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MECHANICAL THROMBECTOMY FOR PATIENTS WITH NIHSS SCORES OF LESS THAN SIX

In 2015, five, randomized, controlled trials supported mechanical thrombectomy (MT) as superior to medical therapy among patients with ischemic stroke (IS) due to large vessel occlusion (LVO). Current guidelines recommend this therapy only for those with National Institute of Health Stroke Scale (NIHSS) scores of six or higher. This study evaluated the safety of MT in patients with NIHSS scores of less than six.

Retrospective data were obtained from a prospectively maintained database of patients treated for an acute ischemic stroke (AIS) due to an anterior circulation LVO who presented with an NIHSS score of less than six. These patients were compared to an equal number of controls. The study's primary outcomes included the efficacy and safety of this procedure, with efficacy assessed as functional improvement with the 90-day modified Rankin Scale (mRS).

Of the 83 eligible patients, 49% underwent MT with medical management (MT+) and 51% received medical management alone (MM-). A good outcome (mRS of 0-2) occurred in 72% of the MT+ group and 62% of the MM- group (p=0.42). Symptomatic intracerebral hemorrhage occurred in two patients in the MT+ group and one patient in the MM- group. Mortality was two percent in the MM+ group and 14% in the MM- (p=0.05). Infarct size averaged 9.3 mm in the MT+ group and 14.6 mm in the MM- group (p=0.08).

Conclusion: This study of patients with a stroke due to a large vessel occlusion found that, among those admitted with an NIHSS score of less than six, those who were treated with a mechanical thrombectomy had reduced mortality.

Abbas, R. et al., Mechanical Thrombectomy in Patients Presenting with an NIHSS Score Less than Six: A Safety and Efficacy Analysis. **J Stroke Cerebrovasc Dis.** 2022, March; 31 (3). 106272.

HUMAN MOTOR CORTEX PLASTICITY BY TRANSCRANIAL ULTRASOUND STIMULATION

Long-term potentiation and depression-like plasticity can be induced with noninvasive brain stimulation, such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS). An emerging method of peripheral stimulation involves transcranial ultrasound stimulation (TUS). This technology can target deep brain areas with millimeter spatial precision by focusing the propagation of acoustic waves onto a selected focal area. This study was designed to develop a TUS protocol to effectively induce brain plasticity in human subjects.

Subjects were 20, right-handed, healthy adults. The motor representation of the right first interosseous (FDI) muscle in the left motor cortex was identified by TMS and was then used as the location for TUS stimulation. To measure the changes in motor cortical excitability, motor evoked potentials (MEPs) of the right first dorsal interosseous muscle were recorded. Each subject was exposed to one of three conditions. These included tbTUS (an 80-second train of 20-millisecond ultrasound bursts, repeated every 200-milliseconds), rTUS (500-millisecond bursts every 1.6 seconds, for a total of 80 seconds), and sham TUS. Changes in MEPs and a visuomotor task were assessed at baseline and at five, 30, and 60 minutes.

The tbTUS produced a consistent increase in corticospinal excitability for at least 30 minutes, whereas rTUS and sham tbTUS produced no significant change. The mean percentage changes in MEP amplitude were 43.1% at five minutes and 27.5% at thirty minutes. The tbTUS resulted in a decrease in movement time during a visuomotor task (p=0.024).

Conclusion: This study found that theta-burst transcranial ultrasound stimulation can induce cortical plasticity in humans.

Zeng, K., et al., Induction of Human Motor Cortex Plasticity by Theta Burst Transcranial Ultrasound Stimulation. **Ann Neurol.** 2022, February;91 (2):238-252.

PNEUMONIA AFTER STROKE

Approximately 30% of patients develop an infection in the first days after stroke, of which one third are pneumonias. This study assessed the temporal profile of pneumonia in a large number of patients hospitalized with acute stroke, and its relationship with outcome.

This retrospective study analyzed prospectively collected patient data from the acute ischemic stroke and intracerebral hemorrhage databases of the VISTA (Virtual International Stroke Trials Archive). The date of onset of pneumonia was defined as the start date indicated on a serious, adverse event (SAE) report. The occurrence of pneumonia or urinary tract infection (UTI) were summarized for the first 90 days after stroke.

Data were completed for 10,021 patients, enrolled in nine, randomized studies between 1995 and 2013. The subjects' mean age was 71 years. The cumulative incidence of pneumonia in the first 90 days was 9.4%. The median time of pneumonia onset was four days after stroke onset. Those with NIHSS scores of >12 had pneumonia earlier than did those with more severe strokes (p=0.02). The median day of UTI onset was six days. Of those with pneumonia after stroke, 47.8% died within 90 days, as compared to 14.7% of those without pneumonia (p<0.001).

Conclusion: This study, using data from a large international database, found that 9.4% of patients hospitalized with a stroke contracted pneumonia in the first 90 days, with nearly 2/3 occurring in the first week.

De Jonge, J., et al. Temporal Profile of Pneumonia after Stroke. **Stroke.** 2022, January; 53 (1): 53-60.

SYSTEMIC INFLAMMATION AND RECOVERY FROM ACUTE LOW BACK PAIN

Recurrence and persistence of low back pain (LBP) are major health issues. A growing body of research points to the involvement of systemic inflammatory responses in many chronic pain conditions, including LBP. This study assessed the association between inflammatory profiles and LBP outcome.

This twelve-month, longitudinal, cohort study included adults with episodes of LBP. The patients completed questionnaires related to LBP, general health, demographics, psychological status, and sleep behavior within 24 hours of providing a blood sample. The participants returned for follow-up blood sampling at three, six and nine months, and reported their "average" levels of LBP (NRS) and LBP-related disability on the Roland Morris Disability Questionnaire (RMDQ). Patients were also assessed for depressive symptoms, pain catastrophizing, fear avoidance beliefs and sleep. Blood was drawn to quantify levels of inflammation, including CRP, TNF, IL-6 and IL-1β. Four clusters were then constructed, including: "inflammatory (high CRP and IL-6) and poor sleep" (Cluster I), "high TNF and depression" (Cluster II), "high pain and high pain-related fear" (Cluster III) and "low pain and low pain-related fear" (Cluster IV).

Pain improvement from baseline was greatest among patients in Cluster I and was significantly better than Cluster II at months three ($p=0.017$) and six ($p=0.044$). At nine months, Cluster IV reported more recovery than Cluster II ($p=0.034$).

Conclusion: This study found that individuals with high baseline levels of CRP and IL-6 recover best from low back pain, while those with high tumor necrosis factor and depressive symptoms demonstrate the worst recovery.

Klyne, D., et al. Relationship between Systemic Inflammation and Recovery over 12 Months after an Acute Episode of Low Back Pain. **Spine J**. 2022, February; 22(2): 214-225.

TAMARINDUS INDICA FOR OSTEOARTHRITIS OF THE KNEE

Previous studies have suggested that *Tamarindus indica (T. Indicia),* combined with an aqueous ethanol extract of *Curcuma longa* rhizome, may mitigate against knee pain among patients with osteoarthritis (OA). This prospective study evaluated the clinical efficacy of *T. indica* combined with *C. longa* for the treatment of patients with OA of the knee (KOA).

Subjects were 96 patients between 40 and 70 years of age with mild-moderate KOA, randomized to one of three groups. These were placebo, NXT15906F6 (250mg) and NXT19185 (300mg) groups. The NXT15906F6 contained six parts *T. indica* seed extract and 3 (w/w) parts *C. longa* rhizome extract. The NXT19185 contained five parts NXT15906F6 and one part *G. mangostana* fruit rind. All groups received one capsule per day. Blood was drawn to measure proinflammatory cytokines and chemokines. The primary outcome was the improvement in the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) scale score.

From baseline to follow up, WOMAC total scores in the NXT15906F6 and NXT19185 groups were reduced by 41.86% ($p<0.05$) and 56.17% ($p<0.05$), respectively. The mean visual analog scale (VAS) of pain scores in NXT15906F6 and NXT19185 groups improved by 42.60% and 54.17% ($p<0.05$ for both) and were superior to placebo ($p<0.05$ for both). Serum proinflammatory cytokines and chemokines were significantly decreased in both treatment groups. Both treatment groups demonstrated improvement in performing functional tasks. Both demonstrated decreased levels of uCTX-II, a cartilage degradation marker.

Conclusion: This 56-day study of patients with mild to moderate OA of the knee found that once daily ingestion of *Tamarindus indica* and *Curcuma longa* rhizome could improve symptoms and function.

Kare, S., et al. *Tamarindus indica* Seed Extract-Based Botanical

Compositions Alleviate Knee Pain and Improve Joint Function in Mild-to-Moderate Osteoarthritis: A Randomized, Double-Blind, Placebo-Controlled, Clinical Study. **Evid Based Compl Alt Med.** 2022. https://doi.org/10.1155/2022/2226139.

AUTOANTIBODIES IN IDIOPATHIC SMALL FIBER NEUROPATHY

Small fiber neuropathy (SFN) is a heterogeneous disease characterized by pain, dysesthesia, and autonomic dysfunction, exclusively involving small nerve fibers. While diabetes and B-12 deficiency are common causes of SFN, 50% remain undiagnosed. As several studies have suggested an autoimmune etiology, this study used a novel autoantibody technology to identify putative autoantibodies associated with SFN.

Subjects were 59, adult patients with neuropathic pain and/or autonomic symptoms and a diagnosis of SFN. Healthy subjects were matched for age and gender. Peripheral blood samples (3ml) were collected from each subject and screened against >1,600 immune-related antigens and for inflammatory markers (ESR, ANA, anti-ENA, ANCA).

Of the 58 patients, SFN was confirmed in 74.1%. Positive autoimmunity, as defined by an ANA of 1:80 or greater, high ESR and presence of anti-ENA or ANCA, was found in 29.3%. Proteomic data showed 11 autoantibodies that were statistically significant ($p<0.05$) when compared to those of controls. Three proteins showed consistently high-fold changes in main and validation cohorts. These were MX1 ($p=0.003$), DBNL ($p=0.009$) and KRT8 ($p=0.043$).

Conclusion: This study of patients with small fiber neuropathy supports the hypothesis that an immune-mediated process may be involved.

Chan, A., et al. Novel Autoantibodies in Idiopathic Small Fiber Neuropathy. **Ann Neurol**. 2022, Jan; 91: 66-77.

VITAMIN K_2 AND D_3 AND SPINE FUSION OUTCOME IN PATIENTS WITH OSTEOPOROSIS

As spine fusion depends on the quality and quantity of bone available for harvest, researchers have sought adjunctive treatments to enhance union at the surgical site. As vitamin K_2 and vitamin D_3 are successful as anti-osteoporotic medications, this study assessed the effect of these vitamins on osseous union after spinal fusion surgery.

This prospective, randomized trial included patients with neurologic symptoms due to lumbar degenerative disease who had low bone mass or osteoporosis. Both the control and the treatment group received calcium 1.2 g per day and vitamin D_3, 250 units. The treatment group also received K_2, 45 mg/day. Fusion was assessed by CT at three to six months. A complete intervertebral osseous union was defined as grade I, whereas an incomplete intervertebral fusion was assessed as grade II or III. Clinical outcomes were assessed with the Japanese Orthopedic Association Back Pain Evaluation Questionnaire (JOA-BPEQ).

Data were complete for 35 patients in the control group and 34 patients in the treatment group. At three months, complete union was found in 88.24% of the treatment group and 68.57% of the control group ($p=0.048$). At six months, these rates were 91.18% and 71.43%, respectively ($p=0.036$). Both groups improved in JOA-BPEQ scores, with no significant difference between the two.

Conclusion: This study of patients with osteoporosis undergoing spinal fusion found that daily ingestion of vitamin K_2 and vitamin D_3 could improve post-surgical fusion more than vitamin D_3 alone.

Zhang, W., et al. Concurrent Treatment with Vitamin K_2 and D_3 on Spine Fusion in Patients with Osteoporosis-Associated Lumbar Degenerative Disorders. **Spine.** 2022, February 15; 47(4): 352-360.

ASSESSING ALCOHOL-RELATED POLYNEUROPATHY WITH MRI

Alcohol-related polyneuropathy (ALN) is the second most common polyneuropathy in the United States. As high-resolution magnetic resonance neurography (MRN) can directly visualize peripheral nerve lesions *in vivo*, this study of alcohol dependent patients (ADP) assessed the efficacy of MRN in the diagnosis of ALN.

This prospective, case control study included 31 consecutive alcohol dependent patients (ADP) and age and gender matched, healthy controls. These were divided into ADP with alcohol-related polyneuropathy (+ALN) and without ALN (Non-ALN). A history and physical was completed including the Total Neuropathy Score (TNS), the Neuropathy Disability Score (NDS), the Neurological Severity Score (NSS) and the Neuropathy Impairment Score of the Lower Limbs (NIS-LL). Motor nerve conduction studies determined distal motor latencies (DML), compound muscle action potentials (CMAP), nerve conduction velocities (NCV) and F waves. MRN exams were used to quantify nerve injury by morphometric cross-sectional area (CSA) and microstructural markers.

The MRN detected nerve damage in ADP with and without ALN. All MRN markers differentiated between ADP subjects and controls. In addition, microstructural markers were able to differentiate between subgroups. Compared to controls, the tibial nerve proton spin density at thigh level was increased in +ALN ($p<0.0001$) and in Non-ALN ($p<0.0052$). The T2 relaxation time was higher in the ALN group compared with controls ($p<0.0001$) and compared to those without ALN ($p=0.0214$).

Conclusion: This study demonstrated that magnetic resonance neurography can detect and quantify peripheral nerve damage in alcohol dependent patients, even in the absence of a formal diagnosis of alcohol related polyneuropathy.

Rother, C., et al. Characterization and Quantification of Alcohol-Related Polyneuropathy by Magnetic Resonance Neurography. **Euro J Neurol.** 2022, February; 29 (2): 573-582.

ORAL MICROBIOME THERAPY FOR RECURRENT CLOSTRIDIOIDES DIFFICILE

Clostridioides difficile (*C.Diff*) infection is estimated to be associated with 20,000 deaths annually in the United States. While vancomycin and fidaxomicin kill toxin-producing *C.Diff* bacteria that cause colonic inflammation, these medications do not kill the spores which can rapidly germinate after treatment discontinuation. As fecal microbiota transplantation for

recurrent *C.Diff* has been effective, this study assessed an oral microbiome therapeutic composed of live, purified *Firmicutes* bacterial spores (SER-109).

This double-blind, placebo-controlled trial included adults with three or more episodes of *C.Diff* within 12 months. The patients were randomized to receive a placebo or a capsule containing SER-109 (approximately 3×107 spore colony-forming units) once daily over three, consecutive days. The subjects were monitored for the occurrence of three or more unformed bowel movements over two consecutive days and a positive *C Diff* stool toxin assay. Stool specimens for whole metagenomic sequencing and targeted bile-acid analyses were obtained at baseline and at weeks one, two and eight.

Data were completed for 149 patients with a mean age of 65.5 years. The percentages of patients with *C.Diff* recurrence were 12% in the treatment group and 40% in the control group (p<0.001). Of the 40 recurrences, 75% occurred within two weeks. No serious adverse events related to the treatment were observed through the eight weeks of the study.

Conclusion: This study of patients recurrently infected with *Clostridioides difficile* found that three days of treatment with purified *Firmicutes* spores can significantly reduce the rate of recurrence.

Feuerstadt, P., et al. SER-109, an Oral Microbiome Therapy for Recurrent *Clostridioides Difficile* Infection. **N Eng J Med**. 2022, January 20; 386(3): 220-229.

DISEASE FLARE IN PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES FOLLOWING COVID VACCINATION

In December of 2020, messenger RNA COVID-19 vaccines (mRNA-1273 and BTN 162b2) were recommended for use by the Advisory Committee on Immunization Practices. Patients with rheumatic and musculoskeletal diseases (RMDs) were not well represented in the vaccine trials, with many hesitant to accept vaccination. This study evaluated disease flare and reactogenicity in individuals with RMDs.

This prospective, observational study included adults with RMD who were receiving immunomodulatory therapy and who received the SARS-CoV-2 mRNA vaccine between December 16, 2020, and April 15, 2021.

A medical history was obtained, including RMD diagnosis, immunomodulatory regimen, and prior SARS-CoV-2 diagnosis. An online questionnaire was distributed seven days after each vaccine dose, wherein participants answered questions concerning local and systemic adverse events. One month after dose two, the subjects completed an online questionnaire about the incidence and prior history of flare and incident flare, as well as symptoms, duration, and treatment.

A total of 1,377 patients with RMD underwent vaccination with BNT162b2 (55%) or mRNA- 1,273 (45%). Of these, 151 (11%) reported flares after vaccination, of which 60% occurred after the second dose. The rate of flares requiring treatment was similar in both vaccine types. Of those treated for the flare, the duration of treatment for the flare averaged 10 days.

Conclusion: This study of 1,377 patients with rheumatic and musculoskeletal diseases who received two doses of Covid vaccinations found that flares of their disease were rare, with none requiring hospitalization.

Connolly, C., et al. Disease Flare and Reactogenicity in Patients with Rheumatic Musculoskeletal Diseases following Two-Dose SARS-Cov-2 Messenger RNA Vaccination. **Arth Rhematol.** 2022, January; 74(1): 28-32.

MIDODRINE TO PREVENT VASOVAGAL SYNCOPE

There is little high-quality evidence for the efficacy of medications for the treatment of vasovagal syncope. Midodrine, an alpha-1 adrenergic receptor agonist and direct vasoconstrictor has been proposed as a potential treatment, although no high-quality studies have demonstrated its efficacy. This clinical trial assessed the efficacy of midodrine to prevent recurrence of vasovagal syncope.

Eligible patients were 18 years of age or older with a Calgary Syncope Symptom score of at least two, and had fainted at least twice in the year before enrollment. The patients were assigned in a double-blinded fashion to receive either placebo or midodrine at a dose of 2.5 mg twice daily up to 10 mg three times daily. The primary outcome variable was the number of episodes of syncope over one year.

At baseline, the subjects reported a median frequency of 4.1 syncopal episodes per year, with a median of six episodes in the year before randomization. At one year, the midodrine group reported 73 syncopal episodes and the placebo group reported 146 episodes. Compared with patients receiving placebo, fewer patients receiving midodrine had at least one syncope episode (p=0.035). A recurrent syncopal episode occurred in 42% of the midrodine and 61% of the placebo group.

Conclusion: This study of young, healthy patients with recurrent vasovagal syncope found that oral midodrine can significantly reduce the risk of recurrent syncope.

Sheldon, R., et al., Midodrine for the Prevention of Vasovagal Syncope. A Randomized, Clinical Trial. **Ann Intern Med.** 2021, October; 174(10): 1349-1356.

MEDICAL OUTCOME 10 YEARS AFTER ARTHROSCOPIC CORRECTION OF FEMORAL ACETABULAR IMPINGEMENT

Femoroacetabular impingement (FAI) is a bony deformity of the hip joint which can obstruct movement of the femoral head. This study reports on the 10-year survivorship and clinical outcomes of patients who underwent hip arthroscopy for symptomatic FAI.

Patients diagnosed with FAI, referred for surgical intervention, underwent arthroscopic surgical repair. All were assessed at baseline and at 10-year follow up using the modified Harris Hip Score (mHHS), the University of California Los Angeles (UCLA) Activity Scale, the 36 -Item Short Form Health Survey (SF-36) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).

Of the 138 cases, 86% were followed for a minimum of 10 years. Of these, 8.4% were converted to total hip replacement at an average of 6.4 years, and 10 required repeat hip arthroscopy at an average of 2.3 years. Significant improvements were noted at 10 years in scores on the mHHS, SF-36 and WOMAC, with high satisfaction noted.

Conclusion: This follow-up study of patients with femoral acetabular impingement found that arthroscopic surgery could produce significant functional improvement, with high satisfaction at 10 years.

Carton, P. et al., Survivorship Rate and Clinical Outcomes 10 Years after Arthroscopic Correction of Symptomatic Femoral Acetabular Impingement. **Am J Sports Med**. 2022, January; 50 (1): 19-29.

ZHENGQING FENGTONGNING FOR KNEE OSTEOARTHRITIS

Sinomenine is a monomer alkaloid extracted from the plant *Sinomenium acutum*, which is thought to have anti-inflammatory, analgesic, and immunomodulatory properties. This literature review was designed to better understand the efficacy of Zhengqing Fengtongning tablets (ZQFTN), a Chinese medicine preparation from the root of Sinomenium acutum.

A literature search was completed for randomized, controlled trials of ZQFTN for the treatment of knee osteoarthritis (KOA). Eighteen studies were chosen, with a combined total of 757 cases and 755 controls.

A meta-analysis was performed on the six studies that used WOMAC scores to assess changes in pain, stiffness and physical functioning of the joints. Improvement in WOMAC pain and stiffness scores were superior in the ZQFTN group compared to the control group ($p<0.001$ for both comparisons). In the studies that assessed serum levels of IL-1β and TNF-alpha, after treatment, serum levels were lower in the ZQFTN group than in the control group ($p<0.001$ for both comparisons).

Conclusion: This study of patients with knee osteoarthritis found that Zhengqing Fengtongning tablets (ZQFTN), from the root of Sinomenium acutum, can effectively relieve knee pain, morning stiffness, and daily activity function disorders, reduce the expression of inflammatory factors in serum and improve the total clinical response rate.

Huang, Z., et al., The Efficacy and Safety of Zhengqing Fengtongning for Knee Osteoarthritis: A Systematic Review and Meta-analysis of Randomized, Clinical Trials. **Evid Based Complement Alternat Med.** 2022. 2768444, 13 pages, 2022. https://doi.org/10.1155/2022/2768444.

ORAL ANTICOAGULANTS AFTER STROKE IN THE OLDEST OLD WITH ATRIAL FIBRILLATION

As the population ages, the number patients 85 years of age and older is steadily growing. Increasing age and atrial fibrillation (AF) are both risk factors for ischemic stroke (IS). This study compared the efficacy of direct oral anticoagulants (DOACs) with vitamin K antagonist (VKA) for patients 85 years of age and older with AF and a recent IS.

Subjects were consecutive patients with an IS or a transient ischemic attack (TIA) within three months, with concurrent nonvalvular AF, who were treated with a DOAC or VKA, initiated after the index event. The primary outcome variable was time to occurrence of the composite of recurrent IS, intracerebral hemorrhage (ICH) or all-cause death.

Data were obtained concerning 5,593 patients with an IS and 391 with a TIA, with a median age of 78 years and a follow-up of 2.5 years. Of these, 1,380 were ≥85 years of age and 4,604 were <85 years of age. Events during the follow-up included 279 recurrent IS events, 69 ICH events and 737 deaths. The risk of a primary event was less among those treated with DOAC in both patients ages ≥85 years (HR 0.46) and <85 years (HR 0.74). These findings were maintained in the adjusted analysis (HR 0.70 for those >85 years and HR 0.87 for those <85 years).

Conclusion: This study of patients with a recent ischemic stroke found that treatment with a direct oral anticoagulant was superior to treatment with a vitamin K antagonist for the prevention of recurrent stroke, intracerebral hemorrhage, or death.

Polymeris, A., et al. Oral Anticoagulants in the Oldest Old with Recent Stroke and Atrial Fibrillation. **Annals Neurol.** 2021, January: 78-88.

OMEGA-3 FATTY ACID, CAROTENOID, VITAMIN E AND WORKING MEMORY IN OLDER ADULTS

Dietary patterns are important for improving cognitive performance and reducing the risk of dementias, including Alzheimer's disease (AD). The cognitive Impairment Study (CARES) examined the potential synergistic effects of a combination of omega-3 fatty acids, carotenoid, and vitamin E supplementation on the cognitive performance of healthy, older adults.

This parallel group, double-blind, placebo controlled, randomized trial included healthy adults, 65 years of age or older, with a personal or family history of memory loss. Baseline tests included the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) and the Montreal Cognitive Assessment (MoCA). Subjects were 60 healthy adults, randomized to either a placebo group or an intervention group. The intervention group received daily supplements of one g fish oil, 22 mg xanthophyll carotenoids and 15 mg vitamin E. Non-fasting blood samples were collected at each study visit. The primary outcome measure was the change in RBANS score from baseline to follow-up.

From baseline to 24-month follow-up, RBANS scores improved by three percent in the control group and six percent in the treatment group. At 24 months, spatial working memory errors improved by 38% in the treatment group and declined by one percent in the placebo group ($p=0.005$). As the cognitive load of the task increased, the treatment group outperformed individuals receiving placebo.

Conclusion: This study of healthy, elderly adults suggests that supplementation with carotenoid, vitamin E and Omega-3 fatty acid may help preserve working memory.

Power, R., et al., Omega-3 Fatty Acid, Carotenoid and Vitamin E Supplementation Improves Working Memory in Older Adults: Randomized, Clinical Trial. **Clin Nutrit.** 2022, February; 41 (2): 405-414.

DEXAMETHASONE AS AN ANALGESIC ADJUVANT AFTER TOTAL KNEE ARTHROPLASTY

Total knee arthroplasty (TKA) is a common procedure, with more than one million performed annually. Small, underpowered studies have suggested that dexamethasone may be a potential analgesic for patients undergoing these procedures. This

study, the Dexamethasone Twice for Pain Treatment after Total Knee Arthroplasty (DEX-2-TKA) trial explored the effect of dexamethasone for patients undergoing primary TKA.

This multicenter, randomized, blinded placebo-controlled trial included adult patients scheduled for primary, unilateral TKA. The subjects were randomized to one of three intervention groups, intravenous dexamethasone, 24 mg, plus placebo (DX1), intravenous dexamethasone, 24 mg, plus intravenous dexamethasone (DX2) or placebo (placebo). The first dose of the trial drug was administered after the onset of anesthesia and the second dose 24 hours after the end of surgery. All participants were provided a patient-controlled analgesia pump for 24 hours and oral opioids for up to 48 hours post-surgery.

Data were collected for 485 patients, with data completed for 97.3%. Median morphine consumption during the first 48 hours was 37.9 mg in the DX1 group, 35.0 mg in the DX2 group and 43.0 mg in the placebo group. Compared to the placebo group, less pain medication was used by patients in the DX1 ($p=0.008$) and DX2 ($p<0.001$) groups. Compared to the placebo group, pain intensity reduction was greater at 24 hours in both treatment groups ($p<0.001$), but did not differ between the two treatment groups.

Conclusion: This study of patients undergoing total knee arthroplasty found that dexamethasone, provided immediately before and 24 hours after surgery, reduced the use of opioids while decreasing pain in the 48 hours after surgery.

Gasbjerg, K., et al. Effect of Dexamethasone as an Analgesic Adjuvant to Multimodal Pain Treatment after Total Knee Arthroplasty: Randomized, Clinical Trial. **BMJ.** 2022; 376: e067325.

POST SURGICAL DELIRIUM PREVENTION FOR THE ELDERLY

Estimates of the rate of postoperative delirium range from 11% to 65%. As postoperative delirium is associated with increased morbidity and mortality, this study assessed the efficacy of a delirium intervention program for patients undergoing elective major surgical procedures.

The Patientensicherheit, Wirtschaftlichkeit und Lebensqualität (PAWEL) study randomized patients at three university hospitals and two tertiary care center clusters. Subjects were 70 years of age or older, undergoing major elective surgical procedures. The subjects were randomized to a control group or a prevention group, which included seven best practice delirium prevention modules (cognitive, motor, and sensory stimulation; meal companionship, diagnostic test and operation room accompaniment, stress relaxation, and sleep promotion). Baseline data included cognitive function, subjective memory impairment, comorbidities, visual impairment, depression, functional status, and frailty. The delirium prevention team (DPT) provided the intervention modules throughout the day, as needed. The primary outcome variable was delirium, assessed daily with the Confusion Assessment Method (CAM).

Over 17 months, 1,470 patients were recruited into the study. For the entire group, delirium occurred in 21.6%, including 35.7% of those undergoing cardiac procedures and 13.6% of those undergoing noncardiac procedures. During hospitalization, delirium was identified in 19.9% of the DPT group and 23.3% of the control group. Among noncardiac patients, delirium occurred in 10.9% of the treatment group and 16.3% of the control group ($p=0.008$). The DPT group did not affect the rate of delirium among cardiac patients.

Conclusion: This large, multicenter study demonstrated the efficacy of delirium prevention in patients undergoing major elective surgery.

Deeken, F., et al. Outcomes of a Delirium Prevention Program in Older Persons after Elective Surgery. A Stepped Wedge Cluster, Random, Clinical Trial. **JAMA Surg.** 2021. doi:10.1001/jamasurg.2021.6370.

MESENCHYMAL STEM CELLS AFTER ISCHEMIC STROKE

While the mechanisms of stem-cell based therapies is unclear, some evidence suggests that this therapy may be able to promote neurobiological and functional recovery after a stroke. This study investigated changes in neuroimaging measures occurring after autologous mesenchymal stem cell (MSC) treatment in patients with ischemic stroke (IS).

The STARTING-2 trial is a prospective, randomized, open-label, controlled trial involving adults 30 to 75 years of age with moderate to severe neurologic deficits resulting from a recent stroke (within 90 days). The patients were randomized to receive IV MSCs or a placebo. Motor function was assessed using the Fugl-Meyer Assessment (FMA) at baseline and at follow-up. An MRI was obtained, with DTI, rs-fMRI, and T1-weighted structural data acquired. Motor-evoked potential response was determined using transcranial magnetic stimulation. From these data, network efficiency and network density were determined, as were ipsilesional, contralesional and interhemispheric motor connectivity. Functional anisotropy (FA) values of the corticospinal tract (CST) and posterior limb of the internal capsule (PLIC) were determined, and individual DTI data points were preprocessed using the FDT [FMRIB's (Functional Magnetic Resonance Imaging of the Brain) Diffusion Toolbox].

At 90 days, improvement ratios of FMA-T, FMA-UL and FMA-LL were 89.9%, 123.1% and 75.9%, respectively, in the MSC group, and 32.8%, 33.4% and 39.8% in the control group. The difference between the MSC and control groups reached significance only for the FMA-T ($p=0.043$). Interhemispheric connectivity and ipsilesional connectivity significantly increased only in the MSC group.

Conclusion: This study of adults with an ischemic stroke within 90 days found that patients who received IV stem cell therapy had improved Fugl-Meyer scores and reduced internal capsule deterioration.

Lee, J., et al. Efficacy of Intravenous Mesenchymal Stem Cells for Motor Recovery after Ischemic Stroke: A Neuroimaging Study. **Stroke.** 2022, January; 53 (1): 20-28.

SYSTEMATIC SCREEN FOR ATRIAL FIBRILLATION

Atrial fibrillation(a-fib) is a leading cause of ischemic stroke. This population-based study was designed to determine whether screening for a-fib and appropriate oral anticoagulation treatment can reduce

the incidence of stroke and all-cause mortality.

The STROKESTOP study is a multicenter, parallel group, unmasked, randomized, controlled trial, completed in Holland and Sweden. All residents, 75 to 76 years of age, without a-fib, were randomly assigned to a control group or an intervention group. Screening was completed by electrocardiogram. Treatment with oral anticoagulation was offered if a-fib was detected. The primary endpoints were ischemic or hemorrhagic stroke, systemic embolism, bleeding leading to hospitalization and all-cause death.

Between March 1, 2012, and May 28, 2014, 13,979 were assigned to a intervention group and 14,383 to a control group. The intervention group underwent intermittent electrocardiograms (ECGs) for 14 days.

After a median follow-up of 6.9 years, fewer primary endpoint events occurred in the intervention group (31.9%) than in the control group (33%), with a hazard ratio of 0.96 (p=0.045).

Conclusion: This study of adults, 75 to 76 years of age, found that systematic screening for atrial fibrillation resulted in a small reduction in ischemic or hemorrhagic stroke, systemic embolism, bleeding leading to hospitalization and all-cause death.

Svennberg E., et al. Clinical Outcomes in Systematic Screening for Atrial Fibrillation (STROKESTOP): A Multicentre, Parallel Group, Unmasked, Randomized, Controlled Trial. **Lancet.** 2021 Oct 23; 398 (10310): 1498-1506.

FUNCTIONAL ACTIVITY TRAINING FOR CHRONIC LOW BACK PAIN.

The primary reason that people with chronic low back pain (LBP) seek healthcare is their difficulty performing daily functional activities. This study compared the efficacy of traditional therapeutic exercises with training in patient-specific functional activities.

This prospective, single-blind, randomized, clinical trial included adults 18 to 60 years of age with LBP of at least 12 months' duration. Those patients were randomized to receive specific motor skills training (MST) or strengthening and flexibility (SFE). MST involved supervised, massed practice of challenging functional activities that were difficult to perform due to LBP. The primary outcome measure was the modified Oswestry Disability Questionnaire (MODQ), with secondary outcomes including the Numeric Pain Rating Scale (NPRS) for average and worst LBP in the prior seven days.

At the post-treatment stage, the MST group had better MODQ scores than the SFE group ($p < 0.001$), with this difference maintained at six and twelve months. At six months, the MST group demonstrated fewer and shorter acute LBP flare-ups and greater adherence, as compared with the SFE group. Post-treatment, the MST group reported higher satisfaction with care, greater improvement in average and worst LBP and physical function, less LBP-related medication use, less absenteeism from usual activities and lower work-related fear-avoidance beliefs, as compared with the SFE group.

Conclusion: This study of patients with chronic low back pain found that those who undergo motor skills training related to their usual activities improved more than did those who underwent traditional strengthening and stretching.

Van Dillen, L., et al. Effect of Motor Skill Training in Functional Activities versus Strength and Stability Exercise on Function in People with Chronic Low Back Pain. A Randomized, Clinical Trial. **JAMA Neurol.** 2021; 78 (4): 385-395.

AMLODIPINE FOR SPINAL CORD INJURY REPAIR

Amlodipine (AM) is an antihypertensive medication which has been found to inhibit neuronal apoptosis and exert neuroprotective effects in various central nervous system diseases. This animal study assessed the effect of amlodipine on recovery after a surgically induced spinal cord injury (SCI).

This animal SCI model involved 45 mice that underwent laminectomy to expose and cut the right hemisphere of the cord at T-10. The mice were randomized to a control group without surgery, a SCI group, or a SCI group that received AM intraperitoneally for seven days beginning immediately after surgery. The viability of ventral spinal cord cells was assessed up to eight hours after surgery and compared between groups. All animals were tested for locomotor recovery at five weeks post-surgery. A TUNEL assay was used to detect autophage activity.

The AM group displayed significantly better motor performance than the SCI group starting on day seven ($p<0.05$). The AM group showed fewer TUNEL-positive cells than the OGD model (the hypoxic-ischemic injury group). In a separate study to investigate whether autophagy was involved in this protective effect against apoptosis, the cells were exposed to the autophage inhibitor 3-MA, which was found to reverse the effects of AM.

Conclusion: This animal study suggests that intrathecal amlodipine can promote structural and functional recovery after traumatic spinal cord injury through an inhibition of apoptosis and neuronal loss.

Huang, Y., et al., Amlodipine Improves Spinal Cord Injury Repair by Inhibiting Motoneuronal Apoptosis through Autophagy Upregulation. **Spine.** 2022. DOI: 10.1097/BRS.0000000000004310.

BLOOD PRESSURE AND COGNITIVE IMPAIRMENT IN ELDERLY WOMEN

The number of people living with dementia was estimated to be 47 million worldwide in 2015 and was projected to reach 135 million in 2050. As studies have demonstrated that hypertension is a risk factor for cerebrovascular disorders and dementia, this study investigated the association between blood pressure (BP) and mild cognitive impairment (MCI) and dementia in older women.

This prospective analysis included 7,207 females, 65-79 years of age, without MCI or dementia at recruitment. The women's BP was measured at the baseline clinic visit. The subjects were screened annually with the Modified Mini-Mental State Examination (MMSE). The study tested three outcomes: MCI, probable dementia, and cognitive loss (defined as the combined endpoint of either MCI or probable dementia or both). Pulse pressure (PP) was defined as the difference between systolic blood pressure (SBP) and diastolic blood pressure (DBP).

At a mean of 11 years follow-up, 1,132 (15.7%) developed MCI, 739 (10.3%) developed probable dementia, and 1,533 (21.3%) had cognitive loss. Elevated SBP and PP were significantly associated with

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increased risk of MCI and cognitive loss ($p<0.01$). Individuals with hypertension, but with controlled SBP of less than 120 mm Hg, did not have a significantly increased risk of MCI ($p=0.071$), or cognitive loss ($p=0.57$) compared with those with normotension. Individuals on anti-hypertensive treatment with PP of less than 50 mm Hg did not have a significantly higher risk of MCI ($p=0.07$) or cognitive loss ($p=0.16$). There were no significant associations between hypertension, SBP, or PP and probable dementia.

Conclusion: This study of community dwelling women 65-79 years of age, found that those with hypertension, with elevated SBP or elevated PP, were at higher risk of cognitive loss and mild cognitive impairment than were women with normotension.

Liu, L. et al., Association between Blood Pressure Levels and Cognitive Impairment in Older Women: A Prospective Analysis of the Women's Health Initiative Memory Study. **Lancet Healthy Longev**. 2022, January; e42-53.

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