cuff tear is among the most common musculoskeletal disorders. Most are treated conservatively, with treatments including nonsteroidal anti-inflammatory drugs, physical/ occupational therapy and subacromial injections. This study compared the effect of suprascapular nerve block to that of subacromial injection among patients with acute rotator cuff tears.

Subjects were 45 years of age or older, all with symptomatic, partial and full-thickness rotator cuff tears. The patients were randomized to treatment with suprascapular nerve block (SSNB) or subacromial injection (SA), with both injections including nine mL of one percent ropivacaine and one mL of betamethasone. All were assessed with a modified Constant-Murley (CM) score, with a secondary outcome of pain, as measured by visual analog scale (VAS) at two, six and 12 weeks after the injection.

Data were collected for 43 patients with a mean age of 65.2 years. At two weeks, there was no difference in CM scores between the two cohorts. At six and twelve weeks, the mean change from baseline CM was significantly greater in the SSNB group than in the subacromial group (p=0.048 and p=0.014 respectively). A 12 weeks, the SSNB group demonstrated a significantly higher mean CM score than did the SA group (p=0.014).

Conclusion: This study of patients with symptomatic rotator cuff tears found that, compared with subacromial injections, those treated with suprascapular nerve blocks enjoyed greater improvements in pain and function at six and 12 weeks.

Coory, J., et al. Efficacy of Suprascapular Nerve Block Compared with Subacromial Injection: A Randomized, Controlled

Trial in Patients with Rotator Cuff Tears. **J Shoulder Elbow Surg.** 2019, March; 28(3): 430-436.

BOTOX VERSUS LOCAL INJECTION FOR MYOFASCIAL PAIN

Myofascial pain is a chronic pain disorder affecting a wide range of patient populations. Local injections are considered a first-line treatment for myofascial pain, with injectates including local anesthetics and botulinum toxin. This literature review and meta-analysis compared the efficacy of injections with botulinum toxin with that of local anesthetic in patients with myofascial pain disorder.

A literature review was conducted for studies of patients with myofascial pain, injected with either botulinum toxin A or local anesthetic, with follow -ups through 24 weeks. From this review were identified 33 studies. Outcome measures included a visual analog scale for pain and the Neck Pain and Disability Scale.

Data from 11 studies found that, one to four weeks after injections, local anesthetic, but not Botox, was effective for pain relief. For studies with follow-up at weeks seven to eight, the pain relief of those treated with local anesthetics was large, while that of botulinum toxin was significant, but small. With follow-up at 11 to 12 weeks, both injections were significantly better than placebo, although clinically small. At 16 weeks, only local anesthetic was significantly better than placebo. A 24 weeks' follow-up, both local anesthetic and botulinum toxin were significantly better than placebo.

Conclusion: This literature review and meta-analysis of patients with myofascial pain found that injections with local anesthetics result in a consistent, large improvement at one to 16 weeks' follow-up, while botulinum toxin injections result in negligible or small effects.

Ahmed, S., et al. Effect of Local Anesthetic versus Botulinum Toxin-A Injections for Myofascial Pain Disorders: A Systematic Analysis. **Clin J Pain.** 2019, April; 35(4): 353-367.

NITRATE SUPPLEMENTATION ON POST EXERCISE BLOOD PRESSURE

Hypertension and obesity are major risk factors for cardiovascular disease. Several studies have found beneficial cardiovascular effects of several different nutrients found in vegetables. This study assessed the dietary effect of nitrate supplementation on post exercise ambulatory blood pressure in obese males.

Subjects were males, 20 to 30 years of age, each with a BMI of 30 to 40 kg/m^2. After determining the maximal heart rate, the subjects were randomized to one of three groups. The high nitrate group received beetroot juice (800 mg nitrate), the low nitrate group received fruit soda (5.4 mg nitrate) and the no-nitrate control group received 200 mL of water. All underwent 40 minutes of aerobic exercise, at an intensity of 50% of their heart rate reserve. Blood pressure was monitored before and after the intervention. Blood was collected to measure plasma nitric oxide concentration before intervention, immediately after intervention and one-hour post-intervention.

The high nitrate group had a significantly reduced ambulatory systolic blood pressure at one to six hours after exercise as compared to the low ($p=0.025$) and the no nitrate ($p=0.05$) controls. No significant difference was noted in ambulatory diastolic blood pressure between groups.

Conclusion: This study of obese males found that ingesting beat root juice prior to exercise can enhance the reduction of systolic blood pressure following moderate intensity exercise.

deLima, B., et al. Effect of Acute Dietary Nitrate Supplementation on the Post-Exercise Ambulatory Blood Pressure in Obese Males: A Randomized, Controlled, Crossover Trial. **J Sports Sci Med**. 2019; 18: 118-127.

ORAL CURCUMIN BEFORE OR AFTER ECCENTRIC EXERCISE

Curcumin is a natural polyphenolic substance extracted from turmeric. Studies have shown various physiological effects of this spice, including membrane protective, anti-inflammatory and antioxidant properties. This study examined the effect of curcumin on muscle damage and inflammatory markers after eccentric exercise.

Two, parallel experiments were conducted. Ten, healthy men ingested either 180 mg per day of oral curcumin or placebo for seven

days before exercise or for seven days after exercise. Each subject performed 30 maximal isokinetic ($120°s^{-1}$) eccentric contractions of the elbow flexors, with the contralateral arm performing the same exercises after at least four weeks. Muscle strength, range of motion soreness and serum CK activity were measured before and one to seven days after exercise. In addition, plasma IL-8 and TNF-α concentrations, serum concentrations of derivatives of reactive oxygen metabolites (d-ROMs), and the biological antioxidant potential (BAP) were measured before, immediately after, 12 hours after, and one, three, five and seven days after exercise.

When curcumin was ingested before exercise, no significant differences in any muscle damage markers were found between the curcumin and placebo trials. However, IL8 was lower at 12 hours after exercise in this group ($p=0.003$). When ingested after exercise, compared to the control group the curcumin group demonstrated superior torque ($p<0.05$), range of motion ($p<0.05$), muscle soreness ($p<0.05$) and CK activity ($p=0.02$).

Conclusion: This study of eccentric exercise found that 180 mg of curcumin, when taken before exercise, can reduce inflammation, and when taken after exercise, can reduce soreness and markers of muscle damage.

Tanabe, Y., et al. Effects of Oral Curcumin Ingested before or after Eccentric Exercise on Markers of Muscle Damage and Inflammation. **Scand J Med Sci Sports**. 2019, April; 29(4): 524-534.

TRANSCRANIAL MAGNETIC STIMULATION AND THETA BURST STIMULATION FOR SPASTICITY IN MULTIPLE SCLEROSIS

Spasticity has been reported in 50 to 70% of patients with multiple sclerosis (MS). Previous studies have demonstrated that high-frequency repetitive transcranial magnetic stimulation (HF-rTMS) or intermittent theta burst stimulation (iTBS) of the primary motor cortex can reduce spasticity among patients with central nervous system insults. This study assessed the effect of these interventions on patients with spasticity secondary to MS.

Patients with spastic secondary progressive MS (SPMS) were randomized to receive HF-rTMS, iTBS or sham stimulation, once per day for five days/week for two weeks. The HF-rTMS was delivered at 20 Hz with a total of 1600 stimuli per session. The iTBS was delivered with a total of 1200 stimuli per session. Outcomes were measured for subjective and objective spasticity as well as pain and fatigue at baseline, at the end of treatment (T1) and at two (T2) and 12 (T3) weeks after the last treatment.

Significant improvements in Modified Ashworth Scale (MAS) scores were noted at T1 for the HF-rTMS ($p<0.001$) and iTBS ($p<0.001$) groups with no such improvement seen in the sham control group. Scores on the Subjective Evaluating Spasticity Scale (SESS) were significantly improved in both treatment groups, persisting at 12 weeks in iTBS group but returning to baseline in the HF-rTMS group. Pain improved in the HF-rTMS group, persisting at two weeks and returning to baseline at 12 weeks, with no significant changes in the other two groups. Scores on the Modified Fatigue Impact Scale improved in the HF-rTMS group at T1, and gradually worsened at two and 12 weeks, with no improvement in the iTBS group.

Conclusion: This study of patients with multiple sclerosis found that treatment with HF-rTMS or iTBS could reduce spasticity, pain and fatigue, with some evidence suggesting a longer lasting effect in those treated with iTBS.

Korzhova, J., et al. High-Frequency Repetitive Transcranial Magnetic Stimulation and Intermittent Theta Burst Stimulation for Spasticity Management in Secondary Progressive Multiple Sclerosis. **Eur J Neurol.** 2019 Apr; 26(4): 680-687.

CEREBELLAR STIMULATION AND GAIT RECOVERY AFTER HEMIPARETIC STROKE

Gait and balance impairments after stroke are associated with poor functional recovery. Studies using magnetic resonance imaging (MRI) have found that activity in the contralesional cerebellum positively correlate with gait recovery in patients with stroke. This study assessed whether cerebellar intermittent theta burst stimulation (CRB-iTBS), a novel form of repetitive transcranial magnetic stimulation (rTMS) could improve gait and balance recovery in patients with stroke.

Subjects were patients with a first ever ischemic stroke in the territory of the middle cerebral artery. The patients were randomized to age-matched groups treated with either CRB-iTBS or sham CRB-iTBS, both coupled with physical therapy. The primary efficacy endpoint was the change from baseline in Berg Balance Scale (BBS) scores.

Patients in the treatment group, but not those in the sham group, showed improvement in gait and balance, with pronounced increases in mean BBS scores at three weeks ($p<0.001$). In addition, those in the treatment group, but not those in the sham group, showed a reduction of step width during gait ($p<0.05$). Non-significant differences were noted between the groups in Fugl- Meyer and Barthel index scores.

Conclusion: This study of patients with ischemic stroke found that intermittent theta burst stimulation directed at the cerebellum can promote gait and balance recovery.

Koch, G., et al. Effect of Cerebellar Stimulation on Gait and Balance Recovery in Patients with Hemiparetic Stroke. A Randomized, Clinical Trial. **JAMA Neurol.** 2019, February; 76(2): 170-178.

DONEPEZIL FOR FALLS AND MILD COGNITIVE IMPAIRMENT

Older adults with mild cognitive impairment (MCI) have a higher prevalence of gait disorders and an increased risk of falls compared to their cognitively normal counterparts. These patients also have a higher dual-task gait cost (DTC), defined as a reduction in gait speed while performing a cognitively demanding task. This study assessed the effect of donepezil on gait speed in patients with MCI.

After a baseline gait assessment, the patients were randomized to receive either donepezil (n=31), titrated up to 10mg/day, or a matching placebo (n=29). Follow-up gait assessments, including gait speed, gait variability and reduction of DTC, were completed at one and six months. Secondary outcomes included the Digit Span subtest, the Trail Making Test, Forms A and B, Letter–Number Sequencing scores and the number of falls.

At six months, the treatment group demonstrated improved dual task gait speed, although this finding was not significant. The treatment group also demonstrated a reduction in DTC compared with placebo, with significant improvement while counting backwards ($p=0.037$). In the

six months after intervention, the treatment group reported 13 falls, while the placebo group reported 21. The percentages of patients who fell during that time were 23% in the treatment group and 41% in the placebo group. Neither comparison was statistically significant. No major adverse events were reported.

Conclusion: This randomized, controlled study of patients with mild cognitive impairment found that Aricept, 10 mg per day, may reduce the risk of falls.

Montero-Odasso, M., et al. Donepezil for Gait and Falls in Mild Cognitive Impairment: A Randomized, Controlled Trial. **Euro J Neurol.** 2019, April; 26(4): 651-659.

PSYCHIATRIC ILLNESS AND ELDERLY FRACTURE PATIENTS

As the population ages, the number of elderly with trauma is expected to grow. Given the emotional burden of trauma, this study investigated the association between traumatic fractures requiring surgery and psychiatric illness among patients 70 years of age or older.

Data from a level I trauma center were reviewed for records of patients 70 years of age or older who underwent surgery for traumatic fractures between 2012 and 2017. The medical record was reviewed to identify patients with ICD codes for psychiatric illness. A multivariable logistic regression analysis was conducted to identify independent associations between hypothesis driven medical characteristics and unplanned readmissions. These variables included age, gender, the Charleston Comorbidity Index, Injury Severity Scale score, fracture location, surgical procedures, number of fractures, nicotine use, substance abuse, dementia, delirium or psychiatric disorders. Data were compared to those of individuals less than 70 years of age.

During the study, data were collected for 1,186 patients. Of these, 44.6% had baseline psychiatric comorbidities, significantly higher than those below 70 years of age (p=0.007). In descending order of prevalence, the comorbidities were anxiety disorder (22.9%), sleep disorder (16%), major depressive disorder (12.9%) and alcohol abuse (8.5%). A higher rate of readmission was noted among those with psychiatric diagnoses, as compared to those without (p<0.001). A multivariate regression analysis demonstrated an independent association between psychiatric illness and unplanned readmission (odds ratio 1.54; p=0.003).

Conclusion: This study of patients 70 years of age or older, admitted for surgical treatment of fractures, found that 44% had a psychiatric comorbidity, with the risk of readmission higher among those with psychiatric diagnoses.

Gitajn, I., et al. Psychiatric Illness is Common in Elderly Fracture Patients. **J Orthop Trauma.** 2019, March; 33 (3): 149-154.

BEMPEDOIC ACID AND LDL-CHOLESTEROL

Studies have shown that Bempedoic acid can lower LDL-cholesterol by inhibiting ATP citrate lyase, a key enzyme in the cholesterol biosynthesis pathway, and may be useful for patients who are insufficiently responsive to lipids. This manuscript presents results of the CLEAR Harmony trial, which assessed the safety and efficacy of Bempedoic acid over one year.

This 52-week, randomized, double-blind, placebo-controlled, parallel group, phase three trial included adult patients with atherosclerotic cardiovascular disease who were taking stable doses of maximally tolerated statin therapy with fasting LDL cholesterol levels >70 mg/dL. The participants were randomized to receive either Bempedoic acid 180 mg/day (n=1488) or matching placebo (n=742). Follow-up visits were conducted at weeks four through 52. The primary endpoint was overall safety, which was assessed according to the incidence of adverse events and changes in laboratory variables.

At one-year, adverse events were reported in 70.5% of the treatment group and in 70.7% of the placebo group, with most of these graded as mild to moderate. The reduction in LDL levels in the Bempedoic group was greater than that in the placebo group at weeks 12 and 24 (p<0.001 for both comparisons). In addition, the Bempedoic group demonstrated superior changes in non-HDL cholesterol, total cholesterol, apolipoprotein B and high-sensitivity C-reactive protein at week 12 (p<0.001 for all comparisons).

Conclusion: This study of patients with LDL levels insufficiently responsive to statins found that treatment with Bempedoic acid can improve LDL level and does not result in increased adverse events.

Ray, K., et al. Safety and Efficacy of Bempedoic Acid to Reduce LDL-Cholesterol. **N Engl J Med**. 2019, March 14;380: 1022-1032.

PRASUGREL VERSUS CLOPIDOGREL FOR NON-CARDIOEMBOLIC STROKE

Guidelines for the management of non-cardioembolic stroke include several antiplatelet agents. Even with these drugs, the one-year stroke recurrence rate is between three and ten percent. Genetic polymorphisms of CYP2C19 have been identified as a major cause of poor responsiveness to Clopidogrel. Prasugrel, a T2 Y 12 receptor antagonist, can inhibit platelet aggregation, independent of CYP 2C19. This Japanese study of patients with a non-cardioembolic stroke investigated the noninferiority of prasugrel compared with clopidogrel.

This randomized, double-blind, active controlled, parallel group study recruited subjects from 224 hospitals in Japan between 2011 and 2015. Subjects were 20 to 74 years of age, each with a documented non-cardioembolic ischemic stroke. The patients were randomized to receive either prasugrel, 3.7 mg, or clopidogrel, 75 mg, once daily for 96 to 104 weeks. The primary efficacy endpoint was the combined incidence of ischemic stroke, myocardial infarction or death from other vascular causes.

The trial was completed by 1,885 patients in the prasugrel group and 1,862 in the clopidogrel group. The combined rates of ischemic stroke, myocardial infarction and death from other vascular causes were four percent in the prasugrel group and four percent in the clopidogrel group. The cumulative incidences of the primary endpoints in patients with large artery atherosclerosis or small artery occlusion at baseline, both considered consequences of platelet thrombus, did not differ between the groups. No significant differences were seen between the groups in any adverse events.

Conclusion: This study of patients with non-cardioembolic ischemic stroke found no significant difference in the rate of recurrent stroke between those treated with clopidogrel and those treated with prasugrel.

Ogawa, A., et al. Comparison of Prasugrel and Clopidogrel in Patients with Non-Cardioembolic Ischaemic Stroke: A Phase 3, Randomised, Non-Inferiority Trial (PRASTRO-I). **Lancet Neurol.** 2019, March 18(3): 238-247.

RELATIVE EFFECTS OF LDL-C ON ISCHEMIC STROKE AND CORONARY HEART DISEASE

Previous studies of statin therapy have demonstrated that reducing low-density lipoprotein cholesterol (LDL-C) will reduce the risk of both ischemic stroke (IS) and coronary heart disease (CHD). Observational studies have found stronger effects of LDL-C on coronary heart disease than on ischemic stroke. This study was designed to use mendelian randomization to better understand the relationship between LDL-C and the risk of IS as compared to that of CHD.

Data were obtained from participants in the Global Lipids Genetics Consortium, including 188,577 participants of European ancestry. The effects on IS and IS subtypes were examined in METASTROKE, a collaboration of the International Stroke Genetics Consortium, which brings together genome-wide data on a total of 12,389 IS cases and 62,004 controls of European ancestry from across 15 studies. The authors identified 62 genetic variants with genome-wide significant associations with LDL-C. They compared the risk of IS and CHD for each genetic variant.

Those with an LDL–C associated variant, had a 50% higher risk of CHD. The effect of these genetic variances on the risk of IS was weaker, with only a 12% increased risk.

Conclusion: This study suggests that LDL-C has a weaker causal effect on ischemic stroke than on coronary heart disease.

Valdes-Marquez, E., et al. Relative Effects of LDL-C on Ischemic Stroke and Coronary Disease. A Mendelian Randomized Study. **Neurol.** 2019; 92(11): e1176-e1187.

METHOD TO STANDARDIZE BLOOD FLOW RESTRICTION

Blood flow restriction (BFR), in combination with low-load resistance exercise, can allow for strengthening with much lower weights. To restrict blood flow, two common cuffs are employed, including elastic and the traditional pressurized nylon cuff. This study compared the efficacy of these two methods.

Subjects were adults, 18 to 35 years of age, including 16 men and 19 women. The circumference of the mid-upper arm was determined, with the arms randomized to receive compression with either the pressurized or the elastic cuff. Resting arterial blood pressure was measured in both arms for all subjects.

In the pressurized cuff condition, the cuff was inflated to 40% of the resting arterial occlusion pressure for one minute. Blood flow was then measured, followed by inflation to 80%. In the elastic cuff condition, the cuff was applied after reducing its length by 10%, and then 20%, with blood flow measurements made after one minute. In both conditions, blood flow in the brachial artery, distal to the cuff, was quantified using a Logiq E ultrasound apparatus with a high-resolution probe.

The mean differences in blood flow between cuffs were -5.9% for low -pressure and -4% for high pressure ($p=0.5$). When the relative changes in pressures for each cuff were separated by sex, there were no differences in the changes ($p=0.5$).

Conclusion: This study of blood flow restriction exercise techniques found that an elastic cuff can be used as a simple means to apply blood flow restriction at 40% or 80% of the systolic blood pressure.

Abe, T., et al. A Method to Standardize the Blood Flow Restriction Pressure by an Elastic Cuff. **Scand J Med Sci Sports**. 2019, March; 29(3): 329-335.

SENSORIMOTOR CONTROL IN CHRONIC ANKLE INSTABILITY

After a lateral ankle sprain, up to 70% experience instability and recurrent ankle sprain. Previous studies have shown that those with chronic ankle instability (CAI) have increased postural sway, prolonged peroneal reaction time and reduced eversion strength. As these factors are dependent on the central nervous system and reflect impaired sensorimotor integration, this study assessed the spinal reflex excitability, presymptomatic and recurrent inhibition in patients with CAI.

Subjects were 12 individuals with a history of at least one significant, lateral ankle sprain resulting in CAI. Controls were patients with no ankle sprain or with an ankle sprain without feelings of instability. Electromyographic data were taken at the soleus, tibialis anterior and peroneus longus muscles. Soleus H reflex pathway activity was measured during static double and single leg stance. Perception of pain and perceived instability were assessed, with a regression analysis completed.

Compared to that of healthy controls, H2 reflexes for the CAI group were 3.3 times greater during double-leg ($p<0.001$) and 1.6 times greater during single-leg stance conditions ($p<0.001$). Presynaptic inhibition was significantly less in patients with CAI as compared to healthy controls. The soleus spinal reflex excitability was greater in the CAI group ($p<0.001$) than in the controls.

Conclusion: This study of patients with ankle sprains found that those with chronic ankle instability exhibit disinhibition of presynaptic mechanisms, that was not evident among those with ankle sprains that did not develop into CAI.

Thompson, C., et al. Altered Spinal-Level Sensorimotor Control Related to Pain and Perceived Instability in People with Chronic Ankle Instability. **J Sci Med Sport.** 2019, April; 22 (4): 425-429.

SPECIALIST VERSUS NON-SPECIALIST INPATIENT REHABILITATION

Previous studies have demonstrated that, for patients with spinal cord injury (SCI), cerebrovascular attack (CVA) and traumatic brain injury (TBI) properly timed treatment in a post-acute rehabilitation specialty unit can improve outcome. This population-based study examined differences in outcomes among patients admitted to special units (SRUs) versus those who were not.

This retrospective, cohort study examined aggregated data from patients hospitalized for TBI, and SCI recorded by the Australasian Rehabilitation Outcomes Centre Registry Database at four discrete time points, 2007, 2010, 2013 and 2016. These prospectively collected data included length of stay and Functional Independence Measure (FIM) scores. A case mixed adjustment was made, and outcomes were compared between those who were treated in SRUs and those who were treated in non-specialized units.

Over the 10 years of the study, compared to patients admitted to non -SRUs, those admitted to SRUs had a longer onset from injury/illness to rehabilitation admission and lower admission FIM scores, as compared to those in non- SRUs. Patients in both the brain injury and spinal cord injury groups had higher absolute functional gains when treated in SRUs, though with lower FIM score gain per day.

Conclusion: This Australian study of patients hospitalized for brain injury or spinal cord injury found that those treated in specialized rehabilitation units had a lower relative functional efficiency per day in rehabilitation, but a higher percentage of gain on the Functional Independence Measure.

McKechnie, D., et al. A Comparison of Patients Managed in Specialist versus Non-Specialist Inpatient Rehabilitation Units in Australia. **Disabil Rehab**. 2019; Feb. 14: 1-8.

APATHY AND SMALL VESSEL DISEASE

Apathy has been defined as a reduction in goal directed behavior, manifesting in decreased initiative and interest. Those with apathy have decreased quality of life and an increased risk of dementia. This study used structural MRI to better understand the pathology associated with apathy.

Subjects were patients with small vessel disease who had white matter disease or lacunar infarctions and who were free of dementia at recruitment. Of those recruited in 2006, 331 were available for follow-up in 2011. All were assessed with the Apathy Evaluation Scale (AES), with depression measured with the Center for Epidemiological Studies Depression Scale (CES). The participants were divided into four groups based on cutoff scores for the AES and the CES. All underwent MRI, with white matter fibers reconstructed with diffusion tensor tractography (DTI). The Automated Anatomical Labeling (AAL) atlas was used to identify 90 regions of the brain for symptom comparison.

A multiple regression analysis, using demographic and clinical variables correlated with apathy, found that predictors of apathy included global efficiency ($p=0.028$) depression ($p<0.001$), cognition ($p<0.001$), and education ($p=0.024$). Patients with apathy, but not depression, had lesions in five distinct topologic clusters. Controlling for depression, cognition and education, apathy was associated with a single cluster in the bilateral SMA, right SMA and left superior frontal gyrus and left superior frontal to right precentral gyrus.

Conclusion: This study demonstrates that apathy is associated with whole brain network density and efficiency, which could be localized to specific structural areas, including the parietal-premotor, frontal-striatal and occipitotemporal connections.

Tay, J., et al. Apathy is Associated with Large-Scale White Matter Network Disruption in Small Vessel Disease. **Neurol**. 2019, March 12; 92(11):e1157-e1167.

BLOOD NEUROFILAMENT LIGHT CHAIN AS A BIOMARKER OF MULTIPLE SCLEROSIS DISEASE ACTIVITY

As a macroscopic reflection of neural axonal damage, elevated cerebral spinal fluid and blood concentrations of neurofilament light (NFL) chain have been found to correlate with an increased number of relapses in patients with multiple sclerosis (MS). This paper used data from two studies to assess the efficacy of NFL as a biomarker for treatment activity and treatment response in patients with relapsing remitting MS (RRMS).

Patients with RRMS were randomized to receive fingolimod or a placebo in a two-year placebo-controlled trial (FREEDOMS) and a one-year active control (TRANSFORMS) trial, with these data compared to normal controls. Blood samples were used to measure concentrations of NFL before and after treatment, with outcomes compared to NFL levels, clinical outcome and MRI changes.

At baseline, patients had significantly higher NFL concentrations than did healthy controls ($p<0.001$). High baseline NFL concentrations were associated with high T2 lesion volume and the presence of Gd+ lesions. The occurrence of new or enlarging T2 lesions was associated with higher baseline NFL ($p=0.0006$). Fingolimod treatment significantly reduced NFL levels ($p<0.001$). Irrespective of treatment, compared to those with <30pg/ml, patients with NFL concentrations of >60pg/ml at baseline had 2.6 times more new or enlarging T2 lesions, 2.5 times more MS relapses and 2.9 times more brain volume loss ($p<0.001$ for all comparisons).

Conclusion: This study found that NFL levels are associated with clinical and MRI related measures of disease activity.

Kuhle, J., et al. Blood Neurofilament Light Chain as a Biomarker of MS Disease Activity and Treatment Response. **Neurol.** 2019, March 5; 92(10): e1007-e1015.

MIND DIET AND SUBJECTIVE MEMORY

Subjective memory complaints are associated with age, as well as with medications and affective issues. Diets, including the Mediterranean diet (MD) and the Dietary Approaches to Stop Hypertension (DASH) have been associated with better cognitive function. The MIND diet combines elements of the MD and DASH. This study assessed the ability of the MIND diet to retard cognitive deterioration.

This study, the Nutrinet study, a large, observational study beginning in 2009, included adults who completed a survey of sociodemographic economic conditions including physical activity, dietary intake, arthrometric data and health status. All subjects completed a twice yearly, 24-hour, dietary record, with the diet rated for adherence to the MIND diet. Every two years until 2017, the subjects completed a cognitive difficulties scale (CDS), which measured daily deficiencies in attention or memory and subjective memory complaints (SMC). Data for this study were reviewed for those over 60 years of age who had no baseline deficits in subjective memory.

At a mean follow-up of six years, SMCs were noted in 15% of those 60 to 69 years of age and in 30% of those over 70 years of age. Among those in the 60 to 69 years old range, greater adherence to the MIND diet trended toward, but was not significantly associated with, improved SMC. However, for those over 70 years of age, compared to the lowest quartile of adherence, the

highest quartile of the MIND diet adherence had a 31% reduction in the risk of SMC (p=0.04).

Conclusion: This study found that adherence to the MIND diet is associated with a reduction in the risk of cognitive decline among those 70 years of age or older.

Adjibade, M., et al. Prospective Association between Adherence to the MIND diet and Subjective Memory Complaints in the French NutriNet-Sante Cohort. **J Neurol**. 2019, April; 266 (4): 942-952.

THIAMINE LEVEL AND COGNITION IN OLDER HOSPITALIZED PATIENTS

While advancing age is associated with cognitive decline, the magnitude and severity may be dependent on behavior related issues such as nutrition and physical activity. As vitamin B1 (thiamine) plays an important role in the function of the nervous system, this study evaluated the effects of thiamine levels on cognitive function.

This cross-sectional study included the results of routine measurements of whole blood thiamine levels in 233 older patients consecutively hospitalized between January and May of 2018. All subjects were assessed for nutritional status with the Mini Nutritional Assessment-Short Form (MNA-SF) at admission, and were categorized as malnourished (zero to seven points), at risk of malnutrition (eight to eleven points) or as having normal nutritional status (12 to 24 points). Whole blood vitamin B_1 levels <20 ng/mL were considered deficient.

From the MNA-SF 47% were at risk of malnutrition and 39% were malnourished. Frailty was present in 82%, while 36% had impaired cognitive function. The mean whole blood vitamin B_1 for the group was 65.3 ng/mL, within the range of no vitamin B_1 deficiency. Patients with dementia (p=0.040) delirium (p=0.002) or depression (p=0.02) demonstrated lower mean B_1 blood levels compared to patients without. A binary logistic regression analysis found that the major independent risk factors for delirium were whole blood vitamin B_1 (p= 0.01) followed by weight loss in the last three months (p=0.005) and female gender (p=0.03), whereas age was the only significant independent predictor for dementia (p=0.002).

Conclusion: This study of elderly hospitalized patients found that blood thiamine was lower in patients with dementia, delirium and depression, as compared to those without.

Pourhassan, M., et al. Blood Thiamine Level and Cognitive Function in Older Hospitalized Patients**. J Geriat Psychiat Neurol.** 2019; 32(2): 90-96.

DURATION OF SYMPTOMS AND OUTCOME AFTER LUMBAR DECOMPRESSIVE SURGERY

While data support the efficacy of decompression for lumbar spinal stenosis, the point at which conservative treatment should be discontinued and surgical intervention initiated is unclear. This study assessed the association between the duration of symptoms and clinical outcomes in patients undergoing lumbar decompression procedures.

Subjects were consecutive patients undergoing primary lumbar decompression for spinal stenosis between January of 2008 and December of 2015. The patients' average age was 54.1 years and the average duration of symptoms was 19.4 months. All participants had undergone the same conservative protocol, including activity modification, anti-inflammatory medications, physical therapy and injections, for a minimum of three months. All underwent a laminectomy at the symptomatic level.

Repeat surgery occurred in 7.5% of those with pain for less than one year and 7.9% of those with symptoms more than one year. No significant difference on any clinical outcome measure was noted between those with less than one year and those with a longer symptom duration. In addition, there was no difference between groups in reoperation rates.

Conclusion: This study of patients undergoing primary lumbar laminectomy found that the length of the symptoms did not affect the surgical outcome or rate of hospital readmission.

Movassaghi, K., et al. The Duration of Symptoms Does Not Impact Clinical Outcomes Following Lumbar Decompression Surgery. **Spine**. 2019; 44(5): 305-308.

CONCUSSION AND RISK OF SUICIDE

Concussion is a transient disturbance of neurologic function caused by trauma. For 80%, neurologic symptoms resolve within seven days of injury. Systematic reviews have demonstrated that severe traumatic brain injury (TBI) is associated with a higher risk of suicide. This study was designed to determine whether concussion and/or mild TBI is also associated with an increased risk of suicide.

A systematic review and meta-analysis were performed using studies assessing the risk of suicide in patients with concussion or mild TBI. Studies published from 1963 through 2017, were reviewed with 17 chosen for inclusion in the analysis.

Data reviewed in the analysis included over 700,000 individuals diagnosed with concussion and or mild TBI and 6.2 million unaffected individuals. From the analysis, the risk of suicide was twofold higher for those diagnosed with at least one concussion and/or mild TBI compared to those without such a diagnosis (p=0.001). Comparing the risk between civilian and military populations, the risk was found to be higher in the civilian than in the military population (p<0.01).

Conclusion: This literature review and meta-analysis found that, compared to the general population, the risk of suicide doubles among those who have had a concussion or mild traumatic brain injury.

Fralick, M., et al. Association of Concussion with the Risk of Suicide: A Systematic Review and Meta-Analysis. **JAMA Neurol.** 2019, February; 76(2):144-151.

HYALURONIC ACID FOR GLENOHUMERAL OSTEOARTHRITIS

Hyaluronic acid has been studied for the treatment of osteoarthritis of the knee while such use in the shoulder is less clear. This systematic review and meta-analysis was designed to better understand the efficacy of HA for patients with shoulder OA.

A systematic review of the medical literature was completed

(Continued from page 2)

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through January 16, 2018. From this review, 15 were chosen for inclusion, including five randomized controlled trials, six prospective cohort studies, 71 retrospective cohort studies and three case series.

This meta-analysis found that the administration of HA resulted in a significant decrease in VAS pain scores, both at three- and six-months' follow-ups. In studies comparing corticosteroid to HA, studies either found no difference or slightly favored the HA group. Studies found similar improvements between the treatment and control groups

Conclusion: This meta-analysis of studies involving patients with osteoarthritis of the glenohumeral joint found that hyaluronic acid can reduce pain at three and six months, although similar improvement was found in control groups.

Zhang, B., et al. Outcomes of Hyaluronic Acid Injections for Glenohumeral Osteoarthritis: A Systematic Review and Meta-Analysis. **J Shoulder Elbow Surg.** 2019, March; 28(3): 596-606.

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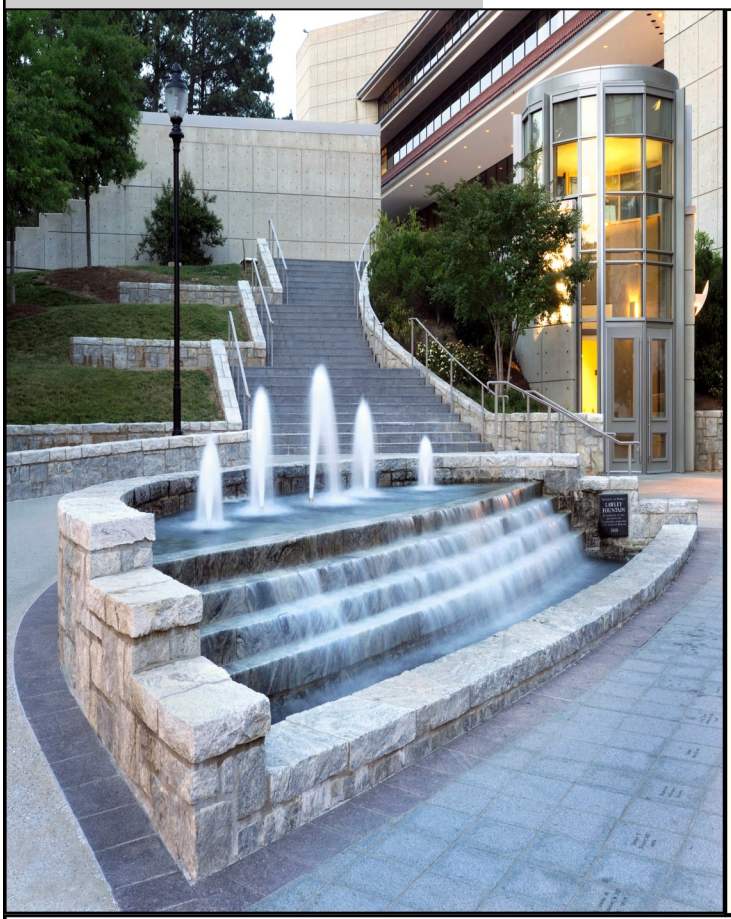

REHAB IN REVIEW

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