MUSCULOSKELETAL

IN REVIEW

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ALLOGENIC PLATELET RICH PLASMA FOR ROTATOR CUFF DISEASE

Comparing studies of platelet rich plasma (PRP) has been difficult because of different PRP mixtures used. In studies using pure PRP, few white blood cells (WBCs) are present, while studies using leukocyte-rich PRP have a large concentration of WBCs. This study was designed to assess the effects of pure PRP on tenocytes, in patients with rotator cuff pathology.

Pure PRP was harvested from healthy donors. Degenerative tenocytes from patients undergoing arthroscopic rotator cuff repair were harvested. Inflammation was induced in these cells with 1 ng/mL IL-1β, with cells then studied with, or without the application of PRP. In a second, clinical study, 17 patients receiving subacromial PRP injections were compared to patients receiving corticosteroid injections. All were followed for six months for pain with range of motion, function and patient satisfaction.

In the in vitro study, PRP caused inflammation in the cells that had not been treated with IL-1β, and reduced inflammation in the cells exposed to IL-1β. In the clinical study, among patients injected with PRP, all pain scores gradually improved over time. The steroid group pain scores were superior to the PRP group at one week ($p = 0.014$), with the best scores for this group at one month, but worsening thereafter. In the PRP group, the mean pain scores reduced gradually over time reaching their lowest levels at six months. Overall satisfaction increased in the PRP group to its highest level at six months, while the steroid group had decreased satisfaction scores to below baseline scores at three months.

Conclusion: This study found that pure PRP induced inflammation in tenocytes in the absence of inflammation whereas it reduced inflammation in the presence of inflammation. In addition, PRP decreased pain and improved shoulder function better than did steroid injections.

Jo, C., et al. Allogenic Pure Platelet Rich Plasma Therapy for Rotator Cuff Disease. A Bench and Bed Study. **Am J Sports Med**. 2018, November; 46 (13): 3142-3154.

CLINICAL COURSE OF CERVICAL RADICULOPATHY

The majority of patients with cervical radiculopathy due to disc herniation will recover within three years. This prospective study describes the clinical course and prognostic models for patients treated non-surgically for cervical radiculopathy. Subjects were consecutive patients with a diagnosis of cervical radiculopathy treated at a multidisciplinary clinic in the Netherlands. The initial visit included a neurologic examination, including MRI, as well as documentation of demographic and prognostic factors. Patients were followed at six and 12 months with a questionnaire regarding their level of symptoms, treatment received, and medication used. The primary outcome measure was perceived recovery at 12 months measured on the seven-point Global Perceived Effect (GPE) scale. Patients were labeled "recovered" if they scored "completely recovered" or "much improved" on the GPE scale.

Subjects were 61 patients with a mean age of 49.5 years, and median symptom duration of 26 weeks. At six months, 42% were "recovered" increasing to 47% at 12 months. At six months, high intensity neck pain was noted by 24%, and 18% at 12 months. A multivariable logistic regression analysis determined that those with a longer duration of symptoms had a higher risk for persistent symptoms (OR 1.01), while those reporting paresthesia had a reduced risk (OR 0.18).

Conclusion: This prospective study of Dutch patients with a diagnosis of cervical radiculopathy found that only half of the patients recovered at one year, with a number of symptoms suggestive of a poor prognosis with conservative treatment.

Sleijser-Koehorst, M., et al. Clinical Course and Prognostic Models for the Conservative Management of Cervical Radiculopathy: A Prospective Cohort Study. **Eur Spine J**. 2018, November; 27 (11): 2710-2719.

EXERCISE PERFORMANCE WITH OVERNIGHT NICOTINE ABSTINENCE

Globally, tobacco abuse includes 933 million daily smokers and 300 million abusers of smokeless

tobacco. Studies of the effects of nicotine on the performance of athletes have produced inconsistent results. This study investigated the effect of an overnight abstinence from nicotine among nicotine-addicted athletes.

Subjects included male regular abusers of smokeless tobacco. At the initial visit, all were assessed for body mass index, VO_2 max, maximal workload at exhaustion, critical power, workload at 80% VO_2 max, and maximal heart rate. In the experimental session, participants pedaled at 80% VO_2 max until exhaustion, either after receiving smokeless tobacco 25 minutes before exercise (nicotine satiety (SA)), or after a 12-hour overnight nicotine abstinence (AB). Blood draws and carbon monoxide levels were used to confirm the use or abstinence.

The mean time to exhaustion during the AB session was 13.1% longer than during the SA session (p=0.031). The perception of effort as measured by the Borg scale did not differ between the conditions.

Conclusion: This study of regular users of smokeless tobacco found that abstaining from use for 12 hours before exercise can significantly improve performance.

Zandonai, T., et al. Exercise Performance Increase in Smokeless Tobacco User Athletes after Overnight Nicotine Abstinence. **Scand J Med Sci Sport**. 2018:1-10.

EXERCISE PLUS MUSIC FOR STROKE PATIENTS

Recent studies have demonstrated that music during exercise can be beneficial in achieving physical goals among elderly populations. This study of patients with a recent stroke assessed the effect of music during exercise.

This prospective randomized study included 65 stroke survivors with a score of 50 or greater on the Barthel Index. All subjects underwent motor and neurologic assessment with screenings at admission to the rehabilitation center and at six months after their stroke. Physical exam included CT Perfusion (CTP) to determine cerebral blood flow (CBF) and cerebral blood volume (CBV), assessed within three-six days of, and at six-months after admission. All subjects underwent 45- minute training sessions, four times per week for six months. Those in the music group (MG) listened to experiential/ traditional music that was common during their youth. Those in the control group (CG) underwent the same exercises without music. Recovery was defined as improvement of cognitive and motor skills of the affected limb, with an increased muscle strength at least by 1/5 accompanied by emotional progress.

Recovery was noted in 26.2% of the music group and in13.8% of the control group (p=0.001). Amultivariable analysis revealed that only lesion size and group were independent predictors of recovery.

Conclusion: This study demonstrates that recovery from stroke was enhanced when music is added to exercise therapy.

Fotakopoulos, G., et al. The Value of Exercise Rehabilitation Program Accompanied by Experiential Music for Recovery of Cognitive and Motor Skills in Stroke Patients**. J Stroke Cerebrovas Dis**. 2018, November; 27(11): 2932–2939.

GABAPENTIN VERSUS PREGABALIN FOR CHRONIC SCIATICA

For chronic sciatica, the medications most often used for treatment are gabapentin or pregabalin. Both are analogues of gamma aminobutyric acid, a substance known to modulate calcium channel subunits. This study was designed to understand the efficacy of these two medications for patients with chronic sciatica.

This prospective double-blind randomized study included patients seen in the neurosurgery clinic with sciatic pain lasting at least three months. The pregabalin group received 150 mg once per day titrated up to a maximum of 300 mg twice per day. The gabapentin group receive 400 mg once per day titrated up to a maximum of 800 mg three times per day. The primary outcome was leg pain intensity using the visual analog scale, with secondary outcome measures including the Oswestry Disability index (ODI), measured at baseline, then at weeks four, eight, 10, and 14.

At the end of eight weeks, pain intensity was reduced by a mean of 7.54/10 for gabapentin (p<0.001), and 7.33/10 for pregabalin (p=0.02). Significant reductions were also found in the ODI scores (p=0.001 for both). In the unadjusted analysis, gabapentin was superior to pregabalin for the reduction of pain (p=0.035), but not for scores on the ODI. There were significantly more adverse events associated with pregabalin than with gabapentin (p= 0.002).

Conclusion: This study suggests that gabapentin is superior to pregabalin for treating the symptoms

Robertson, K., et al. Effect of Gabapentin versus Pregabalin on Pain Intensity in Adults with Chronic Sciatica. A Randomized Clinical

Trial. **JAMA Neurol**. 2018, doi: 10.1001/jamaneurol.2018.3077.

HEMOGLOBIC A1C AND HEMORRHAGIC TRANSFORMATION IN ACUTE ISCHEMIC STROKE

While recent studies have suggested that hyperglycemia may be associated with hemorrhagic transformation (HT) after acute ischemic stroke, the data often rely on acute blood glucose levels which may be influenced by acute circumstances. This study investigated the relationship between hemorrhagic transformation and long-term glycemic control as measured by hemoglobin A1c.

Subjects were consecutive patients diagnosed with acute anterior stroke who were hospitalized between January 2014 and June 2016. All patients were assessed at baseline with computed tomography/ magnetic resonance imaging within 24 hours of symptom onset with hemoglobin A1c obtained the day after admission. Stroke severity was measured by the National Institutes of Health Stroke Scale (NIHSS), with the modified Rankin scale (mRS) used to assess functional outcomes at hospital discharge.

Of the 426 patients included, 93 (21.8%) were noted to have a HT. Of these, 61 (14.3%) were classified with hemorrhagic infarction a with parenchymal hematoma. In a multivariate analysis, hemoglobin A1c was a strong independent predictor of hemorrhagic infarction, with an odds ratio of 1.29. At discharge, 144 (33.8%) of the patients achieved favorable outcomes, defined as mRS score ≤ 2, and 282 (66.2%) achieved unfavorable outcomes (mRS score > 2). A poor outcome was predicted by elevated hemoglobin A1c (OR 1.48).

Conclusion: This study demonstrates of patients admitted for acute ischemic stroke found that an elevated hemoglobin A1c at admission is associated with an increase in the risk of hemorrhagic transformation.

Zhang, G., et al. Hemoglobin A1c Predicts Hemorrhagic Transformation and Poor Outcomes After Acute Anterior Stroke. European J Neurol. 2018, December; 25 (12): 1432-1438nd 32 (7.5%)

DRIVING AFTER HIP ARTHROSCOPY

Numerous studies have examined return to driving after common lower extremity orthopedic surgeries, but none have addressed return to driving after a hip arthroscopy. This study was designed to evaluate patients braking performance after undergoing a right hip arthroscopy. Subjects were 14 patients scheduled for right hip arthroscopy and 17 healthy volunteers. All were assessed with a driving simulator system completed preoperatively (baseline) and at two, four, six and eight weeks postoperatively. The control group underwent five simulator sessions two weeks apart. Multiple parameters of braking performance were assessed, including initial reaction time (IRT), throttle release time (TRT), foot movement time (FMT) and brake travel time (BTT).

The control group had significantly faster reaction times at baseline than did the experimental group. The surgery group did not show any decline in any of the braking performance variables between baseline and two weeks post-surgery. The surgery group demonstrated significant improvements in IRT ($p=0.002$), TRT ($p<0.0001$), FMT ($p<0.0001$) and BRT ($p=0.0002$) between baseline and the two-week postoperative driving session, with no significant changes thereafter.

Conclusion: This study suggests that patients could safely return to driving two weeks after a right-sided hip arthroscopy.

Momaya, A., et al. Return to Driving After Hip Arthroscopy. **Clin J Sport Med.** 2018, May; 28(3): 299-303.

LASER AND SHOCKWAVE THERAPY FOR MYOFASCIAL PAIN

Laser therapy and shockwave therapy are both used clinically to treat musculoskeletal pain. This study compared the relative effects of these interventions on patients with myofascial pain.

The subjects were 61 patients with myofascial pain syndrome of the trapezius. Those randomized to the laser group received daily laser therapy for 15 consecutive business days with a 4W laser. The second group received shockwave therapy once per week for three weeks. In both groups the therapy was directed at the trigger points in the trapezius muscle as well as the region surrounding it. Patients were assessed for resting and spontaneous pain (visual analogue scale), functional impairme Disability Index; NDI), quality of life (SF-36) and pain medication use.

All measured parameters improved significantly from baseline in both groups at the end of three weeks of treatment and at 15 week follow up. When comparing changes between the two groups, both at week three and week 15, improvement in the shockwave therapy group was significantly better than the laser therapy group, except for emotional well-being on week three and physical health at week 15. There were no adverse events noted during the study.

Conclusion: This uncontrolled study of adults with myofascial pain of the trapezius found that both laser and shockwave therapy improved pain tolerance, neck function, and quality of life, though the clinical effectiveness of shockwave therapy was found to be superior.

Kiraly, M., et al. Comparative Study of Shockwave Therapy and Low- Level Laser Therapy Effects in Patients with Myofascial Pain Syndrome of the Trapezius. **Rheumatol In**. 2018, November; 38(11):2045–2052

TRANSCRANIAL MAGNETIC STIMULATION AND ENVIRONMENTAL ENRICHMENT AFTER TBI

Despite the widespread prevalence of traumatic brain injury (TBI), clinical trials of various treatments have shown very limited long-term improvement in functional outcomes. Previous studies have suggested that transcranial magnetic stimulation (TMS) may enhance neuroplasticity, and restore normal cortical excitability levels. This animal study assessed the effect of combining TMS with environmental enrichment in rats with a TBI.

Subjects were 97 rats subjected to a controlled cortical impact to produce a TBI. The animals were then randomized to one of four groups, including: standard housing (SE) environmental enrichment (EE), EE plus TMS (EE-TMS), EE plus sham TMS (EE-S). The TMS was delivered for six days with a total of 280 pulses per day. All animals were trained on a beam walking test, a challenge ladder, tested for motor evoked potentials in response to TMS stimulation, electrophysiological recordings and functional MRI.

The EE-TMS group had significantly better performance on the beam walk test compared to the TBI with the SE group ($p<0.005$). In the electrophysiologic tests, the EE- TMS group demonstrated significantly better LSP amplitude, associated with increases in cortical excitability, compared to the SE group. The EE- TMS group also had a higher MEP amplitude compared to the SE group. **Conclusion:** This animal study demonstrates that a combination of environmental enrichment and transcranial magnetic stimulation can result in functional improvement, as compared to TMS alone.

Shin, S., et al. Transcranial Magnetic Stimulation and Environmental Enrichment Enhances Cortical Excitability and Functional Outcomes After Traumatic Brain Injury. **Brain Stimul.** 2018, November-December; 11(6):1306-1313.

VIRTUAL REALITY FOR PARKINSON DISEASE

The prevalence of Parkinson's disease (PD) in industrialized countries is 0.3% in the general population. This study evaluated the effects of virtual reality training (VRT) on motor and cognitive recovery in patients with PD.

Subjects were 20 patients with PD, with an average age of 69.4 years, randomly assigned to a control group or a VRT group. All patients were assessed with a neuropsychological battery, including tests of cognition and affect. Those in the VRT group used the BTS-Nirvana (BTS-N), which creates three- dimensional multisensory and interactive simulation, to allow the patient to interact with virtual scenarios. Each treatment session lasted 30 minutes, with three sessions per week for eight weeks.

Those in the VRT group demonstrated greater improvements in cognitive function, including executive and visuospatial abilities, as compared to the control group. Compared with the control group, significantly greater improvement was noted in scores on the Mini-Mental State Exam ($p=0.014$), the Frontal Assessment Battery ($p<0.001$), the WEIGL ($p=0.015$), the Addenbrooke Cognitive Examination (ACE)- Revised ($p<0.0001$), the ACE-R Attention and Orientation subtest ($p<0.001$), the ACE-R Memory subtest ($p=0.034$), the ACE-R Fluency subtest ($p<0.001$), the ACE- R Language subtest ($p=0.016$) and the ACE-R Visual-Spatial subtest ($p<0.0001$).

Conclusion: This small study suggests that rehabilitation using virtual reality could be valuable for the improvement of cognition and behavioral outcomes of patients with Parkinson Disease.

Maggio, M., et al. What About the Role of Virtual Reality in Parkinson Disease's Cognitive Rehabilitation? Preliminary Findings from a Randomized, Clinical Trial. **J Geriatr Psychiatry Neurol**. 2018; November 31 (6): 312-31

PROPRIOCEPTIVE TRAINING AND ANKLE SPRAIN

Ankle sprains occur in many sports, and can significantly limit an athlete's performance. While balance training is thought to prevent or treat ankle sprains, the effects of proprioception training are less clear. This literature review and meta- analysis was designed to better understand the effects of proprioceptive training on the risk of ankle sprain.

A literature review was completed for studies of adults, evaluating the effects of proprioception using balance training, as compared with a control condition, on the incidence of ankle sprain. Of the 1,073 studies found in the database, 12 were chosen for the meta-analysis, including 1,722 subjects.

In the meta-analysis, compared to the control condition, balance training resulted in a 38% reduction in the incidence of ankle sprain. Among the studies that examined dynamic neuromuscular control, balance training with proprioceptive training increased the distance reached in the anterior ($p=0.01$), posterolateral ($p=0.0008$) and posteromedial ($p=0.006$) excursion balance tests.

Conclusion: This literature review and meta-analysis supports the conclusion that balance training with proprioceptive training can significantly reduce the risk of ankle sprain and increase balance and joint position sense.

de Vasconcelos, G., et al. Effects of Proprioceptive Training on the

Incidence of Ankle Sprain in Athletes: Systematic Review and Meta- Analysis. **Clin Rehabil**. 2018, December; 32 (12): 1581-1590.

LOW CARBOHYDRATE DIET AND ENERGY EXPENDITURE DURING WEIGHT LOSS

According to the carbohydrate-insulin model of obesity, an increased ratio of insulin to glucagon after a meal with a high glycemic load directs metabolic fuels away from oxidation and toward storage in adipose tissue. Studies exploring this model have not produced conclusive results. This study compared the effects of diets varying in carbohydrate to fat ratios on energy expenditure during weight loss maintenance.

This randomized, controlled trial included adults at Framingham State University, studied between August of 2014 and May of 2017. During a run- in phase, energy intake was restricted to promote 12% weight loss over nine to ten weeks. The subjects who successfully lost this weight were randomized to high, moderate or low carbohydrate test diets for a 20-week phase. During this phase, energy intake was adjusted to maintain weight loss. The diets all contained protein at 20% of total calories, varying the energy contributions of carbohydrates at 60%, 40% or 20%, with the remaining calories obtained through fat. Outcome variables were energy expenditure, physical activity and metabolic hormones.

Of the 234 participants in the weight loss phase, 164 achieved the target 12% reduction in weight loss and were included in this randomized trial. Compared with the high carbohydrate diet, change in total energy expenditures were 91 kcal per day greater on the moderate carbohydrate diet and 209 kcal per day greater on the low carbohydrate diet. The data revealed that energy expenditure increased by 52 kcal/d for every 10% decrease in the contribution of carbohydrate to total energy intake (p=0.002). This effect was most pronounced among those with high insulin secretion, as measured at pre-weight loss.

Conclusion: This randomized, controlled trial found that, with similar calories and similar protein intake, patients who consume low carbohydrate diets have significantly greater total energy expenditure.

Ebbeling, C., et al. Effects of a Low Carbohydrate Diet on Energy Expenditure During Weight Loss Maintenance: Randomized Trial. **BMJ.** 2018:363: k4583.

PAIN IS A RISK FACTOR FOR FRAILTY

Estimates of pain in the general population range from 40% in community dwelling elderly to 80% in institutionalized individuals. While studies have demonstrated an association between pain and frailty, it is not clear whether pain is a risk factor for frailty. This literature review and meta-analysis was designed to better understand the association between persistent pain and the incidence of frailty.

From a literature review, five prospective studies were chosen for inclusion, involving 13,120

participants, ranging from 59 to 85 years of age. All studies used assessments of pain and frailty, with a median follow-up of three to eight years. A random effects model meta - analysis was performed to investigate the association between pain and frailty.

The data revealed that participants with pain at baseline had twice the risk of developing frailty at the time of follow-up (relative risk 2.22) compared to those without chronic pain, even after adjusting for confounding risk factors.

Conclusion: This literature review and meta-analysis demonstrates that persistent pain is associated with a significantly increased risk of frailty.

Saraiva, M., et al. Persistent Pain Is a Risk Factor for Frailty: A Systematic Review and Meta-Analysis from Prospective Longitudinal Studies. Age Aging. 2018, November; 47(6):785-793.

DIACUTANEOUS FIBROLYSIS FOR CARPAL TUNNEL SYNDROME

Diacutaneous fibrolysis (DF) is a technique developed from Cyriax deep friction massage principles. While DF has shown promise for treatment of shoulder pain and lateral epicondylitis, no prior studies have assessed its efficacy for carpal tunnel syndrome (CTS) intervention.

This double-blind, randomized, controlled trial included patients with mild to moderate CTS. The participants were randomized to receive DF or sham DF. All treatment subjects were involved in five sessions of 20 minutes' duration, with an interval of two to five days between sessions. A sham group received similar appearing treatment, but with pressure delivered at a superficial level, without generating mechanical traction on the deep fibers of the soft tissue.

The intensive, nocturnal symptoms of the DF group were significantly reduced compared to those of the sham group. Functional capacity of the upper extremity was significantly improved in the DF group as compared to the sham group. This improvement persisted at one- month follow-up. The DF group demonstrated significantly greater improvement in sensory nerve conduction velocity and motor conduction velocity as compared to the sham group.

Conclusion: This study of DF patients with mild-to-moderate symptomatic carpal tunnel

syndrome found that, after five sessions, significant improvements were achieved on electrodiagnostic, symptomatic as well as functional measures.

Del Barrio, S., et al Effects of Diacutaneous Fibrinolysis in Patients with Mild to Moderate Symptomatic Carpal Tunnel Syndrome: A Randomized, Controlled Trial. **Clin Rehab**. 2018, December; 32(12):1645-1655.

BUTYRATE, DIETARY FIBER AND NEUROINFLAMMATION

Studies have shown that aging results in chronic systemic inflammation, which can accelerate neuroinflammation in the brain. The exact mechanism is not clear, although the overproduction of the pro-inflammatory cytokine interleukin- 1 beta (Il-b1) is known to play a role. As dietary intake is thought to affect this process, this study reviewed the effect of sodium butyrate (NaB), a short-chain fatty acid (SCFA) produced primarily by bacterial fermentation of fiber in the colon, on neuroinflammation.

A group of aged mice were injected with either a saline control or NaB at 1.2 g/kg body weight, as well as saline or LPS at 0.33 mg/kg body weight. At follow-up, the mice were euthanized for tissue analysis, microglial isolation, and RNA isolation. A second group was fed a diet with either a low or high soluble fiber content and underwent a similar post-mortem analysis.

In the first study, immune activation was noted in the microglia after LPS infusion, with increases in *Il-1β*, (p=0.0005). When also infused with butyrate the *Il-1β* expression was attenuated (p=0.0497). These findings were also true for the analysis at the hippocampus, and were more pronounced in the aged mice. In the diet study, cecum and colon analysis indicated severe inflammation associated with immune infiltration in aged animals on a low fiber diet. However, aged mice on a high fiber diet had a decrease in this inflammatory infiltrate. Histology scores supported these findings. Compared to the low fiber diet, the high fiber diet decreased gene expression in the microglia, including *Il-1β, Il-1rn, Il-6, Nlrp3, Tlr4* and *Tnf*.

Conclusion: This animal study found that sodium butyrate can reduce inflammation and immune reactivity in the microglia of the brain, supporting a neuroprotective role of high soluble fiber.

Matt, S., et al. Butyrate and Dietary Soluble Fiber Improve Neuroinflammation Associated with Aging in Mice. **Front Immunol**. 2018. https://doi.org/10.3389/ FIMMU.2018.01832.

BODY MASS INDEX AND LONG-TERM RISK OF REVISION AFTER HIP REPLACEMENT

Studies of the association between body mass index (BMI) and the risk of revision after total hip replacement have produced mixed esults. This study was designed to better understand the effect of BMI on the risk of revision surgery at 11 years following total hip arthroplasty (THA).

Data were prospectively collected for all patients undergoing THA using data from the National Joint Registry, between April of 2003 and December of 2015. Cofounding variables included age at the time of the primary THA, gender, physical status classification, year of primary THA, type of hip replacement and fixation. Data concerning mortality at 90 days and revision were recorded at a maximum follow-up of 11.75 years.

For the 415,598 patients followed, the cumulative probability of death at 90 days, was significantly higher in the underweight than in the normal weight group (p<0.0005). In contrast, compared to the normal weight group 90-day mortality was significantly lower in the overweight (p<0.0005), Obese Class I (p<0.0005), and Obese Class II (p=00.049). At ten year follow up, compared to the normal weight group, the cumulative risk for revision was highest in the Obese Class III (6.7%), and significantly higher than the normal group for Obese Class I, Class II and Class III (p<0.0005 for all). Statistical significance was maintained in the adjusted models.

Conclusion: This population based, longitudinal, cohort study demonstrated that, after total hip replacement, elevated body mass index reduces the short-term risk for mortality, but increases the long-term risk for revision surgery.

Mouchti, S., et al. Long-Term Revision and 90-Day Mortality following Primary Total Hip Replacement. **J Bone Joint Surg.** 2018, December 19: 100(24): 2140-2152.

CEREBELLUM STIMULATION AND GAIT RECOVERY

After a stroke, the contralesional cerebellum is implicated in functional reorganization of the motor network. In animal models, stimulation of the cerebellar-cortical networks has been found to improve recovery. This study assessed the effect of cerebellar intermittent Omega-burst stimulation (CRB-iTBS), a variation of repetitive transcranial magnetic stimulation (rTMS), on gait recovery after a stroke.

Subjects were adult patients with chronic (over six months), first ever middle cerebral artery ischemic stroke with residual gait and balance impairment. Assessments included the Berg Balance Scale (BBS), the Fugl-Meyer (FM) assessment, the Barthel Index (BI) and gait analysis. A combination of TMS and electroencephalogram was used to determine the patterns of cortical reorganization. The patients were randomized to receive either active or sham CRB-iTBS.

All participants underwent three weeks of daily sham or active CRB-iTBS, coupled with physical therapy. The CRB-iTBS was applied over the contralalesional cerebellum. During locomotion analysis, the patients were asked to walk at a comfortable speed. The primary efficacy analysis was the change from baseline in BBS scores, with secondary endpoints including changes in the FM and BI.

At three weeks, patients in the active group demonstrated greater improvement on the BBS (p= 0.03). The treatment group demonstrated significant improvements from baseline by 15.8% at T1 and 23.1% at T2. No significant change was noted in the control group. The gait analysis demonstrated that step width was significantly reduced in the treatment group.

Conclusion: This study demonstrates that cerebellar intermittent omega burst stimulation in patients with chronic stroke can improve gait and balance.

Koch, G., et al. Effect of Cerebellar Stimulation on Gait and Balance Recovery in Patients with Hemiparetic Stroke. Randomized, Clinical Trial. **JAMA Neurol**. 2018; doi:10.1001/jamaneurol.2018.3639.

BENEFITS OF STANDING AT WORK

Sedentary behaviors have been associated with an increased risk of chronic disease and mortality. As office workers spend 70 to 85% of their time sitting, this study assessed the effect of a program designed to decrease sitting time at work.

Eligible subjects were office workers, 18 to 70 years of age, who spent at least 75% of their working day in a seated position. The participants were randomized at the office group level. Those in the intervention group received SMArT work intervention, including a height adjustable desk and education concerning the consequences of sitting. An electronic cushion provided feedback by vibration regarding sitting time. The control group were not given lifestyle advice, guidance or modified work stations.

The primary outcome measure was change in occupational sitting time, as assessed by an ergometer. Secondary outcomes included physical activity, musculoskeletal health, work-related measures and measures of cognition, mood, and quality of life. The subjects were assessed at baseline and at three, six- and 12-months' follow-ups.

At 12-month follow-up, compared to controls, the intervention group had a reduction in sit time of 83.28 minutes per work day, with prolonged sitting time reduced by 44.93 minutes per work day. At 12 months, the intervention group obtained significantly better scores in job performance and recovery from occupational fatigue, but not in job satisfaction. The intervention group also earned better scores in time management and mental-interpersonal demands than did the control group. The intervention group also demonstrated better scores on the Stroop Color Word Test-Reaction Time, quality of life and anxiety. No significant difference was found between groups in musculoskeletal complaints.

Conclusion: This randomized, controlled study of office workers found that an intervention strategy designed to reduce sitting time can reduce sitting time and improve job performance, working engagement, occupational fatigue, anxiety and quality of life.

Edwardson, C., et al. Effectiveness of the Stand More at (SMArT) Work Intervention: Cluster Randomized, Controlled Trial. **BMJ**; 2018: 363: K3870.

WHOLE BODY CRYOTHERAPY FOR FIBROMYALGIA

Fibromyalgia (FM) is a prevalent and disabling disease with unclear pathology, and few effective treatments. Whole body cryotherapy (WBC) has been shown to decrease inflammation and produce analgesia, with positive effects reported for patients with rheumatoid arthritis and ankylosing spondylitis. This study explored the effect of WBC as a treatment for FM.

This randomized, crossover, clinical trial, included patients 25 to 80 years of age with FM for at least one year, all unresponsive to treatment attempts. Those randomized to a treatment arm underwent WBC treatment on alternating days for three weeks. Each session included three minutes in a cabin with temperatures reduced to -196°C. The groups then reversed. The primary outcome measures were a ten-point visual analog scale (VAS) for pain and the FM impact questionnaire (FIQ). Secondary endpoints included disease severity, assessed by the combined Index of Severity of Fibromyalgia (ICAF) and the SF-36.

After the treatment sessions were completed the mean improvements in VAS scores were three in the WBC group and 0.3 in the control group. ($p<0.001$). In addition, better improvement was found in the WBC group in improvement in scores on the FIQ ($p<0.001$) and the ICAF ($p<0.001$). Five patients reported mild adverse events during WBC, notably during the first session, all of which waned in subsequent sessions.

Conclusion: This study of patients with recalcitrant fibromyalgia found that three-minute sessions of cryotherapy every other day for three weeks resulted in significant improvements in pain scores and fibromyalgia impact scores.

Rivera, J., et. Al. The Effect of Cryotherapy on Fibromyalgia: A Randomized, Clinical Trial Carried Out in a Cryosauna Cabin. **Rheum Intern**. 2018, December; 38(12): 2243-2250.

ZOLEDRONATE FOR FRACTURE PREVENTION IN OLDER WOMEN

Bisphosphonates are the primary class of medication used to prevent osteoporotic fractures. However, the evidence for their effects in patients with osteopenia is lacking. Zoledronate can be administered at intervals of one year or longer, and is preferred over oral bisphosphonates by the majority of women. This study assessed the effects of zoledronate on the risk of fractures in postmenopausal women with osteopenia.

Subjects were ambulatory, postmenopausal women, 65 years of age or older, all with osteopenia confirmed by bone mineral density studies. The women were randomized to receive four infusions of either alendronate, 5 mg, or normal saline, at 18-month intervals. All subjects received cholecalciferol, 1.25 mg per month, for the duration of the trial. The primary endpoint was the time to first fragility fracture.

During follow-up, a fragility fracture was diagnosed in 190 women in the placebo group and 122 in the treatment group ($p<0.0001$). Secondary endpoints were also better in the treatment group including symptomatic fractures, [Hazard Ratio (HR) 0.73], death (HR 0.65) and cancer (HR 0.67).

Conclusion: This study of postmenopausal women with osteopenia found that administration of zoledronate every 18 months for six years reduces the risk of fragility fractures, death and cancer.

Reid, I., et al. Fracture Prevention with Zoledronate in Older Women with Osteopenia. **N Engl J Med.** 2018, December 20; 379(25): 2407-2416.

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Produced by the Department of Rehabilitation Medicine, Emory University School of Medicine

Expanding the frontier of medicine in research, teaching, and patient care