

# BONES & BRAIN

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## TRANSCRANIAL MAGNETIC STIMULATION PLUS MOTOR RELEARNING IN STROKE-RELATED SPASTICITY

Stroke is one of the most common neurologic diseases, with limb dysfunction reported by 70%. Repetitive transcranial magnetic stimulation (rTMS) is a noninvasive neuromodulation technique that has been effective in modulating cortical excitability. This study investigated the efficacy of rTMS combined with motor relearning procedures (MRPs), for improving lower limb spasm motor function and cortical excitability.

Subjects were 60 patients with hemiplegia due to ischemic stroke, 30 to 80 years of age. All underwent MRPs involving step-by-step and repeated training for motor dysfunction, 20 to 30 minutes per day for four weeks. A control group participated in MRPs with a placebo rTMS, while a treatment group received 1Hz rTMS for 20 minutes, six days a week for four weeks. Muscle tone was assessed with the modified Ashworth Spasm (MAS) scale, and lower limb function was measured with the Fugl-Meyer Assessment (FMA).

Thirty patients were assigned to each group. Improvements on the MAS and FMA were superior in the treatment group as compared to the control group ( $p < 0.05$  for both). In addition, over time, motor-evoked potential indicators were significantly more improved at four weeks in the treatment group than in the control group.

**Conclusion:** This study of patients with ischemic stroke found that combining repetitive transcranial magnetic stimulation with motor relearning techniques could improve tone and function to a greater extent than motor relearning techniques alone.

Chen, R., et al. Treatment Effects of Low Frequency Repetitive Transcranial Magnetic Stimulation Combined with Motor Relearning Procedures on Spasticity and Limb

Motor Function in Stroke Patients. *Frontiers Neurol.* 2023, Aug 11;14:1213624.

## POST-CONCUSSIVE DRIVING

Studies have shown that, after a concussion, individuals are slower to identify traffic hazards and perform more poorly on driving maze assessments. This study assessed the simulated driving performance of athletes with a concussion.

Subjects were 26 concussed and 23 non-concussed Division I collegiate athletes. The participants underwent driving assessments at three specific points in time, within 72 hours of the concussion, once they were symptom-free, and upon return to their respective sports activities. The control group was tested at similar intervals as the concussion group. This assessment was conducted using a driving simulator which presented various daily traffic scenarios.

Compared to the non-concussed group, at 72 hours post-concussion, the concussion group demonstrated significantly more lane excursions ( $p = 0.003$ ). The concussed group also exhibited a higher Standard Deviation of Lateral Position (SDLP) while avoiding a child crossing the road, displayed greater SDLP when navigating around a car crash, and were closer to the center line while navigating a residential left curve. No significant difference was seen between the groups in the number of collisions.

**Conclusion:** This study of collegiate athletes performing a driving simulation exercise found that, within 72 hours of a concussion, patients demonstrated more lane excursions, but no more collisions, than did controls.

Schmidt, J., et al. Longitudinal Assessment of Post-Concussive Driving. Evidence of Acute Driving Impairment. *Am J Sports Med.* 2023, August; 51(10): 2732-2739.

## GUT MICROBIOME METABOLITES AND ISCHEMIC STROKE

Several microbiome metabolites have been found to be independently associated with incident ischemic stroke. However, a direct relationship has not yet been clarified. This study was designed to better understand this relationship.

The subjects were enrolled in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study, which included 1,075 patients with ischemic stroke and 968 matched controls. The data were adjusted for age, gender, race, and risk factors to determine the relationship between the metabolites and stroke.

An exploratory factor analysis was used to determine associations between metabolite factors and stroke. From this analysis 15 metabolites were identified representing a well-defined metabolic pathway. Of these, factor three, was associated with an increased risk of stroke, with a hazard ratio (HR) of 1.23. Compared to those in the lowest tertile of factor three, those with the highest tertile had a 45% increased risk of stroke.

**Conclusion:** This study, using data from the REGARDS trial identified a gut microbiome metabolism factor, factor three, which was independently related to incident ischemic stroke.

Ament, Z., et al. Gut Microbiota-Associated Metabolites and Risk of Ischemic Stroke in REGARDS. *Cereb Blood Flow Metab.* 2023, July; 43 (7): 1089-1098.

## ASYMPTOMATIC CHRONIC SUBDURAL HEMATOMA

A widely recognized consequence of head injury is chronic subdural hematoma (CSDH). This disorder involves the accumulation of blood and breakdown products within the subdural space and can be spontaneous or post-traumatic. This

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study investigated the natural history of asymptomatic CSDH (asCSDH), to clarify requirements for radiologic follow-up and neurosurgical input.

The database from a single institution was screened over two years for patients fulfilling the criteria for asCSDH with no other significant intracranial traumatic lesions and with no symptoms consistent with a subdural hematoma. The charts were reviewed for past medical history and to calculate the Charleston Comorbidity Index, which estimates the probability of 10-year survival.

Data were reviewed for 106 patients with a mean age of 81.9 years. Of these, 34.9% were taking anticoagulants. The medical teams performed follow-up imaging for 57 patients, predominantly for falls or monitoring purposes. Antithrombotic agents were used by 57.5% of the participants, with these medications held in 70.3% of the cases. Only one patient required neurosurgical intervention at three months from the time of the initial presentation.

**Conclusion:** This study of patients with traumatic subdural hematoma found that asymptomatic chronic subdural hematomas do not require radiological follow-up or neurosurgical intervention in the vast majority of cases.

Parry, D., et al. Asymptomatic Chronic Subdural Haematoma - Does It Need Neurosurgical Intervention? **Br J Neurosurg.** DOI: 10.1080/02688697.2023.2210224.

**APTOLL IN PATIENTS WITH ISCHEMIC STROKE UNDERGOING ENDOVASCULAR TREATMENT**

ApTOLL is a DNA aptamer, an antagonist at toll-like receptor four (TLR4), directly involved in innate immune responses. This study (APRIL) was designed to assess the safety of ApTOLL in patients with acute ischemic stroke who are eligible for endovascular treatment (EVT) within six hours of symptom onset.

This double-blind, randomized, placebo-controlled study involved patients, 18 to 90 years of age, with confirmed anterior circulation, large vessel occlusion stroke. All patients received EVT, and intravenous thrombolysis if indicated. The patients were then randomized to receive a placebo (n=47) or ApTOLL at 0.05 mg/kg (n=36) or 0.2mg/kg (n=36). The primary endpoint was the presence of any of the following

events: death, intracranial hemorrhage resulting in new or worsening symptoms, herniation, neurological worsening, or recurrent stroke.

The primary endpoint occurred in 29% of the placebo group, 36% of the 0.05 mg/kg group, and 14% of the 0.02 mg/kg group. Death by any cause occurred in 18% in the placebo group, 26% of the 0.05 mg/kg group, and 4.8% of those receiving 0.2mg/kg. Lower NIHSS scores at 72 hours were realized in the 0.2 mg/kg group, as were smaller final infarct volumes and a lower incidence of disability.

**Conclusion:** This study found that infusion of ApTOLL, 0.2 mg/kg, in combination with endovascular treatment, in selected patients with stroke, reduced mortality and infarct volume at 90 days, and reduced long-term disability.

Hernández-Jiménez, M., et al. Safety and Efficacy of ApTOLL in Patients with Ischemic Stroke Undergoing Endovascular Treatment: A Phase 1/2 Randomized Clinical Trial. **JAMA Neurol.** 2023, Aug. 80(8): 779-788.

**MAJOR BLEEDING IN ANTICOAGULATION FOR STROKE AND A-FIB**

Individuals with atrial fibrillation (AF) have a five-fold increase in the risk of ischemic stroke (IS). While this risk is reduced with the use of anticoagulants, these medications produce an increased risk of bleeding. This study was designed to determine the independent predictors of major bleeding in patients with AF treated with anticoagulation.

This retrospective study analyzed the nationwide multicenter Korean ATRial fibrillation EvaluationN regisTry in Ischemic strOke patieNts (K-ATTENTION) registry. Data were collected from consecutive patients, 20 years of age or older, with acute ischemic stroke and AF, seen between January of 2013 in December of 2015. The registry included information concerning demographics, risk factors, stroke subtypes, and severity scale scores.

Data were completed for 1,414 patients with median NIHSS Stroke Scale and HAS-BLED scores of seven and two, respectively. Of these, 2.4% experienced major bleeding. A univariate analysis indicated that major bleeding was associated with a common intracranial atherosclerotic stenosis (ICAS), initial NIHSS Stroke Scale score, hypertension, persistent AF,

CHA2DS2-VASc score (HR 1.42, 95% CI 1.10–1.83,  $p=0.007$ ), and HAS-BLED score (HR 2.49, 95% CI 1.56–3.95,  $p<0.001$ ). A multivariable analysis found that significant predictors of bleeding included the initial score on the NIHSS, hypertension, and persistent AF, while the initial hemoglobin level was negatively associated with major bleeding risk. The risk of major bleeding was approximately 1.1-fold higher in patients with NIHSS scores of seven or more compared to scores of less than seven ( $p<0.001$ ).

**Conclusion:** This study of patients with a history of stroke and atrial fibrillation found independent associations between major bleeding and stroke-specific factors, including stroke severity and intracranial atherosclerosis.

Chung, D., et al. Stroke-Specific Predictors of Major Bleeding in Anticoagulated Patients with Stroke and Atrial Fibrillation: A Nationwide, Multicenter Registry-Based Study. *J Clin Neurol*; 2023, Sept;19(5): 429-437.

### EFFECT OF HIGH INTENSITY WARM UP ON 5,000 METER PERFORMANCE TIME

Previous studies have established the potential benefits of high-intensity warm-up (HIWU) protocols before continuous running, primarily for middle-distance runners. This study investigated the impact of such a warm-up technique on long-distance runners.

This randomized, crossover intervention study included adult male runners with at least one year of experience in running 5,000-meter races. At baseline, all underwent evaluation including anthropometric evaluations, estimate of VO<sub>2</sub> Max, measurement of explosive strength capacity, and performance on a 5,000-meter time trial. Those randomized to the HIWU group began with 500 meters of running at 70% intensity, plus three 250-meter runs at 100% intensity. The low intensity warm up (LIWU) group began with one 500-meter run at 70% intensity followed by three 250-meter runs at 70% intensity. The outcome measures included the Counter Movement Jump (CMJ), rating of perceived exertion (RPE), blood lactate concentration (BLA), and total time of the run.

Performance in the 5,000-meter timed trial was significantly better in the HIWU group ( $p=0.03$ ). In addition,

counter-movement jump (CMJ) height was increased only in the HIWU group ( $p=0.008$ ). The rate of perceived exertion during the time trial did not differ between the groups.

**Conclusion:** This study involving trained endurance runners found that a high intensity warm up protocol can improve performance on a 5,000-meter run.

Alves, M., et al. Effects of High Intensity Warm-Up on 5,000 Meter Performance Time in Trained Long-Distance Runners. *J Sports Sci Med*. 2023; 22: 254-262.

### OZONE INJECTION VERSUS PULSED RADIOFREQUENCY FOR ADHESIVE CAPSULITIS

Adhesive capsulitis (AC) is defined as a condition of varying severity, characterized by gradual development of limited active and passive range of motion. Treatment options include nonoperative and operative procedures. This study assessed the efficacy of ultrasound-guided shoulder intraarticular ozone injection by pulsed radiofrequency (PRF) application versus intraarticular steroid injection in patients with idiopathic AC.

The subjects were 45 adults, 30-65 years of age, with primary shoulder AC. All underwent a standard shoulder examination, with baseline visual analog scores (VAS), Shoulder Pain and Disability (SPADI) scores, and range of motion (ROM) documented. Those randomized to the steroid group, received an intraarticular injection of 5 mL of 0.125% bupivacaine plus 40 mg triamcinolone. The ozone group received an intraarticular injection of 5 mL of 0.125% bupivacaine followed by a 10 mL of an oxygen-ozone mixture (15 µg/mL).

All patients in all groups demonstrated statistically significant improvement after intervention in pain, disability, ROM, and inflammatory markers. The PRF/ozone group demonstrated better VAS pain scores and ROM scores than the steroid group.

**Conclusion:** This study of patients with idiopathic adhesive capsulitis found that ozone therapy and radiofrequency were effective in treating pain and range of motion.

Foula, A., et al. Ultrasound-guided Shoulder Intraarticular Ozone Injection versus Pulsed Radiofrequency Application for Shoulder Adhesive Capsulitis: A

Randomized, Controlled Trial. *Pain Physician*. 2023, July; 26(4): E329-E340.

### THE PREVALENCE AND PROGNOSIS OF ASYMPTOMATIC INTRACRANIAL ATHEROSCLEROSIS

Intracranial atherosclerotic disease (ICAD) is a major cause of ischemic stroke worldwide. This study was designed to better understand the prevalence and prognosis of asymptomatic ICAD.

This prospective, community-based study enrolled individuals 35 years or older, living in Shunyi, a rural district of Beijing. Data included demographic characteristics, socioeconomic status, lifestyle habits, medical histories, and physical/neurological examination results, collected via face-to-face interviews. In addition, biological blood tests, brain MRI, and ultrasonography of the carotid arteries were performed at baseline. Imaging was conducted using a 3Tesla scanner to analyze intracranial atherosclerotic plaques. Intracranial atherosclerotic disease was defined as any stenosis or non-stenotic plaques in the MCA-M1 segment or in the BA detected on HR-MRI. Using these data, the groups were divided into those without ICAD (ICAD-) and those with ICAD (ICAD+). The primary outcome variable was ischemic stroke.

Data analysis included 1,060 participants who were stroke free at baseline. The median follow-up time was 53 months in the ICAD<sup>+</sup> group and 55 months in the ICAD<sup>-</sup> group. A stroke event occurred in 26 participants (6.8%) in the ICAD<sup>+</sup> group compared with 10 participants (1.5%) in the ICAD<sup>-</sup> group ( $p=0.0004$ ). In the adjusted analysis, the hazard ratio for stroke among ICAD+ compared to ICAD- was 2.5 ( $p=0.038$ ). The incidence of stroke increased with ICAD severity, with the greatest risk found among those with  $\geq 70\%$  stenosis.

**Conclusion:** This study of community-based, stroke free, Chinese adults found that the incidental finding of intracranial atherosclerotic disease was associated with a significant increase in the risk of stroke.

Li, S., et al. The Prevalence and Prognosis of Asymptomatic Intracranial Atherosclerosis in a Community-Based Population: Results Based on High Resolution Magnetic Resonance Imaging. *Euro*

**J Neurol.** 2023, Sep 22. doi: 10.1111/ene.16057. Online ahead of print.

### **BLOOD FLOW RESTRICTION TRAINING FOR ROTATOR CUFF TENDONOPATHY**

Blood flow restriction exercise (BFRE) has been introduced as a means to strengthen the muscle with less joint torque. This study was designed to assess the efficacy of BFRE in patients with rotator cuff tendonopathy.

The subjects were 28 patients with rotator cuff tendonopathy who were randomized to an eight-week rehabilitation program involving either BFRE or non-blood flow restriction exercises. The primary outcome measures were the strength in the rotator cuff, deltoid scapular retraction and bicep muscle thickness as well as shoulder internal rotation and external rotation strength.

Those in the BFRE group demonstrated greater increases in bicep muscle thickness and shoulder internal rotation strength at 60 degrees than did the non-BFR group. No differences were noted between groups in other measurements. Both groups demonstrated significant improvements in strength of the supraspinatus, infraspinatus, scapular retractor muscle thickness and in shoulder external rotation and internal rotation strength. Shoulder pain and shoulder function improved in both groups without significant differences between them.

**Conclusion:** This study of patients with rotator cuff tendonopathy found that low load blood flow restriction training could produce greater increases in thickness in the biceps and greater internal rotation strength compared to non-blood flow restriction training.

Dilara, K., et al. Blood Flow Restriction Training in Patients with Rotator Cuff Tendonopathy: A Randomized, Assessor Blinded, Controlled Trial. **Clin J Sport Med.** 2023 Sep 14. doi: 10.1097/JSM.0000000000001191.

### **STEROID INJECTION PLUS EXERCISE FOR PLANTAR FASCIOPATHY**

Plantar fasciitis (PF) is the most common musculoskeletal disorder of the foot. Studies of treatment modalities such as stretching, mobilization or electrophysical agents

have often demonstrated insufficient relief. This study assessed the efficacy of exercise, steroid injections and a shoe insert for the treatment of PF.

This randomized single blind study included 180 adults with the diagnosis of PF. Eligible adults reported heel pain of three or more months and pain on palpation of the medial calcaneal tubercle or proximal plantar fascia. The subjects were randomized to groups to receive patient advice plus heel cup alone (PA) versus PA and lower limb exercise (PAX) versus PAX plus corticosteroid injection (PAXI) of 1mL triamcinolone 20mg/ml (PAXI). The exercise included self-dosed lower limb heavy-slow resistance heel raises to exhaustion at no more than an eight-repetition maximum. Outcomes were measured at baseline and through week 52, with the primary outcome measure of pain measured using the Foot Health Status Questionnaire.

Data were analyzed for 180 patients. At 12 weeks, improvement in pain was better in the PAXI than in the PAX ( $p=0.023$ ). This difference persisted at 52 weeks ( $p=0.045$ ). However, at no time did the difference between groups exceed the prespecified minimally important difference.

**Conclusion:** This study of patients with plantar fasciitis found that adding a corticosteroid injection to a treatment strategy involving resistance exercise and an orthotic could improve outcomes.

Riel, H., et al. Does A Corticosteroid Injection Plus Exercise or Exercise Alone Add to the Effect of Patient Advice and a Heel Cup for Patients with Plantar Fasciopathy? A Randomised Clinical Trial. **Br J Sport Med.** 2023, September; 57(18): 1180-1186.

### **MIGRAINE AND TENSION TYPE HEADACHE IN YOUNG ADULTS**

In 2019, headache disorders were listed as the 14th leading cause of disability-adjusted life years globally. The most common forms of primary headaches were migraines and tension type headaches (TTHs). This study was designed to clarify the epidemiology of headache disorders in youths and young adults.

Data were obtained from the Global Burden of Diseases, 2019, an exhaustive study of 369 diseases and injuries, spanning 204 countries.

These data were used to review migraines and TTHs, among those 15-39 years of age. To identify this diagnosis in medical records, the authors used codes G43-G43.919, G44.2-G44.229, and G44.4-G44.41 from the International Classification of Diseases, 10th revision (ICD-10), to represent migraines and TTH.

The global prevalence of migraine was estimated at 581,761,847.2 cases, representing a 16% increase since 1990. The increase occurred across all age groups. The global prevalence of TTH was estimated at 964,808,567.1 cases, representing a 37% increase since 1990. The global incidence of migraine was estimated to be 43,792,977.8 cases, a 36.7% increase since 1990. The global incidence of TTH was 329, 572, 706.8 cases representing a 37.4% increase since 1990. Over this same time the DALYs increased by 38% for TTH-related DALYs and 40% for migraine related DALYs.

**Conclusion:** This study found that, since 1990, among individuals aged 15 to 39 years of age, the prevalence of migraines increased by 16% and of tension-type headaches increased by 37%.

Li, X., et al. Global, Regional, and National Epidemiology of Migraine and Tension-Type Headache in Youths and Young Adults Aged 15 to 39 Years from 1990 to 2019: Findings from the Global Burden of Disease Study 2019. **J Headache Pain.** 2023, September 18; 24(1):126.

### **SAFETY OF EVINACUMAB FOR REFRACTORY HYPERCHOLESTEROLEMIA**

Cardiovascular disease is a leading cause of global mortality and a significant contributor to disability. Studies have shown an association between elevated low-density lipoprotein cholesterol and increased risk of atherosclerotic disease. As angiopoietin-like protein 3 (ANGPTL3) plays an important role in regulating lipoprotein metabolism, this study assessed the efficacy of a monoclonal antibody which inhibits ANGPTL3 (evinacumab) to reduce LDL-C levels in patients with refractory hypercholesterolemia.

Eligible patients were adults with primary hypercholesterolemia and refractory hypercholesterolemia, despite the use of a PCSK9 inhibitor and maximally tolerated statin. During a double-blind treatment period (DBTP) the subjects were randomly

assigned to receive either subcutaneous or IV evinacumab. During the open-label treatment period (OLTP), the treatment group received 15mg/kg IV for 48 weeks, followed by a 24-week follow-up.

At the end of the open-label portion of the study (72 weeks) evinacumab, 15 mg/kg, reduced LDL-C levels from baseline by a mean of 45.5%, apolipoprotein-B by 38.0%, non-high density lipoprotein cholesterol by 48.4%, total cholesterol by 42.6%, and fasting triglycerides by 57%. Treatment-emergent adverse events occurred in 9.4%, with none thought to be related to the study medication.

**Conclusion:** This study of patients with refractory hypercholesterolemia found that evinacumab, an inhibitor of ANGPTL3, can reduce low-density lipoprotein levels, without significant medication-related adverse events.

Rosenson, R., et al. Longer-Term Efficacy and Safety of Evinacumab in Patients with Refractory Hypercholesterolemia. **JAMA Cardiol.** 2023, Sep. 13:e232921. doi: 10.1001/jamacardio.2023.2921. Online ahead of print.

### LIDOCAINE FOR REFRACTORY PRIMARY HEADACHE DISORDERS

Patients with primary headache disorders and trigeminal neuralgia have been found to benefit from inpatient IV lidocaine infusions over the course of several days. This study investigated the effect of a single, 60-minute, outpatient IV lidocaine infusion for refractory primary headache disorders with facial pain and trigeminal neuralgia.

This retrospective analysis investigated treatment-resistant patients meeting the International Headache Society criteria for primary headache disorders, with facial pain or trigeminal neuralgia. The patients were treated with IV lidocaine 5mg/kg diluted in 60 mL saline infused over one hour. The main outcome measure was the change in headache or facial pain, assessed with a ten-point verbal rating scale. Patients were considered responders if they reported a reduction in intensity of at least 50%.

Forty infusions were administered to fifteen patients, including nine with trigeminal autonomic cephalalgia, three with chronic migraine, and three with trigeminal neuralgia. Of these patients, twelve responded positively to the treatment. Complete relief was

experienced by eight of the twelve responders. The average effect duration of the treatment for those who responded was approximately 9.5 weeks. No significant difference occurred in the duration of treatment effect between those with different diagnoses ( $p=0.495$ ).

**Conclusion:** This study demonstrated that a single infusion of IV lidocaine may be clinically effective for the treatment of refractory primary headache disorders with facial pain or trigeminal neuralgia.

Mullins, C., et al. A Single Infusion of Intravenous Lidocaine for Primary Headaches and Trigeminal Neuralgia: A Retrospective Analysis. **Front Neurol.** 2023, Aug 10; 14: 1202426.

### FRAILITY AND NEUROPSYCHOLOGICAL DEFICITS IN OLDER ADULTS

Frailty is defined as the age-related decline in physiological capacity across several organ systems. Frailty has recently been demonstrated to moderate the relationships between neuropathological hallmarks of Alzheimer's disease and the clinical expression of dementia. This study was designed to understand the clinical utility of measuring a patient's degree of frailty and its impact on the interpretation of neuropsychological testing.

Participants were drawn from three large studies of dementia and cognitive decline including the National Alzheimer's Coordinating Center (NACC), the Rush Memory and Aging Project (MAP) and the Alzheimer's Disease Neuroimaging Initiative (ADNI). Global cognitive functioning was assessed in all studies using the mini- mental state exam (MMSE). A separate frailty index operationalized the degree of age-related health-deficit accumulation in each dataset.

After adjusting for possible confounders higher levels of frailty were associated with worse MMSE performance in all study samples. Participants classified as having low frailty had the smallest decrease in MMSE scores, and participants classified as having high frailty had the largest decrease in MMSE scores, such that those with low frailty tended to have relatively preserved overall cognitive functioning despite discrete neuropsychological deficits.

**Conclusion:** This study of 23,819 older adults found that a higher degree of frailty is associated with

worse cognitive function and found a significant relationship between frailty and scores on neuropsychological and global cognitive function.

Canevelli, M., et al. Frailty Is Associated with the Clinical Expression of Neuropsychological Deficits in Older Adults. **Eur J Neurol.** 2023, Sep 22. doi: 10.1111/ene.16072. Online ahead of print.

### PRIMARY HIP ARTHROSCOPY FOR FEMOROACETABULAR IMPINGEMENT

Femoroacetabular impingement (FAI) syndrome is an established cause of hip pain with an increased risk of progression to osteoarthritis (OA). Among athletes the prevalence of this syndrome is increased compared to the rest of the population due to continuous repetitive forces with extreme ranges of motion at the hip. This study assessed the 10-year survivorship after primary hip arthroplasty for FAI syndrome in athletes.

The subjects were athletes who reported participating in sports within one year before surgery. Hip arthroscopy was recommended when the combination of history, physical examination, and radiographic findings indicated evidence of the FAI syndrome. Before surgery the patients had at least three months of nonsurgical treatment. All had preoperative PROMs for the modified Harris Hip Score (mHHS), Nonarthritic Hip Score (NAHS), Hip Outcome Score—Sport Specific Subscale (HOS-SSS), and visual analog scale (VAS) for pain. The athletes were assessed preoperatively, three months postoperatively, and then annually. At 10 years follow up, all were tested with the same patient reported outcome measures. Survivorship was defined as no conversion to total hip arthroplasty.

Data were analyzed for 189 patients of whom 118 (62.4%) received labral repair and 60(31.7%) received labral debridement. At 10 years, the survivorship was 85.7% with significant sustained improvement from baseline measures for the mHHS, NAHS, HOS-SSS, VAS for Pain and iHOT -12 ( $p<0.001$  for all).

**Conclusion:** This study found a high survivorship and significant and sustained improvement in patient reported measures 10 years after primary hip arthroscopy for the surgical management of the

femoroacetabular impingement syndrome.

Domb, B., et al. 10 Year Survivorship, Outcomes, and Sports Participation in Athletes After Primary Hip Arthroscopy for Femoral Acetabular Impingement Syndrome. *Am J Sport Med* 2023, Sept. :51(9):2383-2393.

### CARE ECOSYSTEM COLLABORATIVE MODEL FOR DEMENTIA

The Care Ecosystem is a collaborative dementia care model that uses a multidisciplinary care team, centered around an unlicensed, specially trained, dementia care team navigator who provides telehealth-enabled support to patients with dementia and their primary caregivers. This paper reviewed the cost savings of this program.

Patients were age 45 years of age or older, each diagnosed with dementia. All had active or pending enrollment in Medicare or Medicaid. The program included assignment to an unlicensed dementia care guide who provided caregiver support, standardized education, and connection to licensed dementia care specialists. The primary outcome variable was the sum of all Medicare claim payments during study enrollment.

The sample partner dyads were randomized, with 303 assigned to a treatment group and 157 to usual care. The adjusted effect of the Care Ecosystem on total cost of care was a reduction of \$3,290 from one to six months post-enrollment ( $p=0.02$ ) and a reduction for months seven to 12 of \$3,207 ( $p=0.04$ ).

**Conclusion:** This study of patients diagnosed with dementia and living in the community found that the Care Ecosystem model reduced Medicare costs, exceeding previously estimated program costs.

Guterman, E., et al. Care Ecosystem Collaborative Model and Healthcare Costs in Medicare Beneficiaries with Dementia: A Secondary Analysis of a Randomized, Clinical Trial. *JAMA Intern Med.* 2023, Sep 18:e234764. doi: 10.1001/jamainternmed.2023.4764. Online ahead of print.

### CARPAL TUNNEL SYNDROME DURING PREGNANCY

Pregnancy related carpal tunnel syndrome (CTS) was first reported in 1957 and thought to mainly occur during the third trimester of pregnancy. This study was designed to determine the proportion of severe

CTS that begins during pregnancy and to better understand the electrodiagnostic characteristics of the median nerve lesion at the wrist in pregnancy related carpal tunnel syndrome (PRCTS).

The subjects were pregnant women with CTS symptoms occurring during pregnancy or in the postpartum period. All were examined clinically and underwent electrodiagnostic studies. These studies were performed bilaterally, with median to ulnar fourth digit peak latency differences determined when previous tests were normal. The incidence of conduction block was determined. These results were compared to an age matched control group selected from a previously published series of 676 patients.

Data were obtained from 130 women with PRCTS onset during pregnancy ( $n=80$ ) or after delivery ( $n=50$ ). These were compared to 57 age-matched women with CTS. For the PRCTS group, the first CTS symptoms occurred during pregnancy in 80 (62%) or after delivery in 50 (38%). The clinical assessments found a higher rate of bilateral and diurnal/permanent paraesthesias, as well as more severe symptoms in the patients with PRCTS compared with patients with idiopathic CTS. The electrodiagnostic studies demonstrated more severe clinical features in the PRCTS group. Of those with PRCTS, 90% demonstrated at least one sensory conduction block.

**Conclusion:** This study of women with carpal tunnel syndrome related to pregnancy found that the electrodiagnostic pattern of these women is an acute or subacute median nerve lesion at the wrist identified by conduction block.

Seror, P., et al. Conduction Blocks of the Median Nerve at the Wrist in Pregnancy and Postpartum Carpal Tunnel Syndrome. *Muscle Nerve.* 2023, Oct;68(4):380-387.

### SCALP ACUPUNCTURE AFTER STROKE

Over the past 20 years, the average global lifetime risk of stroke has increased from 22.8% to 24.9%. As scalp acupuncture is widely used in the clinical treatment of stroke and the rehabilitation of stroke, this study evaluated the mechanism of scalp acupuncture treatment in patients with hemiplegia.

The subjects were 21 patients recruited between two weeks and six months from the onset of an ischemic stroke. The patients were divided into a patient control (PC) group and a

scalp acupuncture (SA) group. Twenty healthy controls (HC) were selected for comparison. The stroke patients were treated with conventional interventions including blood pressure management, lipid lowering agents and anti-platelet medicines. The acupuncture was applied at the right anterior oblique line of vertex temporal (MS6), 30 minutes per day for five days. The patients were assessed at baseline and after 14 days of treatment using the National Institutes of Health Stroke Scale (NIHSS) scores and functional MRI (fMRI). Using the fMRI results, a functional connectivity analysis was used to determine the resting-state functional connectivity (RSFC).

Compared with the HCs, the FC between basal ganglia nuclei with the contralateral brain regions was significantly decreased in patients with hemiplegia after stroke. Also found was that the FC was increased between the sensory and visual-related brain areas in the ipsilateral hemisphere on both affected and healthy sides in hemiplegia patients. After acupuncture, increases were found in the RSFC between the left caudate nucleus and the left medial frontal gyrus with decreased RSFC noted between the left caudate nucleus and the left superior gyrus and left marginal lobe.

**Conclusion:** This study of patients with an ischemic stroke found that scalp acupuncture treatment can strengthen functional connections of the bilateral motor cortex and weaken abnormal compensatory connections.

Lin, D., et al. Scalp Acupuncture Regulates Functional Connectivity of Cerebral Hemispheres in Patients with Hemiplegia After Stroke. *Front Neurol.* 2023; 14:1083066.

### COMBINING TESTS TO DETECT UNILATERAL NEGLECT AFTER RIGHT HEMISPHERE STROKE

Unilateral neglect is characterized by an inability to detect, orient, or respond to contralesional stimuli. Currently, there is no evidence-based consensus to choose the appropriate tests to diagnose unilateral neglect. The study was designed to identify the most accurate and efficient combination of tests to detect unilateral neglect in patients with right hemisphere damage (RHD).

Data were analyzed from previous research involving 203 patients with RHD including ischemic stroke (66%), and hemorrhagic stroke (33.5%), with one patient diagnosed with cerebral tumor. All underwent a

comprehensive battery of clinical tests for unilateral neglect. The test results were compared to those of 307 healthy controls. The tests included the bells test, figure copying, clock drawing, line bisection, overlapping figures test, reading test, and a writing test. The scores were analyzed for an optimal combination that would allow the discrimination between healthy controls and patients with RHD.

A logistic regression analysis found that the combination with the greatest performance was the starting point and the difference between the number of omissions on the left and right sides from the bells test, rightward deviation in bisection of long lines, and left-side omissions in a reading test. This combination provided a positive predictive value of 0.90 and a negative predictive value of 0.82.

**Conclusion:** This study of patients with unilateral neglect secondary to a stroke identified a combination of tests that was efficient and accurate for diagnosing unilateral neglect.

Azouvi, P., Discriminative Value of Different Combinations of Tests to Detect Unilateral Neglect in Patients with Right Hemisphere Damage. *Euro J Neurol.* 2023, October; 30 (10): 3332-3340.

### PLASMA NEUROFILAMENT LIGHT CHAIN PREDICTING ALZHEIMER'S DISEASE

Subjective cognitive decline (SCD) and mild cognitive impairment (MCI) are thought to be the first presentations of Alzheimer's disease (AD). However, these are very common and heterogeneous conditions with several possible trajectories and underlying causes. As neurofilament light chain (NfL) has emerged as a promising blood-based biomarker for AD, this study evaluated the efficacy of NfL to predict the progression of cognitive decline.

Subjects were 140 consecutive patients referred for the assessment of cognitive decline to the Center for Adult Cognitive Disorders of Careggi hospital in Florence, Italy. At baseline, all patients underwent a comprehensive clinical and neurologic examination, extensive neuropsychological investigation, and blood collection for the measurement of plasma NfL, and apolipoprotein E genotype (APOE). One hundred ten patients underwent cerebrospinal fluid collection with 28 also undergoing cerebral amyloid positron emission tomography. The patient

data were scored according to the amyloid/tau/neurodegeneration system and followed for a mean of 2.72 years to assess for progression of the disease.

Seventy-seven patients completed a follow up of two years after the initial blood collection and underwent repeat neuropsychological evaluations. At baseline, plasma NfL levels demonstrated high accuracy (area under the curve of 0.82) for detecting patients with biomarker profiles consistent with AD (A+/T+/N+ or A+/T+/N-), revealing significant differences among the SCD, MCI, and AD-D groups ( $p < 0.001$ ). A post hoc analysis confirmed differences between SCD and MCI ( $p = 0.005$ ) and between SCD and AD ( $p < 0.001$ ) as well as MCI and AD ( $p = 0.006$ ). Notably, the rate of NfL change was higher in the progressive-MCI compared to non-progressive SCD and non-progressive MCI.

**Conclusion:** This study of patients with cognitive decline found that plasma NfL concentration and its longitudinal changes could serve as a reliable tool for the early detection of Alzheimer's disease and the progression of cognitive decline in the earliest stages.

Mazzeo, S., et al. Plasma Neurofilament Light Chain Predicts Alzheimer's Disease in Patients with Subjective Cognitive Decline and Mild Cognitive Impairment: A Cross-Sectional and Longitudinal Study. *Euro J Neurol.* 2023, Oct 5. doi: 10.1111/ene.16089. Online ahead of print.

### SARILUMAB FOR RELAPSE OF POLYMYALGIA RHEUMATICA

Polymyalgia rheumatica (PR) is an inflammatory disease that affects persons over 50 years of age. This disease is characterized by pain and morning stiffness of the shoulder and pelvic girdles with significant negative effects on quality of life. While glucocorticoids (GC) have been the mainstay of treatment for this condition, alternative treatments have been trialed. Among these is sarilumab, a human monoclonal antibody that binds the interleukin-6 receptor alpha and efficiently blocks the interleukin-6 pathway. This study assessed the efficacy and safety of this medication for patients with PR who had previously experienced a disease flare while tapering GC treatment.

This phase three multicenter randomized double-blind placebo-controlled trial included patients with a disease flare of PR who were scheduled for treatment with a

tapering dose of glucocorticoids (GC). The patients were randomized to receive 52 weeks of a twice monthly subcutaneous injection of either sarilumab 200 mg, concurrent with a 14-week GC taper, or placebo plus a 52-week GC taper. The primary outcome was sustained remission at week 52.

Data were reviewed for 117 patients of whom 78 completed the treatment. At 16 weeks the proportion of patients with no signs or symptoms of PR was 57% in the treatment group and 49% in the placebo. At week 52, sustained remission had occurred in 28% of the sarilumab group and in 10% of the placebo group ( $p = 0.02$ ). Inflammation, as measured by serum c-reactive protein levels decrease from baseline to week 52 by 6.9 mg/dL in the treatment group and 1.7 mg/dL in the placebo group.

**Conclusion:** This phase three trial of patients with polymyalgia rheumatica found that treatment with sarilumab, a human monoclonal antibody, resulted in a significantly reduced rate of remission.

Spiers, R., et al. Sarilumab for Relapse of Polymyalgia Rheumatica During Glucocorticoid Taper. *N Eng J Med.* 2023, October 5; 389(14): 1263-1272.

### CHRONIC INFLAMMATORY NEUROPATHIES, ACTIVITY AND SOCIAL PARTICIPATION

Chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN) are the most common chronic inflammatory neuropathies. The outcome measures of most of the recent clinical trials lack an evaluation of limitations of activities experienced by patients. This study was designed to evaluate patient-reported limitations in activity and social participation.

This cross-sectional study was conducted between January 2017 and March 2021 at a neuromuscular clinic in the Netherlands. All adult patients with a diagnosis of CIDP or MMN were invited to participate. The patients were provided a survey including the Rasch-built Overall Disability Scales for inflammatory neuropathies and MMN (I-RODS and MMN-RODS), which assessed limitations in activities, restrictions in and satisfaction with participation, self-reported disease severity, average pain intensity in the last week, fatigue and resilience.

Data were obtained from 147 patients with CIDP, and 103 with MMN with a median time since



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diagnosis of seven and 11 years respectively. Among the CIDP patients, limitations in performing activities were reported as mild by 70.7% and moderate to severe by 22.4%, with only 7.5% reporting no limitations. Half reported using an assisted device. Of the MMN patients 52% reported few or no limitations in performing activities with only 5.9% reporting severe or moderate limitations. Participation restrictions were reported by 50% of CIDP and 40% of MMN patients. A multivariate analysis found that limitations in activities were associated with fatigue, moderate to severe pain, increased age and more resilience.

**Conclusion:** This study of patients with chronic inflammatory demyelinating polyneuropathy and chronic multifocal motor neuropathy found that, despite optimal immunomodulating medications, limitations in activity and participation are common, though are less prevalent and severe in those with multifocal motor neuropathy.

Wonink, H., et al. Chronic Inflammatory Neuropathies and Their Impact on Activities and Participation. *Europ J Neurol.* 2023, July; 30(7): 1928-1936.

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