

# REHAB IN REVIEW

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## NEUROTECHNOLOGY TO REPAIR COMPLETE SPINAL CORD INJURY

After a spinal cord injury (SCI), volitional movement during therapy can promote the reorganization of neuronal pathways. The results of this therapy have been far from satisfactory, and are only available to those with incomplete injuries. This study explored the use of neurotechnologies to deliver spatiotemporal epidural electrical stimulation (EES) to promote meaningful functional movement.

The subjects were three males with chronic cervical SCI who displayed severe or complete paralysis. Electrode configurations were identified that targeted the posterior roots projecting to spinal cord regions containing motor neurons. These neurons involved the mobilization of the hip, knee and ankle joints. To identify individual configurations, the subjects were asked to attempt to produce movement of a single joint. Terminal electrode configurations were then adjusted to produce appropriate movement. The subjects were then engaged in a rehabilitation program four to five times per week for five months, focusing on walking on a treadmill and over ground.

Within five days, this procedure led to EES sequences that enabled robust EMG activity in otherwise quiescent muscles while ambulating on a treadmill. All participants improved their walking capacity. After three months the subjects could walk hands-free when provided hip support with a gravity assist harness. Two of the three subjects regained independent walking with 35% body weight support, while the third subject needed a walker to progress over ground. Over time, volitional movements were noted without EES. After months of use, two of the three subjects could transfer from sitting to standing and could walk independently with crutches.

**Conclusion:** This study of three

subjects with chronic spinal cord tetraplegia found that targeted neurotechnology could partially restore meaningful ambulation.

Wagner, F et al. Targeted Neurotechnology Restores Walking in Humans with Spinal Cord Injury. *Nature*. 2018, November; 563 (7729) 65-71.

## ISCHEMIC PRECONDITIONING FOR ACUTE STROKE

Animal studies have suggested that the application of limb ischemia after a stroke can be neuroprotective. This study assessed the tolerability and feasibility of limb ischemia post conditioning (LIPostC) in patients hospitalized with acute stroke.

Subjects were adult patients with ischemic stroke, hospitalized within 24-72 hours. The LIPostC treatment included four cycles of intermittent limb ischemia, alternating five minutes of blood pressure cuff inflation to 20 mmHg above systolic blood pressure, applied to the non-paretic arm. The procedure was repeated every 24 hours from enrollment to day 14. The control group received a sham procedure with a cuff inflation of 30 mmHg. Before and after intervention patients were assessed with a short neurologic examination, NIHSS scoring, ECG, blood tests, and MRI.

At day 90, compared with the control group, the LIPostC group had more improved NIHSS scores ( $p < 0.05$ ), a decrease in cerebral infarct volume (31.3%;  $p < 0.05$ ), an increase in the curative ratio as measured by the modified Rankin scale scores ( $p < 0.05$ ), as well as an increase in regional relative cerebral blood flow ( $p < 0.05$ ). Only one patient was intolerant of the ischemic procedure.

**Conclusion:** This pilot study of patients with acute ischemic stroke found that inducing ischemia to the unaffected limb 15 minutes per day,

for 14 days resulted in improved function and decreased stroke volume.

Li, Y et al. Upper Limb Ischemic Post Conditioning as Adjunct Therapy in Acute Stroke Patients: A Randomized Pilot. *J Stroke Cerebrovasc Dis*. 2018, November; 27 (11): 3328-3335.

## CILOSTAZOL TO PREVENT STROKE-ASSOCIATED PNEUMONIA

Stroke associated pneumonia (SAP) develops in approximately 20% of patients with acute ischemic stroke (IS). The major mechanism of SAP development is the reduction of substance P. As cilostazol induces the upregulation of substance P, this study explored the efficacy of cilostazol for the prevention of SAP.

This retrospective study included 158 patients admitted with IS, who required tube feedings during ICU management. Clinical data were acquired from medical records including the use of cilostazol and the presence of SAP. The primary endpoint was the incidence of SAP within 3-14 days of admission and the number of cilostazol treatments prior to the development of SAP.

Cilostazol was administered as an initial treatment in 28 patients after admission. Of those treated with cilostazol, SAP occurred in 6.1%, compared with 20.8% among those not treated. The length of stay in the ICU was longer in patients with SAP than in patients without SAP ( $p < 0.05$ ), though, in the final analysis, the length of stay in the ICU and the duration of hospitalization were not found to be reduced due to the prevention of SAP by cilostazol.

**Conclusion:** This study of patients with ischemic stroke who required tube feeding suggests that cilostazol may help reduce the incidence of stroke-related pneumonia.

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Netsu, S et al. Cilostazol is Effective to Prevent Stroke Associated Pneumonia. **Dysphagia**. 2018, October; 33 (5):716-724.

## LOW-DOSE TRAZODONE AND NURSING HOME FALLS

Recent studies have shown a decline in benzodiazepine prescribing in nursing homes, thought to be due to the risk of cognitive impairment, falls, and related adverse events. Concurrent with this decline has been an increase in the off-label use of trazodone as a sedative in this population. This study evaluated the comparative risk of fall-related injuries among nursing home residents who are prescribed benzodiazepines or trazodone.

This retrospective study of nursing home residents >65 years of age included 7,791 new users of low-dose trazodone and 7,791 new users of benzodiazepines. The primary outcome was cumulative incidence of a fall-related injuries which resulted in visits to the emergency department (ED) or resulted in acute care hospitalization.

A multivariate analysis found no significant difference in the cumulative incidence of fall-related injuries between the new trazodone users and the new benzodiazepine users ( $p=0.43$ ). Lorazepam was the most commonly prescribed benzodiazepine.

**Conclusions:** This retrospective study of nursing home patients found that the risk of falls did not differ between those newly prescribed trazodone and those newly prescribed a benzodiazepine.

Bronskill, S., et al. Low-Dose Trazodone, Benzodiazepines, and Fall-Related Injuries in Nursing Homes: A Matched-Cohort Study. **J Am Geriatr Soc**. 2018, October; 66 (10):1963-1971.

## STATIN USE AFTER STROKE AND DEMENTIA

Stroke is a leading cause of death and disability in the world. Previous studies have suggested that stroke is associated with an increased risk of cognitive decline and dementia. Among the risk factors for both stroke and dementia is hyperlipidemia. This study investigated the association between statin use and the risk of dementia.

Using data from the National Health Insurance Program in Taiwan, which covers nearly 100% of the Taiwanese population, data were retrieved for one million beneficiaries. Subjects were patients admitted to a hospital with a diagnosis of ischemic or hemorrhagic stroke between 1997 and 2005, who were matched with controls. Data retrieved included prescriptions for statin use, demographics, and comorbidities. The statins were classified as high potency (rosuvastatin, atorvastatin, and simvastatin) and low potency (lovastatin, fluvastatin, and pravastatin). A cumulative duration of statin exposure was assessed. The primary outcome measure was a diagnosis of dementia.

Data were included for 5527 statin users and 9280 non-users. During a median of 7.5 years of follow-up 16.2% were diagnosed with incident dementia among statin users and 23.9% among nonusers ( $p<0.001$ ). Statin use of less than one year did not seem to provide any protective effects against the occurrence of dementia.

**Conclusion:** This retrospective longitudinal study in Taiwan found that after a stroke, the use of a statin was associated with a reduction in the risk of dementia.

Pan, M., et al. Statin Use and the Risk of Dementia in Patients with Stroke: A Nationwide Population based Cohort Study. **J Stroke Cerebrovasc Dis**. 2018, November; 27 (11): 3001-3007.

## 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 impairment (Neck

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.

#### ANTI-FATIGUE EFFECTS OF GINSENG DERIVED OLIGOPEPTIDES

The complaint of fatigue has been reported as related to a number of medical issues. American ginseng (*Panax quinquefolium L.*) has been reported to have a number of biological effects, including the reduction of fatigue. This animal study investigated small molecule oligopeptides (QOPS) isolated from *Panax quinquefolium L.* for their effects on fatigue.

The oligopeptide sample was isolated and purified from American ginseng roots. Subjects were 240 adult male mice divided into five groups. These included a vehicle control group, a whey protein group, and three groups receiving different doses of QOPS; 225 mg per kg BW (LG), 450 mg per kg BW;(MG), and 900 mg per kg BW(HG). The supplements were given once a day for 30 days. After the final treatment mice were assessed for swim time to exhaustion.

Compared to the control group, the swimming time among those given QOPS-LG, QOPS-MG, QOPS-HG were increased by 35.24%, 51.16% and 82.62% respectively.

Compared to the control group, the treatment groups had decreased serum urea nitrogen (SUN) and blood lactate (BLA) levels, and increased lactate dehydrogenase (LDH) activity and hepatic glycogen content ( $p=0.01$  for all comparisons).

**Conclusion:** This study found that animals that were given daily doses of small molecule oligopeptides isolated from American ginseng had a significant reduction in physical fatigue, with the effect increasing with increased doses.

Li, D et al. Anti-Fatigue Effects of Small Molecule Oligopeptides Isolated from *Panax quinquefolium L.* in Mice. *Food Function*. 2018; 9 (8):4266-4273.

#### DRY NEEDLING FOR KNEE OSTEOARTHRITIS

Osteoarthritis (OA) of the knee affects up to 37% of adults in the United States between the ages of 45 and 60 years. Among conservative treatments, electrical dry needling combined with manual therapy has been found to be moderately effective. This study explored the effect of dry needling combined with manual therapy and exercise for patients with symptomatic OA of the knee.

This randomized single blind parallel group study included consecutive individuals with painful knee OA seen in ten different outpatient physical therapy clinics. The participants were randomized to receive manual therapy and exercise, alone or in combination with electrical dry needling. All participants received 8-10 sessions at a frequency of 1-2 times per week over six weeks. In addition, the dry needling group received electrical dry needling using a nine-point protocol for 20-30 minutes at each treatment session. Outcome measures included disability as assessed with the WOMAC total score, with secondary outcomes including knee pain intensity, medication intake, and the global rating of change.

In the adjusted analysis of variance, those receiving dry needling experienced greater improvements in knee-related disability at six weeks ( $p<0.001$ ), and three months ( $p<0.001$ ) compared to those receiving exercise and myofascial therapy alone. The percent change in WOMAC from baseline at three months was 67% in the dry needling

group and 32.9% for the control group ( $p<0.001$  for both comparisons).

**Conclusion:** This randomized uncontrolled study of patients with osteoarthritis of the knee found that dry needling added to exercise and manual therapy could improve patient outcomes.

Dunning, J et al. Periosteal Electrical Dry Needling as An Adjunct to Exercise and Manual Therapy for Knee Osteoarthritis: A Multicenter Randomized Clinical Trial. *Clin J Pain*. 2018, December; 34(12):1149-1158.

#### 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 of chronic sciatica.

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.

### STATIN USE AND KNEE OSTEOARTHRITIS

Several studies have demonstrated the cumulative impact of metabolic disorders on the onset or progression of knee osteoarthritis (OA). Among these were small studies demonstrating that serum cholesterol and triglyceride levels are associated with bone marrow lesions. This study investigated the association between treatment with statins and the progression of OA of the knee.

This randomized double-blind placebo-controlled trial included adult patients from 18 countries presenting with OA of the knee. Subjects were 50 years of age and older with symptomatic and radiographic evident knee OA. Data recorded at baseline included statin use, as well as body mass index and radiographic assessment. Patients were followed for three years for radiographic progression.

Of the 336 patients assessed, 71 were statin users. The statin users had a higher rate of radiographic progression of OA ( $p=0.007$ ). In the adjusted analysis the radiographic progression remained significantly associated with the use of statins ( $p=0.01$ ).

**Conclusion:** This prospective study suggests that among patients with osteoarthritis of the knee, those who take statins are more likely to have radiographic progression.

Eymard, F et al. Statin Use and Knee Osteoarthritis Progression: Results from a Post Hoc Analysis of the SEKOIA Trial. **Joint Bone Spine.** 2018; 85:609-614.

### 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

### HEMOGLOBIN 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 and 32 (7.5%)

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  $\leq 2$ , 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): 1432-1438.

### 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 in 13.8% of the control group ( $p=0.001$ ). A

multivariable 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 Cerebrovasc Dis*. 2018, November; 27(11): 2932-2939.

### IBUPROFEN GEL WITH PHONOPHORESIS FOR KNEE OSTEOARTHRITIS

Phonophoresis combines ultrasound with topical pharmacologic agents. Several studies have demonstrated the effectiveness of nonsteroidal anti-inflammatory drugs (NSAIDs) applied by phonophoresis in patients with osteoporosis (OA) of the knee. As studies have not produced consistent results, this study compares the clinical effectiveness of gel and cream forms of ibuprofen used in phonophoresis for OA of the knee.

Adult patients with clinical OA of the knee were randomized to receive either gel phonophoresis or cream phonophoresis. Both groups received five sessions per week for two weeks to the index knee. Gel and cream forms of five percent ibuprofen were used with ultrasound set at 1 MHz with an intensity of 1 W per centimeter squared for five minutes. All patients were assessed at baseline and follow-up for demographic variables, body mass index, radiographic grading of the index knee, with outcome measures including pain as graded on a visual analog scale (VAS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).

Both groups had significant reductions in VAS pain measures from baseline to follow-up ( $p<0.001$ ). Significant improvement in WOMAC scores was found for the gel ( $p<0.001$ ) as well as the cream ( $p<0.05$ ) groups. The gel group showed more improvement than the cream group in the VAS pain ( $p=0.003$ ) WOMAC-pain ( $p=0.001$ ), WOMAC-stiffness ( $p=0.012$ ), WOMAC-physical function ( $p<0.001$ ) and WOMAC total scores ( $p<0.001$ ).

**Conclusion:** This study of patients with osteoarthritis of the knee

found that ibuprofen phonophoresis is effective, and is best delivered using gel rather than a cream.

Benlidayi, I., et al. Comparative Short-Term Effectiveness of Ibuprofen Gel and Cream Phonophoresis in Patients with Knee Osteoarthritis. *Rheumatol In*. 2018, October; 38 (10):1927-1932.

### 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-1 $\beta$ , 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-1 $\beta$ , and reduced inflammation in the cells exposed to IL-1 $\beta$ . 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.

### OSTEOARTHRITIS, PHYSICAL FUNCTION AND CARDIAC DISEASE

Studies have demonstrated an association between osteoarthritis (OA) and an increased risk of cardiovascular disease (CVD). This study examined the association between symptomatic OA (sxKOA) of the knee, and risk factors for CVD.

This study involves participants in an ongoing community-based study focusing on hip and knee OA. Subjects were 45 years of age and older at admission, without a history of CVD. All were evaluated for physical function using the Health Assessment Questionnaire (HAQ), and were assessed with time to complete five chair stands, and the eight-foot walk. Covariates included age, gender, race, education, body mass index, waist to hip ratio, diabetes, hypertension, hyperlipidemia and use of nonsteroidal anti-inflammatory drugs. The primary outcome measure was incident self-reported CVD.

Analysis was completed for 1709 participants with a mean age of 59.5 years. Of these 15% had sxKOA of the knee. While individuals with sxKOA at baseline had 1.50 times greater odds of incident CVD, in the adjusted analysis there was no significant difference in CVD between those with and those without sxKOA. Comparing those in the lowest quartile of chair stand time, those in the higher quartiles had significantly elevated incident CVD. Slower gait speed was associated with incident CVD, though only for those without sxKOA. Worsening gait speed was also associated with an increased risk of incident CVD.

**Conclusion:** This study suggests that a key contributor to the association between symptomatic knee osteoarthritis and cardiovascular disease among those with painful osteoarthritis of the knee is worsening function over time.

Corsi, M et al. Contributions of Symptomatic Osteoarthritis and Physical Function to Incident Cardiovascular Disease. **BMC Musculoskelet Disor.** 2018; 19:393.

### 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.

### TRANSCRANIAL DIRECT CURRENT STIMULATION FOR PARKINSON'S DISEASE

Compared with the general population, patients with Parkinson's disease (PD) have a higher cumulative risk of dementia and depressive symptoms. This study investigated the effect of transcranial direct current stimulation (tDCS) combined with computerized cognitive training (CCT), on cognitive and mood disorders among patients with PD.

Subjects were 22 patients with PD with mild cognitive impairment (MCI) and dementia. All participants underwent 25 minutes of CCT with concurrent active (a-tDCS) or sham (s-tDCS) tDCS. The stimuli were applied with the anode placed over the dorsolateral prefrontal cortex, five times weekly for two weeks. All subjects were assessed by clinical, neuropsychological and behavioral evaluations at baseline, after the last session, and at three months follow-up. The CCT was completed with BRAINHQ, including five exercises of five minutes each. The primary outcome measure was the change in Beck Depression Inventory-II (BDI-II) score, with secondary outcomes including changes in the cognitive task scores.

Improvement on the BDI-II showed significantly greater improvement in the a-tDCS group than in the s-DCS group at two weeks ( $p = 0.003$ ) and at three months ( $p = 0.007$ ). Better improvement was also noted in the a-tDCS in the PD Cognitive Rating Scale (PD-CRS) total score, and frontal subcortical score at both two- and three-month follow-ups ( $p < 0.001$  for all comparisons). The a-tDCS group was better improved than the s-tDCS in verbal fluency phonemic ( $p = 0.002$ ), semantic ( $p = 0.024$ ), naming of objects ( $p = 0.004$ ), tests of attention ( $p = 0.0009$ ) executive function ( $p = 0.0008$ ) and response flexibility ( $p = 0.0008$ ).

**Conclusion:** This study of patients with Parkinson's disease demonstrates significant additional positive effects of active direct current stimulation on measures of cognitive performance and mood disturbances.

Manenti, R et al. Transcranial Direct Current Stimulation Combined with Cognitive Training for the Treatment of Parkinson Disease: A Randomized, Placebo Controlled

### HIGH INTENSITY INTERVAL TRAINING FOR OVERWEIGHT ADULTS

Current public health guidelines recommend at least 30 minutes of moderate exercise per day. However, time is often cited as a barrier to compliance. An alternative approach is high intensity interval training (HIIT), defined as brief, intermittent bursts of vigorous activity, interspersed by periods of rest. This study investigated the compliance of overweight individuals in a one-year program of unsupervised HIIT, and the outcome of this participation.

Subjects were 18 years of age and older with a body mass index (BMI) of at least 27 kg/m who had no history of cardiovascular disease or serious medical issues. Data collected included weight, body composition, blood pressure, aerobic fitness indices and serum lipids. Participants chose whether to follow current exercise recommendations or HIIT. The HIIT participants used a cycle ergometer to produce three intervals of up to 30 seconds of near maximum effort to obtain perceived effort of 8/10 or greater. The traditional exercise group underwent 30 minutes per day of moderate intensity exercises. Changes in baseline data were compared after 12 months.

Of the initial group, 104 participants (41.6%) elected to try HIIT. At 12 months there were no differences between exercise groups in weight loss, or visceral fat, though the HIIT group reported greater enjoyment of physical activity ( $p=0.01$ ). Compliance with three or more sessions of HIIT per week fell from 40% at week one to 10.8% at 12 months.

**Conclusion:** This study comparing traditional with high intensity interval training exercises found that the high intensity exercise was more accepted than standard exercise, though adherence at one year was low.

Roy, M et al. High Intensity Interval Training in the Real World: Outcomes From a 12-month Intervention in Overweight Adults. **Med Sci Sports Exerc.** 2018, September; 50(9):1818-1826.

### DIRECT CURRENT STIMULATION FOR CHRONIC POST STROKE APHASIA

Recovery from post stroke aphasia is a dynamic process by which undamaged brain networks reorganize adaptively to compensate for the loss of function. Noninvasive brain stimulation has been used to affect recovery of motor function in patients with acute stroke (AS). This study investigated the effects of direct current stimulation (DCS) in patients with chronic aphasia due to stroke.

Subjects were 14 patients with aphasia at least six months after a stroke. All were exposed to three 20-minute treatment sessions including; a) anodal stimulation of the dorsolateral prefrontal cortex (DPFC; A-tDCS), b) cathode stimulation over the DPFC (C- tDCS), and c) a sham stimulation condition (S- tDCS). The primary outcomes included a picture naming task, a phonemic fluency task, and a repetition task. The tDCS interventions were separated by a one-week interval.

As compared to the S-tDCS condition, those in the A-tDCS demonstrated improved phonemic fluency ( $p=0.01$ ), with subjects producing more words after A-tDCS than after S-tDCS. In addition, A-tDCS resulted in faster response in high frequency words ( $p=0.034$ ). There was no effect of the A-tDCS in the repetition and picture naming tasks. Discomfort within the first three minutes of stimulation ranged between zero and 4.5 on a scale of 0-6.

**Conclusion:** This study of patients with chronic aphasia resulting from a stroke found that 20 minutes of anodal stimulation with direct current stimulation could result in improved language performance.

Pestalozzi, M et al. Effects of Prefrontal Transcranial Direct Current Stimulation on Lexical Access in Chronic Poststroke Aphasia. **Neurorehabil Neural Repair** 2018, October; 32 (10): 913-923.

### GRADED EXERCISE PROGRAM IN HEART FAILURE PATIENTS

Less than 50% of chronic heart failure (CHF) patients adhere to prescribed therapy guidelines after cardiac rehabilitation. This study explored whether a gradual increase in exercise volume would help with compliance.

Subjects were 60 Dutch patients with CHF who received individualized gradual exercise training (GET). In the GET group, the training time of aerobic exercises increased incrementally every other week without changing exercise intensity. Resistance exercise training consisted of eight exercises with a durable resistance band. Guidance consisted of a step-down approach from in-hospital to home-based training. Cardiopulmonary exercise tests were performed at baseline, three, six and 12 months. The control group included 117 patients from a CHF registry of patients from the same clinic receiving usual outpatient care.

Compared to baseline, the  $VO_2$  peak was significantly improved at three, six and 12 months (+1.1 mL/min/kg, +2.9 mL/min/kg, and 2.6 mL/min/kg respectively). At the eight year follow up, deaths were reported in 38.3% of the GET patients and in 53.8% of the control patients.

**Conclusion:** This study of patients with CHF suggests that low-intensity, high-frequency exercise therapy with gradual increase in volume can result in long-term increases in fitness and improved survival.

Snoek, Johan A., et al. Impact of a Graded Exercise Program on  $VO_2$  Peak and Survival in Heart Failure Patients. **Med Sci Sports Exer.** 2018, November; 50(11): 2185–2191.

### SIGNIFICANT INCIDENTAL MRI FINDINGS AMONG ASYMPTOMATIC ADULTS

In research, and in clinical practice, magnetic resonance imaging (MRI) results may detect incidental findings. This literature review and meta-analysis attempted to clarify the prevalence of such incidental findings on MRI.

Using data from Medline and Embase through April 2017, the authors reviewed studies reporting on the incidental findings in asymptomatic adults undergoing cardiac, abdominal, brain or body MRI. Of the incidental findings discussed, the authors rated the potential severity of these. Of the studies reviewed, 32 were included involving 27,643 participants.

The pooled prevalence of incidental findings that were rated as potentially serious was 3.9% on brain



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and body MRI, and 1.4% on brain MRI. The prevalence was 1.3% on thoracic MRI and 1.9% on abdominal MRI. When the authors included incidental findings of uncertain potential seriousness, the pooled prevalence rose with approximately half of the findings being suspected malignancies (brain, 0.6%, thorax, 0.6%; abdomen, 1.3%; brain and body, 2.3%).

**Conclusion:** This literature review and meta-analysis outlines the risk of potentially serious incidental findings among asymptomatic patients undergoing magnetic resonance imaging.

Gibson, L et al. Potentially Serious Incidental Findings on Brain and Body Magnetic Resonance Imaging of Apparently Asymptomatic Adults: Systematic Review and Meta-Analysis. **BMJ**. 2018; 363: K4577.

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