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Volume 29 Number 1 | Published by Physicians In Physical Medicine and Rehabilitation | January 5, 2021

HIP EXTENSOR MUSCLE WEAKNESS AND DISABILITY IN EARLY STAGE KNEE OSTEOARTHRITIS

Studies of patients with osteoarthritis (OA) of the knee have shown that knee extensor muscle strength is associated with gait ability and stair ambulation. This study investigated the association between hip extensor muscle weakness and performance of ADLs in patients with early-stage knee OA.

This Japanese study included individuals 65 years of age or older with K/L grade I to II OA of one or both knees. The subjects underwent measurements of ADLs using the Japanese Knee Osteoarthritis Measure (JKOM) and a visual analog scale (VAS) of knee pain. Each also answered questions about the ability to perform stair ambulation, sit to stand motion, and walking on a zero to four scale. All subjects underwent measurements of maximum isometric knee extensor and hip extensor muscle strength. Strength was compared to functional abilities.

Of the 161 participants, those who reported no difficulty performing stair ambulation and sit to stand had significantly stronger knee and hip extensors. The multivariate logistic analysis confirmed that reduced hip extensor muscle strength was significantly associated with a higher presence of difficulty during stair ambulation (OR .33) and sit to stand (OR .32.), but not of walking ability.

Conclusion: This study of elderly Japanese adults with early osteoarthritis of the knee found that hip extensor muscle weakness was significantly associated with difficulty in stair climbing and the ability to perform the sit to stand maneuver.

Shimoura, K., et al. Association between Hip Extensor Muscle Weakness and Disability of Activities of Daily Living in Patients with Early-Stage Knee Osteoarthritis. **Rheumatol Int.** 2020, December; 40(12): 2065-2070.

NEUROFILAMENT LIGHT CHAIN AND PROGNOSIS IN GUILLAIN-BARRE

Neurofilament light chain (NfL) has become an important biomarker of axonal damage. This study assessed the levels of NfL in the serum and cerebrospinal fluid (CSF) of patients with Guillain-Barré syndrome (GBS), to analyze the relationship between baseline levels and outcome at one year.

Data were collected for patients enrolled in a prospective, observational, cohort study which included variants of GBS diagnoses. Patients were included within two weeks of disease onset and compared with age-matched controls. Serum and CSF samples were taken to determine NfL levels at baseline and at 52-week follow-up. A regression was completed to determine the association between levels of NfL and outcome variables.

Data were completed for 90 participants with an average age of 57.4 years. Compared with healthy controls, the mean baseline serum NfL levels were 55.5 in the patients with GBS and 9.83 in controls ($p<0.0001$). This difference was also observed in the CSF ($p=0.034$). Patients with pure motor GBS variant showed higher serum NfL levels than patients with typical GBS ($p=0.025$). Baseline serum NfL levels were higher in patients who were unable to walk independently at one year ($p=0.047$) and in patients unable to run at one year ($p=0.008$). Serum NfL levels lower than 34pg/mL predicted complete recovery, defined as the ability to run at one year.

Conclusion: This study of patients with Guillain-Barre syndrome found that baseline serum levels of neurofilament light can assist in the prognosis of the outcome at one year.

Martin-Aguilar, L., et al. Serum Neurofilament Light Chain Predicts Long-Term Prognosis in Guillain-Barré Syndrome Patients**. J Neurol Neurosurg Psychiat.** 2021, Jan; 92 (1): 70–77.

EGG CONSUMPTION AND CARDIOVASCULAR DISEASE

In 2000, the American Heart Association dietary guidelines recommended that the public consume less than 300 mg per day of cholesterol, to minimize the elevation of blood cholesterol. While one large egg contains 186 mg of cholesterol, recent dietary guidelines no longer provide limits on egg intake. This meta-analysis was designed to help clarify the association between egg consumption and cardiovascular disease.

Data were reviewed for medical publications comparing egg consumption and cardiovascular disease, coronary artery disease, acute myocardial infarction, acute coronary symptoms, stroke, or heart failure. From this literature review, 23 prospective studies were identified with a mean follow-up of 12.28 years. A meta-analysis was completed by combining the findings within the studies.

The pooled subjects were 1,415,839 individuals who experienced 94,975 coronary heart disease episodes, 3,112 heart failure episodes, 19,173 acute myocardial infarctions and 40,064 cases of stroke. There was no significant association between egg consumption and increased rate of overall cardiovascular disease events (hazard ratio (HR) 0.99). Compared with the consumption of zero to one egg per day, higher consumption of eggs per day was associated with a significantly decreased risk of coronary artery disease (HR 0.89). However, the consumption of eggs was not associated with the risk of stroke.

Conclusion: This literature review and meta-analysis found that the consumption of more than one egg per day was associated with a decreased risk of coronary artery disease.

Krittanawong, C., et al. Association between Egg Consumption and Risk of Cardiovascular Outcomes: A Systematic Review and Meta-

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analysis. **Am J Med.** 2021, Jan; 134 (1): 76-83.

BRAIN AGING IN SEPSIS SURVIVORS

Previous studies have demonstrated that survivors of sepsis have an increased risk for long-term cognitive impairment. This study used an analysis of age specific gray matter atrophy across the whole brain to calculate brain age, comparing survivors of sepsis to controls.

This retrospective study included patients with a history of sepsis one year prior to recruitment. All subjects were ventilator dependent for more than 48 hours due to sepsis, suffered from renal failure and needed vasopressors. None of the patients were diagnosed with delirium. All were treated with antimicrobial medication. Each completed a modified form of the informant questionnaire on cognitive decline in the elderly. Those with brain trauma, stroke, Parkinson's disease, or other diseases of the brain were excluded.

At baseline, subjects completed tests of five cognitive domains (alertness, divided attention, selective attention, working memory, and verbal memory). These were combined to create a "cognitive sum score." MRI scanning was completed, with the brain age analysis completed, with the difference between the estimated age and the true chronologic age calculated and labelled as the "BrainAGE." Data from 20 sepsis survivors were compared to those of 40, age-matched, healthy controls.

The BrainAGE of the sepsis survivors was +4.6, while that of the controls was +0.1, demonstrating atrophy 4.5 years beyond that of the controls (p=0.001). A significant, negative correlation was found between the cognitive sum score and the brain age score, indicating that a stronger cognitive impairment was associated with a greater atrophy of the brain (p=0.001).

Conclusion: This pilot study of patients with a history of sepsis one year prior found that the brains of these patients had atrophied at an equivalent to that of 4.5 years of additional aging.

Seidel, G., et al. Accelerated Brain Aging in Sepsis Survivors with Cognitive Long-Term Impairment. **Eur J Neurosci.** 2020, November; 52(10): 4395-4402.

ACUPUNCTURE AND VASOSPASM AFTER SUBARACHNOID HEMORRHAGE

After a subarachnoid hemorrhage (SAH), cerebral vasospasm can result in delayed ischemic neurologic deficit (DIND) in an estimated 50% of cases. As acupuncture has been used in the East for centuries to treat cerebrovascular diseases, this study investigated the efficacy of acupuncture for the prevention of post-SAH cerebral vasospasms.

This randomized, double-blind, placebo-controlled trial included patients hospitalized with SAH. All participants received nimodipine, along with prophylactic therapy and general management. Those randomized to an acupuncture group received 20-minute, daily treatments with electroacupuncture bilaterally at the acupoints PC6 (Neiguan), ST36 (Zusanli), ST43 (Xiangu) and SP4 (Gongsun). The control group received sham acupuncture at the same sites.

The analysis was completed for 22 patients in the acupuncture group and 24 in the control group. A DIND was found in 9.1% of the acupuncture group and 20.8% of the control group (p=0.418). Angiographic vasospasm was detected in 9.1% of the acupuncture group and 25% of the control group (p=0.247). Vasospasm related infarction occurred in 16.7% of the control group and 4.5% of the acupuncture group (p=0.349). Significant changes in the plasma nitric oxide (NO) and endothelin-1 (ET-1) levels were noted at the end of treatment in the acupuncture group, but not in the control group. At long-term follow-up, the modified Rankin Scale (mRS) scores were significantly better in the acupuncture than in the control group (p=0.011).

Conclusion: This pilot study of patients with subarachnoid hemorrhage found that acupuncture treatment was associated with a reduced incidence of delayed ischemic neurologic deficits.

Lee, D., et al. Efficacy of Acupuncture Treatment to Prevent Cerebral Vasospasm after Subarachnoid Hemorrhage: A Double-Blind, Randomized, Placebo-Controlled Trial. **J Altern Complement Med**. 2020; 26(12): 1182-1189.

ACUPUNCTURE AND CORONARY HEART DISEASE

Epidemiological studies have found an association between osteoarthritis (OA) and an increased

risk of developing cardiovascular disease (CHD). As acupuncture has been shown to improve pain and function in patients with OA, this study investigated the effect of acupuncture on the incidence of CHD among patients with OA.

This Taiwanese study randomly sampled the records of one million beneficiaries of the Compulsory National Health Insurance (NIH) program. From the list, individuals were identified with a diagnosis of OA. These patients were further divided as those who also received acupuncture (OA+AP), matched patients who did not receive acupuncture (OA-AP) and a matched non-osteoarthritis (-OA) control group. The primary outcome variable was the development of CHD.

For the 5,046 subjects with OA, 803 were diagnosed with CHD. A Cox proportional hazards regression analysis, after adjusting for gender, age, comorbidities, and drug use, found that the OA-AP group had a greater risk of developing CHD [relative risk (RR) 3.04] as compared with the OA+AP group ($p<0.001$). Also, the –OA group had a 1.88 RR of developing CHD as compared to the OA+AP group ($p<0.001$). The average, daily medical expenditure of hospitalization and outpatient care at five years was significantly greater in the OA-AP group than in the OA+ AP group ($p=0.0001$).

Conclusion: This large-scale investigation of Taiwanese adults found that the risk of coronary heart disease among patients with osteoarthritis was greater than among those without osteoarthritis but was reduced among those who received acupuncture.

Ton, G., et al. Acupuncture Decreased the Risk of Coronary Heart Disease in Patients with Osteoarthritis in Taiwan: A Nationwide, Matched Cohort Study. **J Altern Complement Med**. 2020; doi: 10.1089/acm.2020.0153.

BEETROOT JUICE SUPPLEMENTATION AND MUSCLE POWER

Data have shown that inorganic nitrate (NO3−) increases plasma and muscle nitrite (NO_2−) concentrations which can be further reduced to nitric oxide (NO). This study assessed whether NO_3 − supplementation can enhance power output during concentric (CON) and eccentric (ECC) contractions.

Subjects were 18, active adult males who reported moderate to vigorous-intensity exercise at least three times per week. At baseline lower limb power output was assessed during a half-squat using a flywheel device which allowed participants to maximally complete concentric (CON) and eccentric (ECC) contractions. The subjects were randomized to receive nitrate-rich beetroot liquid (BR), providing 400 mg nitrate/70 mL or a nitrate depleted placebo. These were ingested 2.5 hours before testing to coincide with the peak levels of plasma NO_2. At the time of testing, both groups completed four sets of eight all-out half-squat repetitions, with each set completed with a different moment inertia (0.025, 0.050, 0.075, and 0.100 $kg \cdot m^2$).

Compared to placebo, those in the BR group demonstrated increased mean power (MP) during CON and ECC contractions, at 0.025 and 0.50 $kg \cdot m^2$ ($p<0.001$ for all comparisons), as well as at 0.70 and 0.10 $kg \cdot m^2$ ($p<0.01$ to 0.001 for all comparisons). Similar outcomes were noted for peak power (PP) during CON and ECC contractions ($p<0.01$ to $p<0.001$).

Conclusion: This study found that supplementation with beetroot juice can improve skeletal muscle contractile function.

Rodriguez-Ferandez, A., et al. Beetroot Juice Supplementation Increases Concentric and Eccentric Muscle Power Output. Original Investigation. **J Sci Med Sport.** 2021, Jan; 24(1): 80-84.

CONSUMPTION OF NUTS IN MIDLIFE AND RISK OF COGNITIVE IMPAIRMENT

Previous studies of animals and humans have suggested that nuts may be beneficial for cognition due to the antioxidant, anti-inflammatory, and endothelial vasodilator functions. This study investigated the relationship of nut consumption in midlife to the risk of cognitive impairment in late life.

The Singapore Chinese Health Study involved adult residents of two major dialect groups, the Hokkiens, and the Cantonese. Subjects were recruited between 1993 and 1998 and followed every five years. During the third follow-up visit (2014 to 2016), cognitive testing was completed. Using a 165 item semiquantitative food frequency questionnaire the number of servings per month of nuts was determined.

Data were analyzed for 16,737 participants with an average age of 53.5 years at recruitment and 73.2 years at the time of follow-up cognitive testing. At cognitive testing, 14.3% had cognitive impairment. Compared to those who consumed less than one serving of nuts per month, the odds ratio of cognitive impairment was 0.88 for one to three servings/month, 0.81 for one serving per week, and 0.79 for greater than two servings per week ($p=0.01$). When the data were adjusted for the intake of total unsaturated fatty acids, the association fell to nonsignificance ($p=0.15$).

Conclusion: This large cohort study of Chinese adults living in Singapore found that a higher intake of nuts in midlife was related to a lower risk of cognitive impairment in late life.

Jiang, Y., et al. Consumption of Dietary Nuts in Midlife and Risk of Cognitive Impairment in Late Life: The Singapore Chinese Health Study. **Age Aging**. 2021.afaa267. doi org.proxy.library.emory.edu/10.1093/ageing/afaa267.

VALERIAN ROOT FOR SLEEP DISORDERS

Insufficient sleep leads to reduced stress resilience, decreased quality of life, mood disorders and cognitive, memory and performance deficits. The long-term use of most sedative-hypnotic drugs is limited due to various side effects, such as cognitive and daytime performance impairments. The medicinal use of valerian (V. officinalis) dates to the first century AD. This study evaluated the effectiveness of valerian as a treatment of abnormal sleep and associated disorders.

A literature review was completed for placebo-controlled studies that included V. officinalis treatment. Data included subjective sleep quality improvement, assessed by repeated administration (ranging between five days and eight weeks). The data were compiled, with a meta-analysis completed.

Data were combined from ten studies of subjective sleep quality and included 1,065 subjects. The sleep studies found a benefit in promoting sleep, with a relative risk of 0.35. The multiple active constituents within the supplements used in many of the studies made it difficult to draw strong conclusions. Among those studies that measured anxiety, a positive effect was noted for the whole root as well as the extract.

Conclusion: This meta-analysis of studies of Valerian root found that

this herb is beneficial for assisting with sleep and reducing anxiety.

Shinjyo, N., et al. Valerian Root in Treating Sleep Problems and Associated Disorders - A Systematic Review and Meta-Analysis. **J Evid Based Integr Med**. 2020; 25: 1-31.

TICAGRELOR PLUS ASPIRIN FOR ISCHEMIC STROKE

Two trials have demonstrated that, after a transient ischemic attack (TIA) or minor ischemic stroke, dual antiplatelet treatment can reduce the risk of stroke, myocardial infarction, and vascular death by approximately 30% as compared with aspirin alone. This study, The Acute Stroke or Transient Ischemic Attack Treated with Ticagrelor and Aspirin for Prevention of Stroke and Death (THALES) was designed to understand the factors associated with recurrent, disabling stroke.

Subjects in the THALES trial were 40 years of age or older, had a non-cardioembolic acute ischemic stroke with a National Institute of Health Stroke Scale (NIHSS) score of five or lower or high-risk TIA or ipsilateral atherosclerotic stenosis of 50% or greater. All participants received ticagrelor or a matching placebo every 12 hours for 30 days. In addition, the patients received aspirin at 75 to 100 mg daily. After 30 days, the patients were treated according to the standard of care at the discretion of the investigator and were followed for an additional 30 days. The primary outcome was the time to occurrence of disabling stroke (a modified Rankin Scale (mRS) score of greater than one or death within 30 days).

A primary outcome event at day 30 occurred in 4% of those randomized to ticagrelor and 4.7% of those randomized to placebo (p=0.04). Disability at 30 days, defined as mRS scores of zero or one occurred in 1.3% of the treatment and 1.6% of the placebo group. (p=0.14). The analysis of those patients with recurrent stroke demonstrated less disability at 30 days in the treatment group compared with the control group (p=0.002).

Conclusion: This study of patients with a transient ischemic attack or mild ischemic stroke found that ticagrelor added to aspirin was superior to aspirin alone in preventing stroke or death at 30 days.

Amarenco, P., et al. Ticagrelor Added to Aspirin in Acute Ischemic Stroke or Transient Ischemic Attack in Prevention of Disabling Stroke. A Randomized, Clinical Trial. **JAMA Neurol.** 2020 doi:10.1001/jamaneurol.2020.4396.

BOTULINUM TOXIN FOR DYSTONIC HAND TREMOR

Up to 50% of patients with dystonia have an associated tremor. However, there are few strategies for controlling dystonic tremors. This study assessed the efficacy of botulinum toxin (BoNT) for the control of tremor of the hand.

Subjects were consecutive patients with isolated dystonia and dystonic tremor (DT). From those screened, 15 were randomized to a placebo group and 15 to an active treatment group to receive BoNT, individualized according to tremor severity and the number and size of muscles involved. All were assessed with a structured videotaped neurologic examination to identify the sites and features of dystonia and tremor. The primary outcome variable was tremor, assessed with the Fahn-Tolosa-Marin Tremor Rating Scale (FTM-TRS) at six weeks. Outcome assessments were performed at baseline and at six and 12 weeks after intervention.

Compared to the placebo group, the BoNT group achieved better scores on the FTM-TRS at six ($p<0.001$) and twelve weeks ($p=0.03$). At six weeks, as compared to the placebo group, the BoNT group obtained better scores on the FTM-TRS, part A (tremor severity ($p<0.001$)), FTM-TRS, part B (specific motor tasks ($p<0.001$)) and FTM-TRS upper extremity scores ($p=0.006$). Eight patients (53.3%) in the BoNT group and six (42.8%) in the placebo group reported at least one adverse event. The most frequent was hand weakness, followed by pain.

Conclusion: This randomized, placebo-controlled trial found that botulinum toxin could reduce upper extremity dystonic tremor.

Rajan, R., et al. Assessment of Botulinum Neurotoxin Injection for Dystonic Hand Tremor. A Randomized, Clinical Trial. **JAMA Neurol.** 2020, Dec. doi:10.1001/jamaneurol.2020.476.

CARDIOVASCULAR RISK OF FEBUXOSTAT VERSUS ALLOPURINOL

For the treatment of gout, the most widely used urate-lowering medications are the xanthine oxidase inhibitors, allopurinol, and febuxostat. As previous research suggests that febuxostat may increase the risk of cardiovascular events, this study compared the cardiovascular safety of febuxostat with that of allopurinol.

This prospective trial included 6,051 men with a diagnosis of gout, $\geq$60 years, and with at least one cardiovascular risk factor. The patients were randomly assigned to receive either allopurinol or febuxostat. The medications were adjusted based on urate levels. The primary outcome variable was a composite of hospitalizations for non-fatal myocardial infarction or biomarker-positive acute coronary syndrome, non-fatal stroke, or cardiovascular death over a seven-year period.

The primary event occurred at 1.72 events per 100 patient-years in the febuxostat group and 2.05 events per 100 patient-years in the allopurinol group ($p<0.0001$). Cardiovascular death occurred in 2% of the febuxostat and 2.7% of the allopurinol group ($p=0.018$). All-cause death occurred in 3.5% of the febuxostat group and in 5.7% of the allopurinol group ($p<0.0001$).

Conclusion: This study of patients with gout and at least one cardiovascular risk factor found that those randomized to receive febuxostat had a lower risk of death, cardiovascular death, and hospitalization for nonfatal stroke than those who took allopurinol.

Mackenzie, I., et al. Long-Term Cardiovascular Safety of Febuxostat Compared with Allopurinol in Patients with Gout (FAST): A Multicentre, Prospective, Randomised, Open-Label, Non-Inferiority Trial. **Lancet**. 2020, Nov; 396(10264): 1745-1757.

CEREBELLAR THETA BURSTS FOR STROKE

The cerebellum is a crucial structure involved in balance and motor control. As recent data suggest that cerebellar stimulation may affect cortical spinal excitability, this study of patients with subacute stroke explored the potential benefits of cerebellar intermittent theta burst (iTBS) stimulation using transcranial magnetic stimulation (TMS).

Subjects were adult patients with a stroke at least two weeks from onset. All had motor deficits in the lower limbs, as determined by a score of less than 34 points on the Fugl-Meyer and impaired balance as defined by a score of less than 56 points on the Berg Balance Scale

(BBS). Subjects were randomized to either a sham or treatment group, to receive 50-minute sessions of iTBS of the cerebellum using a transcranial magnetic stimulator, five days per week for two weeks. Sham stimulation was applied at the same location. All subjects underwent standard physical therapy immediately after receiving the sham or active iTBS. The primary outcome measure was the BBS, administrated at baseline and at weeks one and two. Cortical spinal excitability was assessed by the cortical silent period (CSP), resting motor threshold (RMT) and MEP amplitude from the affected side.

At two weeks, compared with controls, the active iTBS group obtained significantly better scores on the BBS ($p=0.045$), and the Trunk Impairment Scale ($p=0.01$). No significant difference between groups was noted on the cortical spinal excitability assessments.

Conclusion: This study of patients with subacute stroke found that intermittent theta burst stimulation using a transcranial magnetic stimulator could improve balance when combined with standard physiotherapy.

Liao, L., et al. Cerebellar Theta Burst Stimulation Combined with Physiotherapy in Subacute and Chronic Stroke Patients: A Pilot, Randomized, Controlled Trial. **Neurorehab Neural Repair.** 2021, January; 35(1): 3-9.

THREE-DIMENSIONAL MAGNETIC RESONANCE SPECTROSCOPY FOR STROKE

After the onset of stroke, MRI with diffusion and perfusion weighting has been used to map ischemic brain tissue damage, and to identify regions of hypoperfusion considered as the salvageable penumbra. However, the accuracy of the observed mismatch is relatively poor. This study assessed the clinical feasibility and efficacy of SPICE (spectroscopic imaging by exploiting spatiospectral correlation) for the identification of ischemic penumbra.

This prospective study included 31 consecutive patients within 24 hours of stroke symptom onset. All underwent an initial MRI scan, repeated at seven to 96 days. High-resolution 3D metabolic imaging was performed with the initial scan using the latest SPICE 1H-MRSI sequence. With an eight-minute scan, the MRSI obtained 3D maps of N-acetylaspartate and lactate levels.

Within the hypoperfused tissue, the lactate signal was higher in areas that ultimately infarcted compared to those that recovered ($p<0.0001$). Both lactate ($p<0.0001$) and N-acetylaspartate ($p<0.001$) differed between infarcted and other regions.

Conclusion: This study of patients with acute ischemic stroke found that using a high-resolution, near whole-brain, 3D magnetic resonance spectroscopy, the lactate signal could separate benign hypoperfusion from the infarct growth region within the area of perfusion-diffusion mismatch.

Yao, L., et al. Fast High-Resolution Metabolic Imaging of Acute Stroke with 3D Magnetic Resonance Spectroscopy. **Brain.** 2020, November;143(11): 3225–3233.

ALLOGENIC GROWTH FACTOR INJECTION FOR PLANTAR FASCIITIS

Plantar fasciitis is usually a self-limiting disease, resolving within 12 months in 90% of patients. Conservative treatments include ice, stretching, night splints, nonsteroidal anti-inflammatory drugs, corticosteroid injections, shockwave therapy and platelet-rich plasma (PRP) injections. The regenerative properties of PRP preparation depend on the amount of growth factors released after platelet activation. This study assessed the effect of lyophilized human platelet growth factors (L-GFs), which were derived from allogeneic pathogen-free platelets.

This prospective study was completed between May of 2017 and November of 2019, involving 150 patients with plantar fasciitis. All participants had failed previous conservative treatment for at least six weeks. They were randomized to a placebo group or an L-GF group. The L-GF was prepared using platelets derived from individual whole blood donations. The patients received a local injection of 3 mL of either the normal saline placebo or the L-GF. The subjects were assessed using the Foot Function Index-Revised Short Form (FFI-R) and a visual analog scale (VAS) for pain. Assessments were completed for up to 12 months post-injection.

At three-month follow-up, the reductions in the mean pain scores were 87% in the L-GF group and 55% in the placebo group ($p<0.001$). Improvements in the FFI-R scores were 62% in the treatment group and 40% in the control group ($p<0.001$).

Conclusion: This prospective study of patients with recalcitrant plantar fasciitis found that allogeneic growth factor injections can improve pain and foot function.

Kandil M., et al. Prospective, Randomized Evaluation of Local Injection of Allogeneic Growth Factors in Plantar Fasciitis. **Foot Ankle Int.** 2020, November; 41(11): 1325-1334.

DRY NEEDLING VERSUS CORTICOSTEROIDS FOR LATERAL EPICONDYLITIS

For persistent lateral epicondylitis, currently used treatments include dry needling (DN) and corticosteroid injections. This study compared the efficacy of these two interventions for the treatment of lateral epicondylitis.

This prospective, randomized, clinical study included patients with lateral epicondylitis for at least three months, all of whom had failed to respond to nonsteroidal anti-inflammatory medications and a forearm brace. The subjects were randomized to receive either dry needling or one injection of 2 mL of Depo-Medrol 40 mg per mL using a 22-gauge needle. The DN treatment included the insertion of 15 stainless steel needles at the lateral epicondyle region and the extensor carpi radialis brevis tendon. The needles were placed to the bone and rotated three or four times and maintained for 10 minutes. The DN was repeated twice weekly for a total of five sessions. The patients were assessed by a blinded rater at baseline and three and 24 weeks after the intervention using the Patient-Rated Tennis Elbow Evaluation (PRTEE).

Data were available for 52 patients in the DN group and 49 in the steroid group. Both groups demonstrated significant improvement from baseline. At week three and week 24, the DN group obtained significantly better PRTEE scores than did the corticosteroid group ($p<0.01$).

Conclusion: This study of patients with lateral epicondylitis recalcitrant to conservative treatment found that dry needling was superior to corticosteroid injections for symptom improvement at both three and 24 weeks.

Uygur, E., et al. The Use of Dry Needling versus Corticosteroid Injection to Treat Lateral Epicondylitis: A Prospective, Randomized, Controlled Study. **J**

Shoulder Elbow Surg. 2021, Jan; 30(1): 134-139.

VASCULAR EFFECTS OF WATER WALKING IN OLDER ADULTS

Endothelial dysfunction is known to occur early in atherosclerotic cardiovascular disease. Exercise training can induce improvements in cardiovascular risk factors, including endothelial function. Studies have demonstrated several benefits of water-based walking on vascular function. This randomized trial examined the effects of a water-based exercise intervention, as compared to those of a land-based intervention on endothelial function.

Subjects were community-dwelling individuals, 50 years of age or older, with less than 60 minutes per week of purposeful physical activity. Those participants were randomized to a non-exercise control (CG) land-based (LB) or water-based (WB) exercise program, three times per week for 24 weeks. The exercise intervention progressed to 50 minutes at a heart rate reserve of 55 to 65%. Water exercises occurred at a depth reaching the xiphoid process. Brachial artery endothelial function (flow-mediated dilation; FMD) and smooth muscle cell function (glyceryl trinitrate administration) were tested before (week zero) and after (week 24) the intervention.

The FMD increased in the LW group but decreased in the CG group (p= 0.035). The FMD difference between the WB and the CG failed to reach significance (p=0.79). Compared to the WB group, the FMD change was superior in the LB group (p=0.009).

Conclusion: This study of individuals 50 years of age or older found that walking on land may be superior to walking in water for the improvement of endothelial function.

Haynes, A., et al. Effects of Land versus Water Walking Interventions on Vascular Function in Older Adults. **Med Sci Sports Exer**. 2021 Jan; 53(1): 83-89.

TRANSCRANIAL DIRECT CURRENT STIMULATION EFFECTS ON GABA AND DOPAMINE

Transcranial direct current stimulation (tDCS) to the dorsolateral prefrontal cortex (DLPFC) has attracted attention as a treatment for neuropsychiatric disorders, Alzheimer's disease, and depression. This study investigated the tDCS-induced changes in dopamine and γ-aminobutyric acid (GABA) levels in the brain.

This randomized, sham-controlled, double-blind, crossover study included 17, healthy, right-handed Japanese men 20 to 26 years of age. An active group received 26 minutes of tDCS with a current intensity of 2 mA, applied to the DLPFC. Within 140 minutes of the stimulation, positron emission tomography (PET), magnetic resonance imaging (MRI) and GABA-magnetic resonance spectroscopy (MRS) were performed. At least one month later, the participants crossed to the other group, receiving either sham or active tDCS. Spectroscopy measurements with the MEGA-PRESS sequence were used for detecting GABA and other brain metabolites.

After active tDCS with the anode over the left DLPFC, GABA was elevated in the left striatum and moderately reduced in the right striatum. Also, GABA was reduced in the left DLPFC. PET analysis demonstrated that, after tDCS, reductions were found in [11C]-raclopride binding potentials (increases in dopamine release) in the right striatum which were inversely correlated with those in the left striatum.

Conclusion: This study demonstrated that tDCS with the anode over the left DLPFC and the cathode over the right DLPFC, caused significant increases in dopamine release in the right striatum and GABA concentrations in the left striatum, suggesting that tDCS can modulate the monoaminergic systems in the deep brain structures.

Bunai, T., et al. tDCS -Induced Modulation of GABA Concentration and Dopamine Release in the Human Brain: A Combination Study of Magnetic Resonance Spectroscopy and Positron Emission Tomography. **Brain Stim**. 2021, January-February; 14 (1): 154-160.

TRANSCRANIAL DIRECT CURRENT STIMULATION AND SJOGREN'S SYNDROME

Primary Sjögren's syndrome (pSS) is the second most common autoimmune disease. Fatigue affects between 67% and 85% of these patients. As transcranial direct current stimulation (tDCS) has shown promise for reducing fatigue in patients with multiple sclerosis, this study investigated the effect of tDCS on fatigue among patients with pSS.

This parallel, randomized, sham-controlled, double-blind study included women between the ages of 18 and 65, all diagnosed with pSS and scoring greater than five on the Fatigue Severity Scale (FSS). A structured interview was used to collect demographic and biomedical information at baseline. Subjects were randomized to receive five sessions of sham tDCS or tDCS, with a constant current intensity of 2 mA for 20 min/day. Outcome measures were assessed at baseline (T1), after five tDCS sessions (T2) and then 15 days (T3) and 30 days (T4) after the end of tDCS sessions. The primary outcome measure of fatigue severity was documented by using the FSS. As a secondary measure of Sjögren-specific symptoms of fatigue, pain, and dryness, subjects used the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI).

Data were completed for 36 participants. Improvements in the FSS were significantly greater in the treatment group than in the sham group at T2 and T4. These improvements were larger than the clinically important difference of 0.6 determined for the FSS in patients with systematic lupus erythematosus.

Conclusion: This study of female patients with primary Sjögren's syndrome found that transcranial direct current stimulation could be useful for the treatment of fatigue. One month after the tDCS protocol was completed (T4), the active group showed significantly greater reductions in pain as measured by the ESSPRI.

Pinto, A., et al. Transcranial Direct Current Stimulation for Fatigue in Patients with Sjögren's Syndrome: A Randomized, Double-Blind, Pilot Study. **Brain Stimul.** 2021, January-February: 14 (1): 141-151.

GREATER OCCIPITAL NERVE STIMULATION AND ASSOCIATIVE MEMORY

Recent trials involving vagus nerve stimulation have shown that improvements in associative memory occur via the ascending fibers of the vagus nerve that synapse with neurons in the nucleus of the solitary tract (NTS). These project to the locus coeruleus (LC) and promote noradrenaline (NA) release, which plays a key role in driving neuroplasticity and related memory processes (the LC-NA pathway). This study assessed the efficacy of tDCS

for improving associative memory, and the effect of tDCS on NA release.

Subjects were thirty healthy adults who were randomized to a sham tDCS group (S-tDCS) or an active tDCS (A-TDCS) group. The A-tDCS group received a constant current of 1.5 mA intensity during each of the three-study phases (250 seconds × 3 blocks) with electrodes placed over the left and right C2 dermatomes. All subjects underwent a wide range of mood, executive function, and memory tests.

The subjects performed the Swahili-English Word Association Task, during which they were asked to learn 50 Swahili English word pairs across a total of three blocks of study (S) and test (T) phases. Saliva was collected to assess changes in alpha-amylase, a biomarker for NA, before, immediately after, and at seven and 28 days after stimulation.

Compared to the S-tDC group, more words were correctly recalled by the A-tDCS group at seven and 28 days. In addition, α-amylase levels in the A-tDCS group demonstrated a greater increase immediately after stimulation ($p<0.001$) and at seven ($p<0.001$) and 28 ($p=0.007$) days. No effect was noted for cortisol levels.

Conclusion: This study found that transcranial direct current stimulation of the greater occipital nerves improved associative memory.

Luckey, A., et al. Greater Occipital Nerve Stimulation Boosts Associative Memory in Older Individuals: A Randomized Trial. **Neurorehab Neural Repair.** 2020, November; 34 (11): 1020-1029.

DORSAL ATTENTION NETWORK AND MEMORY AFTER BRAIN INJURY

After a traumatic brain injury (TBI), episodic memory (the ability to remember discrete events), is impaired. This study investigated memory network function in patients with TBI, with and without episodic memory impairment.

Subjects were 35 patients with TBI and a mean of 127 months since the injury, matched to healthy controls. All underwent a detailed neuropsychological battery to assess cognitive function. Also, all underwent a memory task, reviewing a series of abstract art images while undergoing a functional MRI. A diffusion analysis was also used, with FA values extracted. For each task, the white matter that was specifically related to the task was used to create a structural connectome of the underlying white matter architecture.

Healthy controls performed the memory task with 72.5% accuracy, while patients with TBI scored 64.9% accuracy. Those with TBI who were in the lower half of memory scores (impaired memory (IM)), were compared with those with normal memory (NM). The IM patients showed impairments in intellectual ability ($p<0.001$), processing speed ($p<0.001$) executive function ($p=0.005$), and verbal [immediate ($p=0.003$); delayed ($p<0.001$)], associative [immediate ($p=0.017$); delayed ($p=0.004$)] and visuospatial memory [immediate ($p<0.001$); delayed ($p=0.001$)] compared to healthy controls. The IM patients were also impaired relative to the NM TBI group in intellectual ability ($p=0.005$), executive function ($p=0.011$), associative memory [immediate ($p=0.017$); delayed ($p=0.004$)] and visuospatial memory [immediate ($p< 0.001$); delayed ($p=0.006$)]. In contrast, NM patients were impaired compared to controls only in processing speed ($p=0.003$). Compared to the IM group, the NM group showed greater activation in the right precuneus, right intraparietal sulcus, left inferior temporal gyrus, and bilaterally in the temporal-occipital fusiform cortex, PHG, and lingual gyrus.

Conclusion: This study of patients with traumatic brain injury demonstrates a relationship between abnormal activation of functional networks during encoding and specific areas of damage.

Mallas, E., et al. Abnormal Dorsal Attention Network Activation in Memory Impairment after Traumatic Brain Injury, **Brain.** 2020 awaa380, https://doi-org.proxy.library.emory.edu/10.1093/brain/awaa380

LUMBAR DISC HERNIATION TREATMENT WITH MICRODISCECTOMY VERSUS ENDOSCOPIC DISCECTOMY

For lumbar disc herniation (LDH), open lumbar microdiscectomy (OLMD) has become the gold standard among surgical treatments. As this surgery can result in muscle damage and requires partial laminectomy and nerve retraction, percutaneous endoscopic lumbar discectomy (PELD) was introduced as an alternative. This study compared the outcomes of patients treated with these two surgeries.

This retrospective, matched cohort analysis included patients with LDH treated with PELD or OLMD. The groups were matched for age, disc herniation level, and characteristics. Patients were asked to complete a 10-point visual analog scale (VAS) for lower back pain preoperatively, on postoperative day one, and at each follow-up visit.

Data were completed for 29 consecutive patients undergoing PELD for a single level unilateral LDH, and 29 patients undergoing OLMD. The day after surgery, the VAS scores for LBP and leg pain were better in the PELD group ($p=0.01$ and $p=0.06$, respectively) Three months after surgery, the VAS scores for low back pain remained better in the PELD group ($p=0.026$). At 12 and 24 months after surgery, the VAS pain scores did not significantly differ between the groups. The mean lengths of hospital stays were 2.55 in the PELD group and 3.21 in the OLMD group ($p=0.037$).

Conclusion: This study of patients with lumbar disc herniation found that, compared with open lumbar microdiscectomy, those treated with percutaneous endoscopic lumbar discectomy had a more rapid recovery and earlier reductions in low back pain.

Jarebi M., et al. A Matched Comparison of Outcomes between Percutaneous Endoscopic Lumbar Discectomy and Open Lumbar Microdiscectomy for the Treatment of Lumbar Disc Herniation: A Two-Year, Retrospective, Cohort Study. **Spine.** 2021 Jan; 21(1): 114-121.

NUSINERSEN FOR MOTOR FUNCTION IN ADULT SPINAL MUSCULAR ATROPHY

Spinal muscular atrophy (SMA) is an autosomal recessive, lower motor neuron disease causing progressive muscular atrophy and weakness. Nusinersen is an antisense oligonucleotide administered intrathecally and able to modify the pre-mRNA splicing of survivor motor neuron 2 (SMN2) increasing functional SMN protein levels. This study investigated the efficacy of this medication on the motor function of patients with SMA2 and SMA3.

This retrospective study included patients with a diagnosis of SMA2 or SMA3 treated with Nusinersen after the age of 18 years. All were treated with intrathecal loading of 12 mg at baseline, and then at day 14, 20 and

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63 followed by maintenance doses every four months. Clinical assessments of motor function and safety data were collected at each injection interval. The primary outcome the Hammersmith Functional Rating Scale Expanded (HFMSE), the revised upper limb module, and the 6-minute walk test. Secondary outcomes included timed function tests and pulmonary function tests.

The mean age at onset of the 116 patients was three years. The HFSME score in SMA3 increased from baseline by a median of one point at T6 ($p<0.0001$), two points at T10 ($p<0.0001$), and three points at T 14($p<0.0001$), This was not true for the SMA2 group. The 6-minute walk test distance increased significantly at T6, T10 and T14. The number of patients with clinically significant improvement increased from 53% at T6 to 69% at T14.

Conclusion: This study of patients with spinal muscular atrophy supports the safety and efficacy of nusinersen, particularly for adult patients with SMA3

Maggi L, Bello L, Bonanno S, *et al.* Nusinersen Safety and Effects on Motor Function in Adult Spinal Muscular Atrophy Type 2 and 3 **J Neurol, Neurosurg Psych.** 2020, November;91:1166-1174.

***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