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## CONCURRENT STRENGTH AND ENDURANCE TRAINING FOR RUN PERFORMANCE

Training to improve distance running performance has traditionally been through aerobic training. However, new evidence suggests that concurrent strength and endurance training may have added benefits. This study assessed the effects of a 10-week program of concurrent strength and endurance (CSE) exercises on running performance and biomechanics.

Subjects were 28 distance runners assessed at baseline for demographics, event specialization, weekly endurance training loads, and results of a $VO_2$ max test. The participants were randomly assigned to either a CSE training group or a control group. In addition to their normal running training, the CSE group undertook strength training two days per week for 10 weeks. Hip and knee extensors were targeted using 70% of the one-repetition maximum. Running performance was measured using a 2km timed trial. Biomechanical and muscle activity data were collected while the subjects were running on a synthetic track. A motion analysis system assessed kinetics and kinematics during running.

Running time improved more in the CSE group than in the control group (p= 0.006). After the intervention, 64% of the CSE group and 36% of the control group had improved in $VO_2$ max by at least 2.2%. Time to exhaustion during the $VO_2$ max test was 12% longer in the CSE group (p= 0.024) than in the control group.

**Conclusion:** This study found that hip and knee extensor strength training, when added to endurance training, can improve running performance.

Trowell, D., et al. Effect of Concurrent Strength and Endurance Training on Run Performance and Biomechanics: A Randomized, Controlled Trial. **Scand J Med Sci Sports.** 2021, November 12. doi: 10.1111/sms.14092. Epub ahead of print.

## DIRECT CURRENT STIMULATION AND NEUROTROPHIC FACTOR IN KNEE OSTEOARTHRITIS

Previous studies have demonstrated the positive effects of transcranial direct current stimulation (tDCS) for the treatment of chronic pain. As brain-derived neurotrophic factor (BDNF) has been implicated in pain modulation, this study assessed the effect of tDCS on BDNF levels among patients with symptomatic osteoarthritis of the knee (KOA).

Subjects were 50 to 70 years of age with symptomatic KOA. The patients were randomly assigned to active or sham tDCS for 20 minutes for five consecutive days. At baseline and after the final treatment session, BDNF was measured for comparison between groups. Follow-up analyses evaluated change in log-BDNF as a function of change in pain scores (NRS; WOMAC).

Compared with baseline, the sham tDCS treatment resulted in significantly higher BDNF levels than did the tDCS group. A positive relationship was found between changes in pain scores and changes in BDNF. For the NRS, strong evidence (posterior probability (PP) =91.2%) supported this relationship. For the WOMAC, moderate evidence (PP=88.1 %) supported this relationship.

**Conclusion:** This randomized, controlled trial found that transcranial direct current stimulation for 20 minutes on five consecutive days significantly decreased levels of brain -derived neurotrophic factor.

Suchting, R., et al. Changes in Brain-Derived Neurotrophic Factor from Active and Sham Transcranial Direct Current Stimulation in Older Adults with Knee Osteoarthritis. **Clin J Pain.** 2021, December 1; 37(12): 898-903.

## ATRIAL FIBROSIS IN EMBOLIC STROKE OF UNDETERMINED SOURCE

Embolic stroke of undetermined source (ESUS) accounts for up to 30% of ischemic strokes. Atrial fibrillation (AF) is a common cause of embolic stroke and has long been suspected to account for many cases of ESUS. However, extended cardiac monitoring using an implantable loop recorder has resulted in a reported detection rate of 30% after three years, leaving two thirds without an etiology. This study assessed whether left atrial (LA) cardiac disease is a risk factor for a stroke independent of AF.

Subjects were 203 patients from three centers. These included 103 patients without known AF (35 healthy controls, 15 with lacunar strokes and 53 with ESUS) and 100 patients with AF (50 with and 50 without prior stroke). To measure LA fibrosis, a cardiac LGE-MRI was completed within three months of stroke diagnosis. The primary outcome variable was the combination of recurrent ischemic stroke, incident AF or both.

The MRI findings indicated LA fibrosis in 15% of those with ESUS, 8.1% of healthy controls (p=0.001), and 10.8% of lacunar stroke patients (p=0.034). At 19-month follow-up, 16.9% of patients with LA fibrosis experienced a recurrent stroke or incident AF. A Cox regression demonstrated that LA fibrosis of ≥12% was associated with a hazard ratio of 4.90 for the combined outcome of recurrent ischemic stroke, incident AF or both. (p = 0.02).

**Conclusion:** This study of patients with embolic stroke of undetermined source found that left atrial fibrosis is associated with recurrent stroke.

Künhnlein, P., et al. Atrial Fibrosis in Embolic Stoke of Undetermined Source: A Multicenter Study. **Eur J Neurol**. 2021 Nov; 28(11): 3634-3639.

## LOWERING BLOOD PRESSURE AND RISK OF TYPE 2 DIABETES

Although blood pressure control is an established strategy for preventing microvascular and macrovascular events in people with type 2 diabetes, its benefit for preventing diabetes is less clear. This literature review and meta-analysis assessed data from large-scale, randomized trials to establish the comparative effects of five major blood pressure-lowering drug classes, and the risk of type 2 diabetes.

Data were gathered from all primary and secondary prevention trials which used a specific class or classes of antihypertensive drugs, with at least 1,000 person-years of follow-up in each randomly allocated arm.

Data for the meta-analysis included 80,500 men and 57,429 women. The rate of a new-onset type 2 diabetes events per 1,000 person-years was 16.44 in the comparison group and 15.94 in the intervention group. Each five mm Hg medically influenced lower systolic blood pressure was associated with a 12% lower risk of type 2 diabetes. By drug type, a decrease in risk was noted with angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs). The risk was increased with the use of thiazide diuretics and β blockers. No change in risk was found for calcium channel blockers.

**Conclusion:** This meta-analysis, comparing blood pressure-lowering treatment with the risk of new-onset type 2 diabetes found that each five-mmHg reduction in blood pressure resulted in a 12% reduction in the risk of type 2 diabetes.

Nazarzadeh, M., et al. Blood Pressure Lowering and Risk of New Onset Type 2 Diabetes: An Individual Participant Data Meta-analysis. **Lancet.** 2021, November 13; 398: 10313.

## ROLE OF OPHIOPOGONIN D IN ATHEROSCLEROSIS

Ophiopogonin-D is a steroidal saponin isolated from the root of the Chinese medicinal plant Ophiopogon japonicas. Previous studies have demonstrated pharmacological activities including anti-oxidative, inhibition of venous thrombosis, and anti-inflammatory. As ophiopogonin D (OPD) has been shown to alleviate the metabolic syndrome, this animal study investigated the potential for OPD to alleviate atherosclerosis.

Subjects were 25, eight-week-old, ApoE negative, male mice. All were fed a high fat diet containing 21% fat and 0.15% cholesterol for 12 weeks. The subjects were divided into three groups: a model group, an OPD group (0.5 mg/kg/d) and a simvastatin group (5 mg/kg/d). Blood was collected throughout the study and histologic tissue samples were collected after the 24-week experiment. The composition of the gut microbiota were assessed at baseline and follow-up.

After 12 weeks of treatment, those in the OPD group had a significantly greater reduction in plaque formation and lipid levels than those in the model group. The treatment group also demonstrated improved oral glucose tolerance and insulin resistance, as well as reduced hepatocyte steatosis. In addition, the OPD group had a reduced abundance of gut *Erysipelotrichaceae genera* associated with cholesterol metabolism.

**Conclusion:** This animal study found that the use of Ophiopogonin D, a pharmacological compound of *Ophiopogonin japonicus*, could slow plaque progression and improve lipid metabolism.

Zhang, Y., et al. The Role of Ophiopogonin D in Atherosclerosis: Impact on Lipid Metabolism and Gut Microbiota. **Am J Chinese Med.** 2021; 49: 1449-1471.

## RESTARTING ANTIPLATELET THERAPY AFTER HEMORRHAGIC STROKE

Approximately one third of adults in high income countries with stroke caused by spontaneous intracerebral hemorrhage (ICH) are already taking oral antithrombotic drug therapy at the time of the event. This study, using data from the Restart or Stop Antithrombotics Randomized Trial (RESTART) extended follow-up time to better understand the effects of restarting oral antithrombotic drug therapy.

The RESTART trial included adults who had survived for at least 24 hours after a spontaneous ICH. Those in a treatment group started antiplatelet therapy, including oral aspirin, dipyridamole or clopidogrel, administered within 24 hours of randomization. The primary outcome variable was fatal or nonfatal,

recurrent symptomatic ICH. The patients were followed up to seven years.

Of the 537 patients, the primary outcome variable occurred in 8.2% of the antiplatelet therapy group and 9.3% of the controls. A major vascular event affected 72 participants (26.8%) allocated to antiplatelet therapy compared with 87 participants (32.5%) allocated to avoid antiplatelet therapy with an adjusted hazard ratio of 0.79 (p=0.14).

**Conclusion:** This study of survivors of an intracranial hemorrhage found that restarting antiplatelet therapy did not increase the risk of recurrent intracerebral hemorrhage and decreased the risk of major vascular events.

Al-Shahi Salman, R., et al. Effects of Antiplatelet Therapy after Stroke Caused by Intracerebral Hemorrhage: Extended Follow-Up of the RESTART Randomized, Clinical Trial. **JAMA Neurol**. 2021, October 1; 78(10): 1179-1186.

## CHINESE MEDICINE FOR OSTEOARTHRITIS OF THE KNEE

In 2013, The Chinese Public Welfare Industry Research Project approved the Triple Rehabilitation Therapy Chinese Medicine (CM) method for treating knee osteoarthritis (KOA). This multicenter, prospective study assessed the efficacy of this intervention.

Subjects were patients 40 to 75 years of age with symptomatic KOA. Those randomized to the CM group received electroacupuncture, Chinese medicinal herb fumigating-washing of the knee (mixture containing *Cortex erythrinae* 15 g, *Speranskia tuberculata* 15 g, *Artemisiae argyi folium* 15 g, *Lycopodii herba* 15 g, *Aconiti radix* 10 g, Aconiti kusnezoffi *i radix* 10 g, *Zanthoxyli pericarpium* 8 g, *Angelicae dahuricae radix* 10 g, *Clematidi radix et rhizome* 10 g, *Carthami flos* 5 g, *Chuanxiong rhizoma* 5 g, *Taxilli herba* 15 g, *Drynaria rhizoma* 15 g and *Dipsaci radix* 15 g) and traditional exercises six days per week for four weeks. Those in the control group received "three-step-six style" knee exercises (based on Tai Chi, Baduanjin, and Yijinjing), electromagnetic wave therapy 20-30 minutes per day, joint movement training, and muscle strength training. Outcome measures were the Lequesne Index scores, VAS pain scores, range of motion, lower limb muscle strength, knee joint circumference, quantitative scores of KOA symptoms, and the Short Form-36 Health Survey Questionnaire.

Data were completed for 696 outpatients. At two and four weeks, greater improvement was noted in the CM group than in the control group for scores on the Lequesne Index ($p<0.01$), VAS pain scores, and SF-36 scores of physical functioning, role -physical, body pain, social functioning, and role-emotional ($p<0.05$ or $p<0.01$).

**Conclusion:** This study of adults with osteoarthritis of the knee found that Chinese medicine involving triple rehabilitation therapy was superior to conventional therapy for improving pain and function.

Jie-mei, G., et al. Chinese Medicine Involving Triple Rehabilitation Therapy for Knee Osteoarthritis in 696 Outpatients: A Multicenter, Randomized, Controlled Trial. **Chin J Integr Med**. 2021; Oct; 27(10): 729-736.

## PHANTOM EXERCISES FOR LOWER LIMB AMPUTEES

Phantom limb pain (PLP) is a common complaint after lower limb amputation. While PLP subsides with time in most patients, it may persist for years in up to 10%. This study assessed the effect of phantom exercises on PLP.

This randomized trial included 24 lower extremity amputees, 18 to 60 years of age, with phantom limb pain of four or greater on a visual analog scale (VAS). All participants received daily mirror therapy for 15 minutes and routine physical therapy for 20 minutes. Those randomized to an experimental group engaged in phantom motor execution (phantom limb exercises) for an additional 15 minutes. These exercises included imagining movement of the phantom limb and attempting to execute these movements. Evaluations were completed at baseline and after two and four weeks of intervention using the VAS for pain, the AMP Mobility scale, and the RAND SF-36 Quality of Life Questionnaire.

The VAS pain scores significantly improved in both treatment groups after two and four weeks. At four weeks, the experimental group enjoyed greater pain relief than the control group ($p= 0.003$). Quality of life scores significantly improved in both groups, although the domain of bodily pain was superior in the experimental group at four weeks ($p=0.012$).

**Conclusion:** This study of patients with phantom limb pain found that phantom exercises, added to traditional intervention, could accelerate recovery from pain.

Zaheer, A., et al. Effects of Phantom Exercises on Pain, Mobility and Quality of Life among Lower Limb Amputees; A Randomized, Controlled Trial. **BMC Neurol.** 2021; 21: 416.

## LATERAL ANKLE INSTABILITY–INDUCED NEUROPLASTICITY

After an initial acute ankle sprain, up to 40% experience recurring ankle injuries, termed lateral ankle instability (LAI). As researchers have found that neuroplasticity occurs in musculoskeletal disorders, this study assessed the morphological brain differences associated with LAI.

Subjects were 35 patients seen for unilateral LAI and 35 without a history of ankle injury. All underwent MRI brain scans. From these scans, regional grey matter volume was determined and compared between groups.

The grey matter volume within a cluster in the cerebellar vermis was significantly lower in the LAI group than in the control group ($p<0.001$). A multivariable analysis revealed that lower grey matter volumes were associated with a longer duration of LAI ($p=0.092$).

**Conclusion:** This study of patients with lateral ankle instability found that these patients had reduced grey matter volume within the cerebellar vermis, and that the degree of this reduction was associated with the duration of the instability.

Xue, X., et al. Lateral Ankle Instability -Induced Neuroplasticity in Brain Grey Matter: A Voxel Based, Morphometry MRI Study. **J Sci Med Sport.** 2021, December; 24 (12): 1240-–1244.

## RETURN TO SPORT AFTER ACUTE LATERAL ANKLE SPRAIN

Lateral ankle sprains are one of the most common injuries sustained during sport. No criteria-based guidelines are available to inform decisions to return to sport following an acute ankle sprain. This study was designed to establish a

consensus opinion from a panel of experts.

The panels were chosen from among health and exercise professionals, working with athletes competing on nationally selected teams in field or court sports, wherein acute lateral ankle sprain injuries are the most prevalent. The authors used the three-round Delphi approach to establish a consensus of opinion. For each survey round, the level of agreement was calculated for each item.

Data were completed for each round by 119 participants. Using a consensus of return to sport assessment items, five domains were created and proposed to the panel. These were pain, ankle impairments, athletic perception, sensorimotor control, and sports/function performance. Items for which there was at least 90% agreement included sports specific activities, pain severity during sport participation and ankle range of motion. Items for which there was at least 85% agreement included completion of a full training session, agility, hopping and ankle muscle strength.

**Conclusion:** This consensus of experts in ankle sprain determined that the items that should be used to inform return to sport after an acute ankle sprain include assessment of pain severity, ankle impairments, sensorimotor control, athletic perception/readiness, and sport/ functional performance.

Smith, M., et al. Return to Sport Decisions after an Acute Lateral Ankle Sprain Injury: Introducing the PAASS Framework: An International Multidisciplinary Consensus. **Br J Sports Med.** 2021; 55: 1270-1276.

## EARLY CARDIAC REHABILITATION FOLLOWING ACUTE MYOCARDIAL INFARCTION

One of the leading causes of congestive heart failure (CHF) is acute myocardial infarction (AMI). Research has shown that secondary prevention through comprehensive cardiac rehabilitation (CR) is a cost-effective means to ensure a favorable outcome after an MI. This study evaluated the effects of CR on patients with CHF after an AMI, following percutaneous coronary intervention (PCI).

This retrospective study included patients with AMI with CHF following PCI. Patients were divided according to those with heart failure with reduced ejection fraction (HFrEF; n = 54) and those with heart failure with mid-range ejection fraction (HFmrEF; n = 178). Seventy-eight patients who participated in two-week cardiac rehabilitation were further divided into two subgroups based upon major adverse cardiovascular events. Patients were followed every three months from discharge. The CR included three supervised regular exercise sessions per week on a bicycle and four supervised electrical stimulation sessions per week on alternate days. The primary outcome variable was major adverse cardiac events (MACE), including cardiogenic death and rehospitalization.

For the HFrEF group, a MACE occurred in 59.4% of the control group and 18.2% of the CR group (p=0.005). For the HFmrEF group, a MACE occurred in 29.5% of the controls and in 3.6% of the CR group. For patients with HFrEF, rehospitalization occurred in 28.1% of the control group and in 18.2% of the CR group. For those with HFmrEF, rehospitalization occurred in 22.1% of the control group and in 3.6% of the treatment group.

**Conclusion:** This study of patients with heart failure after an acute myocardial infarction found that a two-week program of early cardiac rehabilitation involving active and passive exercise could reduce major cardiac events and rehospitalization.

Cai, H., et al. Effect of Early Cardiac Rehabilitation on Prognosis in Patients with Heart Failure following Acute Myocardial Infarction. **BMC Sports Science, Med Rehabil**. 2021; 13: 139.

## LONG-TERM TRAJECTORIES OF COGNITION AND FUNCTION BEFORE AND AFTER STROKE

Data have demonstrated that after a stroke, patients show an acute accelerated decline of cognitive and daily functional activity, continuing for up to 10 years. This study compared the long-term temporal patterns of declining cognition and daily functioning before and after a stroke.

Data were obtained from the Rotterdam study, a large, prospective, population based, cohort study in the Netherlands. The cohort was initiated in 1990 and was expanded from 2000 to 2006, with a total of 14,926 participants 45 years of age or older. All patients were interviewed every four years, with tests including the Mini-Mental State Examination (MMSE), routine cognitive assessment and measurement of activities of daily living. Those who suffered a stroke during follow-up were matched with three, stroke free participants.

During a mean 12.5 years' follow-up, 1,662 participants suffered a first ever stroke. At eight years before the stroke, the cognitive scores of future stroke patients began to deviate from those of the controls. This difference was noted on the Stroop Test, the Verbal Fluency Test, and the Purdue Pegboard Test. Basic and instrumental activities of daily living (BADL and IADL) trajectories of future stroke patients began to deviate from their stroke-free status at eight and seven years, respectively. Those with the APOEe4 genotype and lower education levels were most vulnerable to cognitive and functional deterioration before their stroke.

**Conclusion:** This data from the Rotterdam study found that patients who suffer a first ever stroke will have experienced a decline in cognition and activities of daily living beginning several years prior to the stroke diagnosis.

Heshmatollah, A., et al. Long-Term Trajectories of Decline in Cognition and Daily Functioning before and after Stroke. **J Neurol Neurosurg Psychiat.** 2021, Nov;92(11):1158-1163.

## INFLUENCE OF COHABITATION ON FAMILY CAREGIVERS OF PEOPLE WITH DEMENTIA

Previous studies have demonstrated that family caregivers of people with dementia experienced high emotional stress, depression, and reduced quality of life. This study compared the effects on caregivers when living with the patient with dementia.

Data Were Acquired from The Korean Community Health Survey (CHS). Three groups were identified for comparison. Group one comprised families with no members diagnosed with dementia (D-). Group two included families with a member diagnosed with dementia, who were not living together (D+L-). Group three included those who were living with a family member diagnosed with dementia (D+L+). All answered questions concerning depressive symptoms, stress perception rate,

subjective health, subjective happiness, and the EuroQol-5.

Data were obtained from 306,609 D- families, 12,540 D+L- families and 4929 D+L+ families. For depressive symptoms and stress recognition, the highest scores occurred in the D+L+ group, the second highest in the D+L- group and lowest scores in the D- group ($p<0.001$ for all comparisons). Subjective health and happiness were worst in the D+L+ group, second worst in the D+L- and best in the D- group ($p<0.001$ for all comparisons).

**Conclusion:** This Korean study found that, among families with a member diagnosed with dementia, those who lived with that family member had worse scores on depression, stress recognition, subjective health, happiness, and quality of life than did family members who did not cohabitate.

Park, M., et al. The Influence of Cohabitation Type on the Psychological Vulnerability of Family Caregivers of People with Dementia: Results from a Community Health Survey of 324,078 People in Korea. **Arch Gerontol Geriatr**. 2022, January-February: 04558.

## MIRTAZAPINE FOR AGITATION IN DEMENTIA

Mirtazapine is among the most commonly prescribed antidepressants for older people and those with dementia. The study was designed to understand the clinical efficacy and safety of mirtazapine in patients with Alzheimer's disease (AD) with agitation.

This multicenter, parallel group, double-blind, placebo controlled, randomized trial included patients with probable or possible AD and coexisting agitation. The Cohen-Mansfield Agitation Inventory (CMAI) was used to measure agitation. The subjects were randomized to receive either the placebo or mirtazapine, with a target dose of 45 mg per day. Caregivers were contacted at weeks two and four to complete questionnaires concerning adverse effects and adherence. The primary outcome variable was the reduction of agitation, as measured by the CMAI at 12 weeks.

Data were completed for 102 patients in the mirtazapine group and 102 in the placebo group. The severity of agitation decreased in both groups by week six and continued to be lower than baseline at week 12. At no point in the unadjusted or adjusted analyses did the CMAI scores differ between groups.

**Conclusion:** This study of patients with Alzheimer's disease and agitation found that mirtazapine, given with normal clinical care, is not clinically effective for the treatment of agitation.

Banerjee, S., et al. Study of Mirtazapine for Agitated Behaviors in Dementia (SYMBAD): A Randomized, Double-Blind, Placebo Controlled Trial. **Lancet.** 2021; 398: 1487-1497.

## ANXIETY RELATED CONCUSSION PERCEPTIONS OF COLLEGIATE ATHLETES

Increased awareness of sports related concussions has resulted in a number of positive changes. This study was designed to identify anxiety that is related to concussion perceptions of collegiate athletes and factors associated with this anxiety.

This cross-sectional study included athletes between 18 and 26 years of age from four NCAA division I, two division II and one division III university. The participants completed a survey regarding personal and sports demographics, diagnosed concussion history, mood disorder history, concussion knowledge, injury perceptions and sources of concussion information. Participants were instructed to identify concussion signs and symptoms and to answer general concussion knowledge questions. Injury perceptions were assessed using the Perception of Concussion Inventory for Athletes (PCI-A).

Data were provided by 482 athletes with an average age of 19.7 years. Of these, 291 (60.7%) agreed or strongly agreed that the possibility of sustaining a concussion is upsetting to them. In addition, 222 (46.7%) stated that they were worried about concussions, 194 (40.7%) were fearful of sustaining a concussion and 119 (25.0%) felt anxious at the thought of sustaining a concussion.

**Conclusion:** This study found that negative, anxiety related perceptions about concussions are prevalent in the collegiate athlete population.

Beidler, E., et al. Anxiety Related Concussion Perceptions of Collegiate Athletes. **J Sci Med Sport.** 2021, December; 24(12): 1224-1229.

## AEROBIC EXERCISE AND POSTCONCUSSIVE SYMPTOMS

Current sport-related concussion recommendations emphasized the importance of physical activity, and sub-symptom aerobic exercise as a key component of active recovery. These recommendations are vague and do not account for exercise dosing. This study sought to determine the optimal volume of exercise associated with symptom resolution at one month.

Study participants were 14 to 21 years of age, seen at a medical facility for the treatment of a concussion. Those randomized to a treatment group were instructed to exercise at a target heart rate determined at an exercise test at the initial visit. Sessions occurred five days per week, 20 minutes per day. At each visit, the patients were assessed with the Post-Concussion Symptom Inventory (PCSI). Activity logs were used to determine exercise volume each week. Those with volumes of <100 minutes per week (low volume) were compared to those with > 100 minutes per week (high volume).

Those in the high-volume group reported significantly lower symptom severity scores at one month than those in the low volume group ($p=0.03$). A volume of 160 minutes per week successfully discriminated between those with and those without symptoms at one month after study commencement.

**Conclusion:** This study of patients newly diagnosed with concussion found that a greater aerobic exercise volume within the first month is associated with lower symptom burden at one month.

Howell, D., et al. Influence of Aerobic Exercise Volume on Postconcussive Symptoms. **Am J Sports Med.** 2021, July; 49 (7): 1912-1920.

## GREY MATTER CHANGES WITH DIRECT CURRENT STIMULATION FOR EPISODIC MIGRAINE

After low back pain, migraine is the second most disabling condition worldwide. Several studies have demonstrated the efficacy of transcranial direct current stimulation (tDCS) for the treatment of migraine. As patients with migraine also undergo structural changes in several cortical and subcortical areas related to perception and pain processing,

this study investigated the effects of tDCS on those structural changes.

The subjects were 18 to 80 years of age, all diagnosed with episodic migraine (EM). The participants were randomized to receive 20 minutes per day for 28 days of either true or sham tDCS with anode stimulation over the visual cortex. All subjects underwent structural MRI at baseline and then again at 1.5 months and 5.5 months after completion of the treatment protocol. Headache diaries were completed throughout the duration of the trial. Controls were 31, healthy matched subjects without a history of migraine.

Compared to the sham group, the tDCS treatment group experienced a reduction of 1.9 migraine days per month. Compared to healthy controls, the patients with migraines showed significantly increased grey matter volume in the left lingual gyrus (p=0.003). This volume decrease paralleled the reduction in migraine days per month.

**Conclusion:** This study demonstrated that patients with episodic migraine headaches have increased grey matter volume in the left lingual gyrus, which can be reduced through treatment with transcranial direct current stimulation.

Schading, S., et al. Tracking tDCS Induced Grey Matter Changes in Episodic Migraine: A Randomized, Controlled Trial. **J Headache Pain**. 2021; 22: 139.

## MIGRAINE PAIN INTENSITY IN PATIENTS TREATED WITH ERENUMAB

Previous studies have demonstrated that erenumab can reduce monthly migraine days among patients with episodic and chronic migraine. This *post hoc* analysis reports on two studies of erenumab in patients with episodic migraine (EM) or chronic migraine (CM).

Data were obtained from two, randomized, double blind, placebo-controlled trials, including patients with EM and or CM. Those in the EM study were randomized to receive placebo or erenumab, 70 mg or 140 mg, once monthly for three months. Those in the CM study were randomized (3:2:2) to receive placebo, erenumab 70 mg or erenumab 140 mg, once monthly for three months. In the analysis, a series of pain intensity-related outcomes were included. These were cumulative monthly migraine pain (CMMP), summing the peak pain intensity scores, the monthly average migraine pain (MAMP), averaging the peak pain intensity scores, and the monthly average migraine pain in MMD responders (those who achieved over 50% improvement in pain).

For the CMMP, compared to placebo group, the 70 mg and 140 mg treatment groups had a greater reduction in cumulative pain. Values for the MAMP were significantly more improved in the treatment group than in the placebo group for the EM group (p<0.001) but were non-significant for the CM group.

**Conclusion:** This *post hoc* analysis of two, randomized, double blind, placebo-controlled trials found that cumulative monthly migraine pain can be reduced by once per month intake of erenumab.

Lipton, R., et al. Reduction in Migraine Pain Intensity in Patients Treated with Erenumab: A *Post Hoc* Analysis of Two, Pivotal, Randomized Studies. **Cephalalgia.** 2021, 41 (14): 1458-1466.

## METHYLPHENIDATE FOR APATHY IN ALZHEIMER'S DISEASE

Apathy is one of the most prevalent neuropsychiatric symptoms experienced by patients with Alzheimer's disease (AD). The Apathy in Dementia Methylphenidate Trial (ADMET-2) suggested that treatment with methylphenidate could improve global cognition, with minimal adverse events. This study assessed the efficacy of methylphenidate for the treatment of apathy.

Subjects were diagnosed with possible or probable AD with clinically significant apathy. The participants were randomized to receive either placebo or methylphenidate at five mg twice per day for three days, followed by 10 mg twice per day for the remainder of the study. The primary outcomes were changes in Neuropsychiatric Inventory Apathy (NPI Apathy) scores from baseline to six months and the odds of an improved rating on the Alzheimer's Disease Cooperative Study Clinical Global Impression of Change (ADCS-CGIC).

Data were available for 72 patients in the methylphenidate group and for 80 in the placebo group. At six months, the change in NPI apathy scores was greater in the methylphenidate group than in the placebo group (p=0.002). The odds ratio of having an improved rating on the ADCS-CGIC for the methylphenidate group compared to placebo was 1.90.

**Conclusion:** This study of patients with Alzheimer's disease found that methylphenidate could significantly improve apathy scores.

Mintzer, J., et al. Effect of Methylphenidate on Apathy in Patients with Alzheimer's Disease: The ADMET 2 Randomized, Clinical Trial. **JAMA Neurol.** 2021, Nov 1; 78 (11): 1324-1332.

## CUBITAL TUNNEL PERFUSION AND POSTURE

Cubital tunnel syndrome is the second most common compression mononeuropathy. Treatments include splints to inhibit elbow flexion and patient education to avoid predisposing upper extremity postures. This cadaveric study assessed cubital tunnel perfusion at different upper extremity postures designed to progressively increase the tension of the ulnar nerve.

The axillary artery of 30 cadaveric upper extremities was injected with an ultrasound contrast agent for 30 seconds at a constant pressure of 140 mmHg. Ultrasound was performed to record the perfusion at each of five different arm postures. Joint positions were chosen that caused elongation of the ulnar nerve and, thus, created increased tension with each progressive position. Maximum relaxation was noted in posture one with the shoulder at 30° abduction, elbow maximum extension, the radioulnar joint at neutral, wrist at neutral, and fingers at neutral.

Elbow flexion alone did not significantly reduce perfusion but caused significant narrowing of the cubital tunnel. Significant narrowing was also found with elevation of the shoulder. Compared with posture one, posture five resulted in a significant decrease in perfusion (p<0.001). Compared with posture one, representing maximum relaxation, shoulder elevation plus elbow flexion (posture three) impeded perfusion significantly.

**Conclusion:** This cadaveric study demonstrated that, as increased tension is placed on the ulnar nerve,

decreased perfusion occurs at the cubital tunnel.

Rossmann, T., et al. Cubital Tunnel Perfusion at Different Postures-An Anatomical Investigation. **Musc Nerve.** 2021, December; 64(6): 749-754.

## THE 14-3-3 EPSILON COMPONENT OF TNFR2 AND OSTEOARTHRITIS

Despite the prevalence of osteoarthritis (OA), effective disease modifying treatments are not currently available. Research has demonstrated that TNFR2 can inhibit inflammation and prevent bone loss in inflammatory arthritis.

This study used biochemical, copurification and proteomics screens to isolate the intracellular cofactors of the TNFR2 complex. Eight proteins were found to specifically bind to TNFR2. The protein ranking first was 14-3-3ε. The authors then created 14-3-3ε deficient mice to validate the interaction between TNFR2 and 14-3-3ε.

The mice with 14-3-3ε deficiency were found to have an exaggerated OA. Both global and chondrocyte-specific deletion of 14-3-3ε largely abolished PGRN's therapeutic effects against OA. Ensuing experiments indicated that 14-3-3ε was specifically recruited to TNFR2 following PGRN treatment in chondrocytes and exert chondroprotective effects as an essential mediator of PGRN/TNFR2 signaling in regulating chondrocyte metabolism. These results suggest a previously unrecognized TNFR2 pathway in the pathogenesis of OA.

**Conclusion:** This study found that 14-3-3ε is a crucial component of the TNFR2 receptor complex in chondrocytes and osteoarthritis, establishing a novel signaling paradigm to combat the inflammatory and catabolic components of osteoarthritis.

Fu, W., et al. 14-3-3 Epsilon is an Intracellular Component of TNFR2 Receptor Complex and its Activation Protects against Osteoarthritis. **Ann Rheum Dis**. 2021, December; 80 (12): 1615-1627.

## MUSCLE POWER, ADIPOSITY AND ALL CAUSE MORTALITY

Research has found that maintaining an adequate cardiorespiratory fitness at an older age decreases the risk of all-cause mortality, independently of overall or abdominal adiposity. However, muscle power has been found to be more strongly related to functional status in older adults than has cardiorespiratory capacity. This study evaluated a group of older individuals to compare the all-cause mortality risk between those with different combinations of adiposity and muscle power.

This prospective study included a representative sample of non-institutionalized adults, 65 years of age or older, living in Spain. Data were collected by personal interviews and physical examinations. During the physical examination, anthropometrics, body composition and muscle power were assessed. Those with a BMI of ≥30 kg/m$^2$ in both men and women were labelled "fat" (F). Weak (W) was defined as a normalized muscle power value, determined during a sit to stand protocol, of < 75.4 W/m$^2$ in men and <61.5 W/m$^2$ in women. The participants were assigned to one of four groups: lean and powerful (LP), fat and powerful (FP), lean and weak (LW) or fat and weak (FW). All-cause mortality was collected through the Spanish National Death Index over a median follow-up of 8.9 years.

Compared to the FW group, the risk of all-cause mortality was significantly lower in the FP, and LP groups (p=0.044 and p=0.043, respectively). When introduced as a continuous variable, higher relative muscle power significantly reduced mortality risk, independently of age, gender, hypertension, smoking and walking and sitting times (p=0.025).

**Conclusion:** This study of Spanish adults, 65 years of age or older, found that muscle power is inversely related to the risk of mortality, independent of age, gender, hypertension, smoking and activity levels.

Alcazar, J., et al. Fat but Powerful Paradox: Association of Muscle Power and Adiposity Markers with All-Cause Mortality in Older Adults from the EXERNET Multicentre Study. **Br J Sport Med.** 2021; 55 (21): 1204-1211.

## PELVIC FLOOR DISORDERS STOP WOMEN FROM EXERCISING

Pelvic floor (PF) disorders affect one in four Australian women. During sports/exercise, a load may be placed on the PF, resulting in symptoms of PF disorders. This study investigated the impact of PF symptoms on women's physical activity.

This cross-sectional survey included Australian women 18 to 65 years of age who had experienced current, past or a fear of PF symptoms while exercising. Data were collected to document body mass index (BMI), educational level, medical comorbidities, pelvic conditions, menstrual and menopause status, obstetric history, and symptoms of PF. The short form of the International Physical Activity Questionnaire was used to assess current activity levels.

Data were collected for 4,556 responders with a mean age of 41.9 years and a mean BMI of 29.9 kg/m². Of these, 46% had discontinued a form of exercise due to symptoms of PF, 53% had modified their participation and 48% continued to participate in a form of exercise while experiencing symptoms. The most common PF symptom experienced during exercise was urinary incontinence, causing 41% to stop exercising. Symptoms of anal incontinence during exercise were experienced by 45% of the women, resulting in 26% ceasing a form of exercise.

**Conclusion:** This survey of women with self-identified pelvic floor symptoms during exercise found that 46% had stopped exercise due to their symptoms.

Dakic, J., et al. Pelvic Floor Disorders Stop Women Exercising: A Survey of 4,556 Symptomatic Women. **J Sci Med Sport**. 2021, Dec; 24 (12): 1211 -1217.

## FLYWHEEL RESISTANCE TRAINING FOR ELITE SOCCER PLAYERS

Soccer requires the player to perform a great number of accelerations, decelerations, and changes of direction (COD), as well as quick and decisive jumps and sprints. The "COD deficit" refers to the additional time that a COD requires compared to a linear straight sprint test over the same distance. As flywheel resistance exercises have been found to enhance the load of the eccentric phase during resistance exercises, this study assessed the effect of flywheel resistance exercises for improving the COD deficit.

*(Continued from page 2)*

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The study included 24 young elite under 16-year-old (U-16) soccer players. Those subjects were randomized to either a control group or a flywheel group, with the flywheel group engaging in 10, weekly sessions of 75 minutes' duration. At baseline, and after the 10 weeks of training, all participants were measured for unilateral counter movement jumps (CMJ), with a 30 m linear sprint test and a COD sprint test.

Compared with the control group, significant within-group improvements in CMJ, COD and COD deficit performance for dominant and non-dominant limbs were found for the flywheel group. No significant improvement was seen in linear sprint performance.

**Conclusion:** This study of elite, U-16 soccer players found that a once-a-week flywheel resistance exercise program could improve change of direction and jumping ability.

Raya-Gonzalez, J., et al. The Effect of a Weekly Flywheel Resistance Training Session on Elite U-16 Soccer Players' Physical Performance during the Competitive Season. A Randomized, Controlled Trial. **Res Sports Med.** 2021; 29 (6): 571-585.

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