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EXOSOMAL TAU AND AMYLOID-BETA 42 IN TBI

Studies have demonstrated that, when cytokines, including interleukin are elevated after a traumatic brain injury (TBI) patients are less likely to recover. This study was designed to better understand the role of neuronal proteins and inflammatory cytokines, in chronic post-concussive military personnel.

Subjects included 42 military personnel with a mild TBI (mTBI) and 22 healthy matched controls. For each participant the Neurobehavioral Symptom Inventory (NSI) was administered to measure post-concussive symptom severity. Blood samples were taken to determine concentrations of tau, amyloid-beta ($A\beta_{42}$) and cytokines which included tumor necrosis factor alpha (TNF- α), interleukin 6 (IL-6) and interleukin10 (IL-10).

In the TBI group, the mean number of injuries was 2.5 with 30% reporting four or more previous TBIs. The time since the last TBI was three months to over three years. Compared to controls without TBI, those with mild TBIs had elevated concentrations of exosomal tau ($p < 0.01$), $A\beta_{42}$ ($p < 0.01$) and IL-10 ($p < 0.05$). PTSD scores and depression scores were significantly correlated to exosomal IL-10 ($p < 0.01$ and $p = 0.063$ respectively).

Conclusion: This study found that exosomal levels of tau, $A\beta_{42}$ and IL-10 were elevated in military personnel with chronic mild traumatic brain injury, with elevated tau related to chronic post-concussive symptoms and elevated interleukin10 levels related to symptoms of post-traumatic stress disorder.

Gill, J., et al. Higher Exosomal Tau Amyloid-Beta 42 and IL-10 are Associated with Mild TBIs and Chronic Symptoms in Military Personnel. *Brain Injury*. 2018, September; 32(11):1359-1366.

TAI CHI QUAN FOR FALL PREVENTION IN HIGH-RISK ADULTS

Overall, 20% of community dwelling adults 65 years of age or older report a history of fall. This trial compared the efficacy of two proven interventions, tai chi (TC) and multimodal exercise, for the prevention of falls in high-risk, elderly adults.

Participants were 70 years of age or older with either a history of fall within the past 12 months or evidence of impaired mobility. Eligible subjects were randomized to a) TC, using modified tai chi quan forms, b) multimodal exercises, including integrated aerobic, strength, balance and flexibility activities or, c) a control group engaged in stretching exercises. All subjects were assessed for fall related information and physical activity. Outcome measures were collected at baseline and at four and six months.

At six months, among the 1,147 participants, 733 falls were recorded, involving 85 in the TC group, 112 in the exercise group and 127 in the stretching group. Falls were significantly lower in the TC group than in the exercise group ($p = 0.04$). At six months, the TC and exercise groups performed significantly better than did the stretching group on functional performance measurements, as well as in cognitive function.

Conclusion: This study of community dwelling older adults, thought to be at high risk of falling, found that a six-month intervention of tai chi quan is effective in reducing the incidence of falls, and is superior to conventional, multimodal exercise.

Li, F., et al. Effectiveness of a Therapeutic Tai Chi Quan Intervention versus a Multimodal Exercise Intervention to Prevent Falls among Older Adults at High Risk of Falling: A Randomized, Clinical Trial.

JAMA Intern Med. 2018, October; 178 (10): 1301-1310.

TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION FOR PRESSURE ULCERS

Several studies have reported on improvements in wound healing using electric stimulation. This study investigated the effectiveness of local and spinal transcutaneous electrical nerve stimulation (TENS) on healing and symptoms of pressure injuries (PIs).

Subjects were 22 patients with a PI of the distal third of a lower extremity. All were 50 years of age or older, with a PI of grade II or higher, which had failed healing with standard wound care. Those in an experimental group received standard wound care, with electrical stimulation applied for 30 minutes at the local level and 30 minutes on the back for 20 sessions over two months. A control group underwent placebo TENS with low energy stimulation. Outcome variables were pressure injury volume, blood flow, skin temperature, oxygen saturation and pain. Wound healing was assessed with the Expected Results for the Healing of Chronic Wounds Index.

Analysis of variance revealed that wound area decreased more in the experimental than control group ($p = 0.023$), as did pain ($p = 0.004$) and foot temperature ($p = 0.007$).

Conclusion: This study of older adults with pressure injury ulcers found that spinal and local electrical stimulation with a TENS unit can accelerate wound healing and decrease pain.

Garcia-Perez, S., et al. Effectiveness of Transcutaneous Electrical Nerve Stimulation Energy in Older Adults: A Pilot Clinical Trial. *Adv Skin Wound Care*. 2018, October; 31(10): 462-469.

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GLOBAL BURDEN OF MIGRAINE AND TENSION HEADACHE

In the Global Burden of Diseases, Injuries and Risk Factors (GBD) study, headache emerged as a major, global, public health concern. This study provides an overview of the change in headache burden throughout the world between 1990 and 2016.

The GBD derived data from population based, cross-sectional surveys on migraine and tension-type headaches. Prevalence was determined for each gender and by age group. Disease burden, measured in years of life lived with disability (YLD), was calculated from the prevalence and average time spent with headache, multiplied by disability weights.

In 2016, three billion individuals were estimated to have a headache disorder, with 1.89 billion experiencing tension-type headaches and 1.04 billion experiencing migraine headaches. Migraine was estimated to have caused 45.1 million YLD in 2016, an increase of 51.2% from the 29.8 million YLD in 1990. Tension-type headache caused 7.2 million YLD in 2016, an increase of 53.1% from the 4.7 million YLD in 1990. The peak prevalence occurred between 35 and 39 years of age. Globally, migraine and tension-type headaches accounted for 6.5% of all YLD.

Conclusion: This study estimates that, in 2016, almost three billion individuals were affected by a migraine or tension-type headache, with these headaches accounting for 6.5% of all years lived with disability.

GBD 2016 Headache Collaborators. Global, Regional and National Burden of Migraine and Tension-Type Headache, 1990-2016: A Systematic Analysis for the Global Burden of Disease Study 2016. *Lancet Neurol.* 2018, November; 17(11): 954-976.

CALCITONIN GENE-RELATED PEPTIDE AND CLUSTER HEADACHES

Cluster headache attacks feature a combination of extreme unilateral pain accompanied by prominent cephalic autonomic symptoms (CAS) such as tearing, conjunctival redness, rhinorrhea, nasal congestion and ptosis. As the signaling molecule calcitonin gene-related peptide (CGRP) has gained attention for its

migraine inducing abilities, this study was designed to determine whether infusion of CGRP would effect the onset of cluster headaches.

This Danish study included participants 18 to 65 years of age, diagnosed with episodic or chronic cluster headaches. The patients were randomly assigned to receive 1.5 mcg/m of CGRP or a placebo on two study days, separated by at least seven days. If a headache of any type occurred after the infusion, the headache intensity was recorded beginning before infusion and every 10 minutes until 1.5 hours after an infusion. Data gathered included headache intensity, time of onset and autonomic symptoms.

Of the 37 participants recruited, nine were diagnosed with episodic cluster headaches in the active phase (EC-A), nine with episodic cluster headaches during remission (EC-R) and 14 with chronic cluster headache (CC). After the infusion, eight of nine patients with EC-A reported a cluster-like attack, as compared with one of nine after placebo infusion ($p=0.05$). Conversely, no patients with EC-R reported cluster-like attacks after CGRP or placebo infusion. Seven of 14 patients with CC reported an attack after CGRP, as compared with zero after placebo ($p=0.02$).

Conclusion: This study of patients with episodic cluster headaches found that an infusion of CGRP provokes cluster headache attacks only during the active phase.

Vollesen, A., et al. Effect of Infusion of Calcitonin Gene-Related Peptide on Cluster Headache Attacks. A Randomized Clinical Trial. *JAMA Neurol.* 2018, October; 75 (10): 1187-1197.

GALCANEZUMAB FOR THE PREVENTION OF EPISODIC MIGRAINE

Calcitonin gene related peptide (CGRP) is widely expressed throughout the nervous system, acting as a sensory neurotransmitter, vasodilator and mediator of neurogenic inflammation. Galcanezumab is a humanized monoclonal antibody that binds CGRP and prevents biologic activity without blocking the receptor. This study was designed to determine the efficacy of Galcanezumab for the prevention of migraine headaches.

This phase three study included patients who were 18-65 years of age with a diagnosis of migraine for at least one year. The patients were randomized to receive a monthly injection of placebo or Galcanezumab at a dose of 120 mg or 240 mg. Migraine headaches days were recorded for one month before injections and then monthly for 10 months.

Among the 703 patients studied, patients who received both the 120 and the 240 mg doses of Galcanezumab had significantly better reductions in mean headache days ($p<0.001$) than did those receiving the placebo, with these effects beginning within month one. The proportion of patients that maintained at least a 50% reduction in monthly mean headache days for six consecutive months was 20.5% in the 120 mg group ($p<0.001$), 19.2% in the 240 mg group ($p<0.001$) and 8.9% in the placebo group.

Conclusion: This study of patients with chronic episodic migraine found that monthly injections of Galcanezumab can reduce monthly migraine headache days.

Stauffer, V., et al. Evaluation of Galcanezumab for the Prevention of Episodic Migraine. The EVOLVE-1 Randomized Clinical Trial. **JAMA Neurol.** 2018, September; 75 (9): 1080-1088.

ASPIRIN AND ALL CAUSE MORTALITY IN THE HEALTHY ELDERLY

This study, the Aspirin in Reducing Events in the Elderly (ASPREE) trial, was a primary prevention trial to determine whether the daily use of 100 mg of enteric-coated aspirin could prolong the healthy lifespan of older adults.

Subjects were 19,114 healthy adults, 65 years of age or older, residing in community settings in Australia. Those recruited had no cardiovascular disease, dementia or disability. The subjects were randomized to receive either 100 mg of enteric-coated aspirin or a placebo. Mortality was confirmed by two independent sources, with the underlying cause of death and the proximal cause of death both determined.

Subjects included 9,525 randomly assigned to the aspirin group and 9,589 to the placebo group. During

the study, 5.5% died, with the risks of death from any cause determined to be 12.7 events per 1,000-person years in the aspirin group and 11.1 events per 1,000-person years in the placebo group, [hazard ratio (HR) 1.14]. Among those who received aspirin, the major contributor to higher, all-cause mortality was an increased risk of death for which the underlying cause was cancer (HR 1.31). This higher cancer-related mortality was not confined to a specific tumor location or pathologic type.

Conclusion: This randomized, controlled trial found that 100 mg of aspirin per day results in a higher all-cause mortality, mostly as a result of an increased risk of cancer.

McNeil, J., et al. Effect of Aspirin on All-Cause Mortality in the Healthy Elderly. **N Engl J Med.** 2018, October 18; 379 (16): 1519-1528.

ASPIRIN, CARDIOVASCULAR EVENTS AND BLEEDING IN HEALTHY ELDERLY

Low-dose aspirin is among the most widely used agents for the prevention of cardiovascular disease. As an increased risk of bleeding has been observed in the elderly, this study was designed to better understand the effects of prophylactic aspirin on cardiovascular and bleeding events in the healthy elderly.

Subjects were 65 years of age or older and free of overt coronary heart disease, cerebrovascular disease, atrial fibrillation, dementia, physical disability, high risk of bleeding or anemia. The subjects were randomized to receive either a placebo or 100 mg of enteric coated aspirin, once per day. Annual in-person visits and medical record reviews were supplemented by regular telephone calls. The primary endpoints were major adverse cardiovascular events, fatal coronary heart disease, nonfatal myocardial infarction or fatal/nonfatal ischemic stroke. The primary adverse event was a composite of hemorrhagic stroke, symptomatic intracranial bleeding, or clinically significant extracranial bleeding.

Subjects were 9,525 individuals assigned to receive aspirin and 9,589 to received placebo. After 4.7 years of follow-up, the rates of major adverse cardiovascular events were 7.8 per 1,000-person years in the

aspirin group and 8.8 per 1,000-person years in the placebo group (hazard ratio 0.89). The rates of major hemorrhagic events were 8.6 per 1,000-person years in the aspirin group and 6.2 per 1,000-person years in the placebo group ($p<0.001$). Approximately 50% of the bleeding events were gastrointestinal.

Conclusion: This randomized trial involving healthy, elderly adults found that the use of low-dose aspirin does not significantly lower the risk of cardiovascular disease, but does result in a significantly higher rate of major hemorrhage.

McNeil, J., et al. Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly. **N Engl J Med.** 2018, October 18; 379(16): 1509-1518.

HIGH FAT DIET, POSTOPERATIVE PAIN AND INFLAMMATION

Studies have shown an association between obesity and the incidence as well as severity of chronic pain conditions. This animal study was designed to understand the effect of diet on postoperative pain.

In an animal model of postoperative pain, rats were randomized to be fed for six weeks before surgery with either a high fat diet (40% of calories from butter fat) or a low-fat diet. Before and after surgery, the animals were assessed for pain, including the mechanical path withdrawal threshold using six applications of Von Frey filaments at the side of the wound, and for spontaneous pain behavior.

In male rats fed a high fat diet, mechanical hypersensitivity was prolonged and the threshold for paw withdrawal remained significantly lower than that of normal diet rats for over one week after surgery. In females, the effect of the diet was much more modest. A three-way analysis showed a main effect of diet ($p<0.001$) and gender by diet ($p=0.046$) for the Von Frey filament test. Spontaneous pain scores showed a main effect of diet ($p=0.04$). In a secondary experiment, when given a high fat diet for seven weeks, and switched back to a normal diet for two weeks before incision, there were no effects of diet on either mechanical or spontaneous pain.

Conclusion: This animal study suggests that a high fat diet may

exacerbate pain post-surgically, but when switched to a normal diet for two weeks, this effect was mitigated.

Song, Z., et al. High Fat Diet Exacerbates Postoperative Pain and Inflammation in a Sex Dependent Manner. **Pain**. 2018, September; 159 (9): 1731-1741.

KNEE OSTEOARTHRITIS AND METABOLIC SYNDROME

The metabolic syndrome (MetS) has been found to be associated with cardiovascular disease and mortality. There is some evidence of a relationship between MetS and osteoarthritis (OA). This Egyptian study further examined the relationship between MetS and characteristics of OA of the knee.

Subjects were 60 adults with a diagnosis of MetS and 60 obese subjects without MetS. All subjects were assessed for pain with the Western Ontario and McMaster University (WOMAC) index, and underwent laboratory assessment of triglycerides, HDL cholesterol and glucose. All underwent plain radiographs of the knee to diagnose and assess OA.

The frequency of OA and the severity of OA, hypertension and diabetes were significantly higher in the MetS group than in the control group ($p=0.034$, $p<0.001$ and $p<0.001$, respectively). In addition, among those in the MetS group, those with OA of the knee were more likely to have hypertension ($p=0.009$), diabetes ($p=0.002$) and greater weight ($p=0.01$).

Conclusion: This study of patients with the metabolic syndrome found that osteoarthritis of the knee is prevalent among these patients, and is associated with worse pain, function, and advanced radiographic changes.

Afifi, A., et al. Osteoarthritis of Knee Joint in Metabolic Syndrome. **Clin Rheum**. 2018, October; 37(10): 2855-2861.

COMORBIDITIES TWO YEARS AFTER ARTHROSCOPIC HIP SURGERY

Surgery of the lower extremities can limit the patient's ability to bear weight for weeks, and can limit physical activity for months. This

study was designed to determine the rate of medically diagnosed comorbidities developing within two years of arthroscopic hip surgery.

Data were obtained from claims made within the United States Military Health System (MHS). The MHS data repository (MDR) was used to identify all cohort and health care utilization variables for individuals undergoing arthroscopic hip surgery over a ten-year period. For this study, age was restricted to 18 to 50 years, with data reviewed for two years after surgery.

The final cohort comprised 1,870 participants with a mean age of 32.2 years. Compared to baseline, within two years of hip surgery, a significant increase was noted in the diagnoses of mental health disorders, posttraumatic stress disorder, chronic pain, substance abuse disorder, cardiovascular disease, metabolic syndrome, systemic arthropathy, sleep disorder, insomnia, and breathing related sleep disorder (all $p<0.001$). The total number of individuals with a chronic pain diagnosis increased by 166%, with PTSD increasing by 149% and sleep disorders by 111%.

Conclusion: This study found that, after arthroscopic hip surgery, the incidence of seven major comorbidities increases significantly.

Rhon, D., et al. Comorbidities in the First Two Years after Arthroscopic Hip Surgery: Substantial Increases in Mental Health Disorders, Chronic Pain, Substance Abuse and Cardiometabolic Conditions. **Br J Sports Med**. 2018, September; 0:1-8. doi:10.1136/bjsports-2018-099294.

DEMENTIA AND ONE YEAR MORTALITY AFTER HIP FRACTURE

Fractures of the hip in the elderly are associated with higher rates of morbidity and mortality. This study assessed the rate of mortality during the year following hip fracture surgery in patients with Parkinson's disease (PD) or other dementias.

Using data from the Taiwan National Health Insurance Research Database (NHIRD), the authors identified individuals who were 65 years or older and who had been surgically treated for a non-traumatic, acute fracture of the hip between 1997 and 2012. From this group, patients diagnosed with dementia and/or PD up to two years before the

hip fracture surgery were compared to patients with hip fractures but without dementia or PD. The subjects were followed until one year after the date of fracture or until the end of 2013, death or withdrawal from the insurance program.

Of the 6,626 patients in the cohort, 676 had dementia and 371 had PD, with 127 having both. Patients with dementia, or both dementia and PD, had significantly higher mortality than did those with neither condition, hazard ratio (HR) of 1.45 and 1.57, respectively. There was no significant effect of PD alone on the risk of death.

Conclusion: This study of elderly patients undergoing surgical repair of a hip fracture found that dementia is an independent risk factor for death in the year following surgery.

Chiu, H., et al. Dementia Predicted One-Year Mortality for Patients with First Hip Fracture. **Bone Joint J**. 2018, September; 100B(9): 1220-1226.

CIRCULATING OMEGA-3 FATTY ACIDS AND HEALTHY AGING

Healthy aging is defined as living a meaningful lifespan without chronic disease and with intact physical and mental function. As human trials with omega-3 polyunsaturated fatty acids (n3-PUFAs) have shown favorable effects on blood pressure, endothelial function, plasma triglycerides, heart rate and inflammation, this study was designed to understand the relationship between n3-PUFAs and healthy aging.

The Cardiovascular Health Study is a multicenter, prospective cohort of older adults. From 1989 through 1993, 5,888 ambulatory, independent adults were recruited from four United States communities. Trained personnel performed annual clinical examinations to assess demographics, health status, hospital stays, medical history and lifestyle. The subjects were followed through June of 2015 to determine health status and incident cardiovascular disease events. Data included 12-hour fasting blood samples to determine n3-PUFA levels, other fatty acid biomarkers and lipid levels. Healthy aging was defined as survival without cardiovascular disease, cancer, lung disease or severe chronic kidney disease, and the

absence of cognitive and physical dysfunction.

With an average age at baseline of 74 years, 89% experienced unhealthy aging during follow-up. Participants in the highest group of total, long chain n3-PUFAs had an 18% lower risk of unhealthy aging ($p=0.001$) as compared to those in the lowest group. When the n3-PUFAs were analyzed separately, those in the highest eicosapentaenoic acid or docosapentaenoic acid groups had a 24% ($p=0.001$) and 18% ($p=0.003$), respectively, lower risk for unhealthy aging, as compared with the lowest group.

Conclusion: This prospective study of healthy, elderly Americans found that circulating levels of omega-3 polyunsaturated acids are associated with healthy aging.

Lai, H., et al. Serial Circulating Omega-3 Polyunsaturated Fatty Acids and Healthy Aging Among Older Adults in The Cardiovascular Health Study: Prospective, Cohort Study. **BMJ**. 2018; 363: K4067.

TRANSCRANIAL DIRECT CURRENT STIMULATION AND COGNITIVE FUNCTION IN THE ELDERLY

Previous studies of healthy adults have demonstrated that one 20-minute session of transcranial direct current stimulation (tDCS) at the dorsolateral prefrontal cortex can enhance performance on tests of executive function. This study was designed to determine whether tDCS could induced lasting improvements in dual-task performance, cognition and mobility in older adults with mild to moderate impairments in cognitive and motor function.

Participants were 65 years of age or older who exhibited both slow gait and executive dysfunction. The participants were randomized to receive either tDCS or sham intervention delivered with the anode placed over the dorsolateral prefrontal cortex (DLPFC). Cognition, mobility and dual-task performance were assessed at baseline, post-intervention, and at two weeks after completion. The primary outcome measures included the Montreal Cognitive Assessment (MoCA), and the Timed up and Go (TUG), with dual task performance defined by the decrement in performance between

single and dual task conditions of walking speed and sway.

At two-week follow-up, the tDCS group had significantly better scores than the sham group in the total MoCA scores ($p=0.03$). A subgroup analysis revealed that the tDCS improved performance within the visuospatial executive function subscore ($p=0.002$), with other subscores unchanged. The tDCS group also showed better mitigation of dual task costs to sway speed ($p=0.0009$) and area ($p<0.0001$).

Conclusion: This pilot, sham controlled trial found that 10 sessions of direct current stimulation, with the anode over the left dorsolateral prefrontal cortex, may be helpful in reducing impairments in gait and executive function.

Manor, B., et al. Transcranial Direct Current Stimulation May Improve Cognitive-Motor Function in Functionally Limited Older Adults. **Neurorehabil Neural Repair**. 2018, September; 32(9): 788-798.

EXTERNAL COUNTERPULSATION IN CHRONIC CEREBROVASCULAR OCCLUSIVE DISEASE

External counterpulsation has been shown to improve cerebral perfusion velocity in patients with acute stroke and is thought to stimulate collateral artery growth. It is not known however whether non-acute but at-risk patients with high-grade carotid artery disease may benefit from counterpulsation.

Patients were 60 years of age and older with unilateral internal carotid artery stenosis or occlusion. The patients were randomized to a dual course of counterpulsation treatment of either 20 minutes active followed by 20 minutes sham, or vice versa. At baseline, cerebrovascular CO₂ reactivity was determined via inhalation of 7% CO₂-enriched air for two minutes. Near-infrared spectroscopy monitoring (NIRO-300; Hamamatsu) of the bilateral prefrontal cortex was used to obtain the tissue oxygenation index (TOI).

During the counterpulsation cycle the mean blood flow velocity increased significantly in the ipsilateral middle cerebral artery ($p<0.01$) with little change in the contralateral side. Counterpulsation also increases the TOI of the ipsilateral hemisphere compared to baseline ($p<0.01$), with insignificant

changes contralaterally. No Changes in PetCO₂ were recorded in any condition.

Conclusion: This study of patients with chronic stenosis of the internal carotid artery found that short-term counterpulsation treatment can cause an immediate increase in cerebral oxygenation and intravascular flow velocity – the latter being the pivotal mechanism by which cerebral arteriogenesis is thought to be triggered.

Buschmann, E., et al. Short-term External Counterpulsation Augments Cerebral Blood Flow and Tissue Oxygenation in Chronic Cerebrovascular Occlusive Disease. **Eur J Neurol**. 2018, November; 25 (11):1326-1332.

HEAD OF BED POSITIONING AFTER ACUTE ISCHEMIC STROKE

After an acute ischemic stroke (IS), cerebral perfusion pressure is known to decrease when the brain is elevated above the level of the heart. While at a group level this effect seems to last no more than 24 hours, the individual effect is quite heterogeneous and often paradoxical. This study was designed to determine whether the cerebrovascular response to head of bed manipulation depends on cerebral autoregulation performance.

Consecutive patients hospitalized with acute IS were compared to matched reference subjects. All underwent bilateral transcranial Doppler ultrasound (at the proximal middle cerebral artery) to determine cerebral blood flow velocity (CBFV) and near-infrared spectroscopy of total hemoglobin tissue concentration (total Hb), and local cerebral blood volume (CBV) assessed with the head-of-bed positioned at 30° and 0°. Continuous blood pressure was measured in the non-paralytic hand. Cerebrovascular autoregulatory performance was expressed as the phase difference of the arterial pressure-to-CBFV transfer function.

Following the head of bed lowering, CBF increased in patients with autoregulatory performance at less than 50th percentile, but decreased in the hemispheres of patients with better autoregulatory performance ($p<0.05$). The CBV was inversely related to autoregulatory performance in the patients with IS,

with no such relationship observed for CBV velocity.

Conclusion: This study of patients with acute ischemic stroke found that lowering the head of the bed from 30 to zero degrees increased cerebral blood flow among those with poor autoregulatory performance, but decreased cerebral blood flow among those with good autoregulatory performance.

Truijen, J., et al. Cerebral Autoregulatory Performance and the Cerebrovascular Response to Head of Bed Positioning in Acute Ischemic Stroke. *Euro J Neurol.* 2018, November; 25 (11): 1365-1371.

SURGICAL VERSUS NONSURGICAL TREATMENT OF MENISCAL TEARS

Previous studies of meniscal tears which compared surgical to nonsurgical care have failed to demonstrate the superiority of surgery. This study was designed to determine whether physical therapy (PT) is noninferior to arthroscopic partial meniscectomy for improving self-reported knee function after a meniscal tear.

This multicenter trial was performed in nine hospitals in the Netherlands. Participants were 45-70 years of age with knee pain and a nonobstructive meniscal tear confirmed by MRI. Subjects were randomized to receive either surgical removal of the torn portion of the meniscus followed by therapy or to a PT exercise protocol consisting of 16 sessions of 30 minutes each over eight weeks. The primary outcome was patient reported knee function on the subjective knee form of the international knee documentation committee (IKDC) from baseline to 24 months.

Of the 321 patients enrolled, 159 were randomized to surgery and 162 to PT. At 24 months, knee function scores in the surgical group improved 26.2 points compared with improvement of 20.4 points in the PT group, suggesting a noninferiority of PT. Knee pain during weight-bearing improved more in the surgical group ($p=0.01$), with no difference between groups in general health and activity levels.

Conclusion: This multicenter randomized controlled trial of patients 45 years of age or older with painful meniscal tears found that physical

therapy was noninferior to partial meniscectomy for improving knee function in the two years after the injury.

Van de Graff, V., et al. Effect of Early Surgery Versus Physical Therapy on Knee Function among Patients with Nonobstructive Meniscal Tears: The ESCAPE Randomized Clinical Trial. *JAMA.* 2018, October 2; 320 (13): 1328-1337.

VESTIBULAR REHAB IN SUBACUTE STROKE

Vestibular rehabilitation is a growing field of interest; though, few randomized, controlled trials have investigated the outcomes of such programs. This preliminary study investigated the effectiveness of vestibular exercises for patients with subacute stroke.

Twenty-five patients with stroke resulting in unilateral hemiplegia were randomized into two groups, including 12 to a control group (CG) and 13 to a vestibular rehabilitation group (VR). These patients met the additional inclusion criterion of being able to ambulate independently without an assistive device. Both groups performed four weeks of standard physiotherapy twice weekly. Additionally, the CG performed sessions dedicated to balance exercises focusing on weight bearing through the paretic limb. The VR subjects performed an equal number of sessions of gaze stability and upright postural control exercises. A 10-meter walk test and traditional clinical scales, including the Functional Ambulation Classification, Tinetti Balance and Gait, Berg Balance Scale and Barthel Index were administered before and after the four-week training. The participants were followed at three and twelve months to evaluate for reported falls.

Statistically significant increases in walking speed ($p=0.043$) and stride length ($p=0.009$) were seen in the VR group as compared to CG subjects. Improvements on all clinical indices were generally more pronounced in the VR group, with statistically significant findings in the Tinetti Gait ($p=0.014$) and Tinetti total scores ($p=0.011$). In the CG, three patients experienced at least two falls at twelve-month follow-up, whereas only one VR patient had one fall over the same period.

Conclusion: This study of patients with subacute stroke found that adding vestibular rehabilitation to a comprehensive rehabilitation program may help improve dynamic balance, and reduce falls.

Tramontano, M., et al. Vestibular Rehabilitation Training in Patients with Subacute Stroke: A Preliminary Randomized Controlled Trial. *Neurorehabil.* 2018; 43(2):247-254.

SPLINTS VERSUS STEROIDS IN CARPAL TUNNEL SYNDROME

While carpal tunnel syndrome (CTS) is the most common compression neuropathy affecting the upper limb, no consensus exists concerning the best primary care management for mild to moderate cases. This study, the Injection versus Splinting in Carpal Tunnel Syndrome (INSTINCTS) trial, compared the efficacy of splints with steroid injections as a primary intervention.

Subjects were 18 years of age or older, presenting with a new episode of primary, idiopathic, mild to moderate CTS. The participants were randomly assigned to receive either one treatment with 20 mg methylprednisolone acetate, injected into the carpal tunnel or to volar cock-up splints, to be worn at night for six weeks.

Baseline data were collected from self-completed questionnaires immediately before randomization and at six weeks and six months after study initiation. The primary outcome variable was the overall score for symptom severity and limitations in hand function on the Boston Carpal Tunnel Questionnaire (BCTQ) at six weeks.

Participants were 234 patients, with 118 assigned to the splinting group and 116 to the injection group. At six weeks, significantly greater improvement was found in the corticosteroid group as compared to the splinting group in the BCTQ overall score ($p=0.0001$), functional limitations score ($p=0.0031$), hand-wrist pain intensity score ($p=0.049$), and insomnia due to wrist problems ($p=0.018$). At six months, no significant difference was noted between groups.

Conclusion: This prospective study of patients with mild to moderate carpal tunnel syndrome found that corticosteroid injections

into the carpal tunnel produce outcomes at six weeks that were superior to those of nighttime splinting.

Chesterton, L., et al. The Clinical and Cost Effectiveness of Corticosteroid Injection versus Night Splints for Carpal Tunnel Syndrome (Instincts Trial: An Open Label, Parallel Group, Randomised Controlled Trial. **Lancet**. 2018, October; 392 (10156): 1423-1433.

SMOKING DURING PREGNANCY AND RISK OF DIABETES IN CHILDREN

Several previous, small studies have suggested a potential decreased risk of type 1 diabetes following maternal smoking during pregnancy. This large, prospective, cohort study was designed to better evaluate the effects of smoking during pregnancy on the risk of type 1 diabetes in children.

Eligible women were recruited from among participants of the Norwegian Mother and Child Cohort Study (MoBa) and the Danish National Birth Cohort (DNBC). The subjects were asked to self-report on maternal smoking before, during, and for six months after pregnancy. Cord blood from the MoBa biobank was sampled in 154 cases with type 1 diabetes and 476 randomly selected controls.

Smoking during pregnancy after gestational week 12 was associated with decreased risk of childhood-onset type 1 diabetes, with a pooled, adjusted HR of 0.66, as compared to mothers who did not smoke. Neither maternal smoking before pregnancy nor maternal smoking during the first six months after birth was associated with the risk of type 1 diabetes.

Conclusion: Sustained maternal smoking during (but not before or after) pregnancy is associated with a lower risk of development of type 1 diabetes in children.

Magnus, M., et al. Parental Smoking and Risk of Childhood Onset Type 1 Diabetes. **Epidem**. 2018, Nov; 29 (6): 848-856.

TELEPHONE BASED FOLLOW-UP AFTER STROKE AND TIA

Stroke survivors are at an increased risk for recurrent vascular

events, with guidelines established for targets for blood pressure and low-density lipoprotein cholesterol (LDL). This study was designed to determine whether telephone-based follow-up could improve blood pressure values and LDL values 36 months after stroke or TIA.

Subjects were patients seen at one Swedish Hospital with ischemic stroke, intracerebral hematoma or TIA between 2010 and 2013. All subjects had blood pressure and blood lipids measured at a healthcare facility at one, 12, 24 and 36 months after discharge. Those randomized to the intervention group received telephone-based counseling, with medications adjusted to stabilize blood pressure and LDL-C. The control group received secondary care according to local standards, most often in the office of the general practitioner. Outcome measures were compared between groups.

At 36-month follow-up, the mean adjusted systolic blood pressures were 128.1 mmHg in the intervention group and 134.2 mmHg in the control group ($p<0.001$). The mean diastolic blood pressure was 75.3 mmHg in the intervention and 78.8 mmHg in the control group ($p<0.001$). The mean adjusted LDL-C was 2.2 mmol per liter in the intervention group and 2.5 mmol per liter in the control group ($p<0.001$).

Conclusion: This prospective study of patients hospitalized with a stroke or transient ischemic attack found that a telephone follow-up could improve blood pressure and cholesterol better than the usual care in the control group.

Ögren, J., et al. Long-term, Telephone based Follow-Up after Stroke and TIA Improves Risk Factors: 36-month Results from the Randomized Controlled NAILED Stroke Risk Factor Trial. **BMC Neurol**. 2018, September; 18(1):153.

SMOKING AND HEALING OF ROTATOR CUFF TEARS

The incidence of rotator cuff tears has increased dramatically over the past several years. The healing failure rate after rotator cuff repair has been estimated to be between 20% and 94%. This study was designed to determine whether tobacco abuse a well-known metabolic risk factor, is also a risk factor for poor healing of a rotator cuff tear.

This retrospective cohort study included patients undergoing arthroscopic repair of full thickness rotator cuff tears. Subjects identified were current smokers with a greater than 20-pack-year smoking history. The control group included 34 nonsmokers matched for age, fatty infiltration and tear size. All patients had follow-up at a minimum of six months with magnetic resonance imaging or ultrasound, and a functional assessment at a minimum of one year.

At final follow-up, 29.4% of the smoking group and 5.9% of the nonsmokers had failed to heal ($p=0.023$). In the final regression analysis, failure to heal was correlated with rotator cuff tear size ($p=0.02$) and tobacco abuse ($p=0.012$). The final functional assessment found no difference between the smoking group and the nonsmoking group.

Conclusion: This study found that current heavy smoking resulted in a significant increase in healing failure as compared with nonsmokers.

Park, J., et al. Effect of Smoking on Healing Failure after Rotator Cuff Repair. **Am J Sports Med**. 2018, October; 46 (12): 2960-2968.

SURGICAL TREATMENT OF SUBACROMIAL PAIN SYNDROME

Subacromial pain syndrome (SPS) is a common shoulder disorder, viewed as a condition wherein tightness and friction in the subacromial space can lead to bursitis, tendinopathy and eventual cuff tears. Some have suggested that those with rotator cuff tears have more advanced pathology and, thus, are less likely to respond to intervention. This study investigated the long-term results of an isolated subacromial decompression surgery, as compared to those of rotator cuff repair combined with subacromial decompression.

Subjects were patients with symptomatic, chronic SPS, or small to medium size rotator cuff tears. All underwent a subacromial decompression, with those with rotator cuff tear also undergoing repair. The primary outcome measure was performance on the Disabilities of Arm, Hand and Shoulder (DASH), with a visual analog scale (VAS) of pain and function included as a

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pain and function included as a secondary outcome.

Data were obtained for 180 patients undergoing combined surgery and 180 undergoing subacromial decompression only.

Significant improvement was noted in both treatment groups in DASH scores ($p < 0.001$) and VAS scores for function ($p < 0.001$) and pain ($p < 0.001$). Interestingly, post-operative function was significantly more improved in patients > 55 years of age ($p = 0.038$) than in younger patients.

Conclusion: This long-term, follow-up study of patients who underwent decompressive surgery for subacromial pain syndrome found no evidence of inferior outcome as compared to those who underwent combined decompressive surgery and rotator cuff repair surgery.

Inderhaug, E., et al. Long-Term Results after Surgical Treatment of Subacromial Pain Syndrome with or without Rotator Cuff Tear. **J Orthopaed.** 2018, September 15(3): 757-760.

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