

# REHAB IN REVIEW

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## TREATMENT OF CHRONIC DIZZINESS AFTER ISCHEMIC STROKE

Previous studies have demonstrated that dizziness is a common complaint among patients with chronic ischemic cerebral lesions. In some cases, this dizziness is associated with supratentorial lesions for which the underlying mechanism is unknown. Cilostazol, a phosphodiesterase three inhibitor, prevents platelet aggregation and dilates vessels by increasing cyclic adenosine monophosphate levels. This medication increases cerebral blood flow and cerebral function in patients with chronic stroke. This study was designed to compare the efficacy of this medication with that of aspirin for chronic, post-stroke dizziness.

This prospective, randomized, open label trial included 209 patients diagnosed with non-cardioembolic ischemic stroke who subsequently complained of persistent dizziness. The patients were randomly assigned to one of two treatments: cilostazol, 200 mg per day, or aspirin, 100 mg per day, for six months. The primary outcome measure was a subjective assessment of chronic dizziness. Dizziness was considered to have improved when the patient reported that the symptom no longer disturbed activities of daily living. In addition, measures included fixation suppression of the vestibulo-ocular reflex (Fr Index) and regional blood flow in the cerebrum, cerebellum and brainstem, as measured by a SPECT scan.

After six months, subjective dizziness had significantly improved in 83.3% of the cilostazol group and in 39% of the aspirin group ( $p < 0.0001$ ). After therapy, scores on the Fr Index were decreased only in the cilostazol group ( $p < 0.0001$ ). Blood flow in the cerebrum was relatively increased only in the cilostazol group ( $p = 0.012$ ).

**Conclusion:** This study of patients with chronic dizziness after ischemic stroke demonstrates that cilostazol can reduce subjective dizziness while increasing supratentorial cerebral blood flow.

Johkura, K., et al. Cilostazol versus Aspirin Therapy in Patients with Chronic Dizziness after Ischemic Stroke. *Clin Neurol Neurosurg*. 2012, September; 114(7): 876-880.

## GROWTH HORMONE FOR FIBROMYALGIA

Fibromyalgia (FM) is a chronic, noninflammatory pain syndrome, characterized by chronic, widespread pain, fatigue and sleep disturbance. The current consensus for treatment includes medications, exercise and psychological support. Previous studies have documented that 50% of patients with FM have a growth hormone deficiency, with 30% having a deficit in insulin-like growth factor I (IGF-1). This study reviewed the effects of treating FM with low-dose growth hormone.

This study included 120 patients diagnosed with severe FM and IGF -1 levels  $< 150\text{ng/ml}$ . The subjects were randomized to receive either low-dose, subcutaneous growth hormone for 12 months (group A) or a placebo for six months, followed by low-dose growth hormone for six months (group B). Both groups continued standard doses of amitriptyline and tramadol, which were initiated six months prior to the beginning of the study. Patients were assessed at nine time points using the Fibromyalgia Impact Questionnaire (FIQ), the EuroQol 5 Dimensions Test (EQ5D), a visual analogue scale (VAS) for pain and the number and intensity of tender points.

At the end of six months, no significant difference was seen between the groups in the percent of patients with fewer than 11 positive tender points, the mean number of

tender points, intensity of pain or total FIQ scores. However, at 12 months 53% of patients in the treatment group and 33% of the control group had fewer than 11 positive tender points ( $p < 0.05$ ). In addition, group A had a 40% reduction in the number of tender points, as compared to 28% in group B ( $p = 0.07$ ). Pain intensity on the VAS averaged 5.2 in group A and 6.21 in group B ( $p = 0.03$ ). In addition, group A demonstrated greater improvements in FIQ scores, EQ5D scores and VAS scores at 12 months ( $p = 0.02$ ,  $p = 0.047$ ,  $p = 0.01$ , respectively)

**Conclusion:** This study of patients with fibromyalgia and growth hormone deficiency suggests that growth hormone replacement may be an effective treatment for pain reduction and improved quality of life.

Cuatrecasas, G., et al. Growth Hormone Treatment for Sustained Pain Reduction and Improvement in Quality of Life in Severe Fibromyalgia. *Pain*. 2012, July; 153 (7): 1382-1389.

## TRENDS IN SERUM LIPIDS AMONG UNITED STATES YOUTHS

The process of atherosclerosis begins during childhood and is associated with adverse lipid concentrations. Serum lipid concentrations in childhood are associated with lipid concentrations in adulthood. This study examined the trends in serum lipid concentrations among children and adolescents over the past 20 years.

Data were obtained from the National Health and Nutrition Examination Surveys (NHANES) from three time periods, 1988-1994, 1999-2002 and 2007-2010. As a component of this study, participants received a detailed, in-person home interview, followed by physical examinations, including laboratory measures. The laboratory evaluations included serum total cholesterol and

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HDL-C levels, in participants at least six years of age, as well as triglycerides in participants at least 12 years of age. Also collected were demographic variables and body mass index calculations.

Among those ages six to 19 years, a decrease in total cholesterol was noted between the earliest and latest data, from an average of 165 mg per deciliter to 160 mg per deciliter ( $p < 0.01$ ). In addition, the mean HDL-C levels increased from the earliest to the latest reporting period. Among adolescents ages 12 to 19 years, decreases were seen in mean serum LDL-C between the earliest and latest reporting period, from 95 mg per deciliter to 90 mg per deciliter ( $p = 0.003$ ), and in mean serum triglycerides, from 80 mg per deciliter to 73 mg per deciliter ( $p < 0.001$ ). Despite these improvements, more than 20% of children ages nine to 11 years of age had either a low HDL-C or a high non-HDL-C concentration in the range indicating the need for additional clinical evaluation.

**Conclusion:** This study, using data from the NHANES trials, found a favorable trend in the past 20 years for lipid concentrations among youths in the United States.

Kit, B., et al. Trends in Serum Lipids among U.S. Youths Aged 6 to 19 Years, 1988-2010. *JAMA*. 2012; August 8; 308 (6): 591-598.

### **VIRTUAL REALITY GAMING AND BALANCE IN THE ELDERLY**

Falls are the leading cause of death by injury among the elderly in the United States. Exercises that increase functional strength and balance have been shown to reduce falls in this population. Virtual-reality gaming is a new technology that has been used to assist with balance. This study evaluated the utility of using a virtual reality gaming system, the Wii Balance Board, to improve dynamic balance in older individuals.

Forty, community dwelling adults between the ages of 60 and 95 years of age were studied. After baseline testing, the subjects were randomized to a control group or a virtual-reality group. The virtual-reality group received three different Nintendo Wii FIT Balance interventions, three times per week for six weeks. The control group received no intervention. Both groups were

followed over six weeks, with pre-and post test evaluations including the 8-foot Up and Go Test (UG), the Activities Specific Balance Confidence Scale (ABC), and the Geriatric Depression Scale (GDS).

The mean change on the 8-foot UG decreased by one second in the treatment group, as compared to 0.2 seconds in the control group ( $p = 0.038$ ). The mean increases on the ABC were 6.9% for the treatment group and 1.3% for the control group ( $p = 0.038$ ). Although GDS improved more in the treatment group, that difference did not reach statistical significance.

**Conclusion:** This study of community dwelling elderly individuals found that a six-week program using the Wii Fit Balance can improve balance and confidence in performing functional activities.

Rendon, A., et al. The Effect of Virtual Reality Gaming on Dynamic Balance in Older Adults. *Age Aging*. 2012; 41: 549-552.

### **GAMING IN CHILDREN WITH BRAIN INJURY**

Patients with acquired brain injury (ABI) report problems with motor, cognitive, behavioral and emotional function. Previous studies have suggested a beneficial effect of virtual reality and interactive video gaming for patients with stroke, although the results have been mixed. This study explored the effect of the use of a Nintendo Wii in children with ABI.

This multi-center, observational study included patients six to 29 years of age, diagnosed with ABI. A total of 50 patients were recruited for this 12-week intervention. Baseline data included neuropsychological tests, sociodemographic and disease characteristics, physical, recreational and social activity history, cognitive/neuropsychological function and quality of life measures. Assessments were completed at baseline and after the 12-week intervention. After baseline testing, three Nintendo Wii games were determined to match the patient's main limitations. Treatment goals were individualized and included physical, mental and/or social functioning. The participants were encouraged to play each game a minimum of 20 minutes per week, with a total game time of at least two hours per week.

A total of 45 patients were

available for follow-up. At follow-up, improvements were noted in physical activity, information processing speed, attention, response inhibition and parent perceived quality of life. At follow-up, two thirds of the patients reported improvements in gross motor functioning and information processing. In addition, the majority of the subjects indicated improvement in their major treatment goals.

**Conclusion:** This uncontrolled study of patients with acquired brain injury found that the use of Nintendo Wii may improve physical, cognitive and social functioning.

Kloet, A., et al. Gaming Supports Youth with Acquired Brain Injury? A Pilot Study. *Brain Inj.* 2012, July; 26 (7-8): 1021-1029.

### KINESIOTAPING AND MUSCLE STRENGTH

Since its development in the 1970s, kinesiotaping has become an increasingly popular treatment, purported to enhance muscle function, improve circulation and decrease pain through neurological suppression. This study assessed the immediate effect of kinesiotaping on quadricep strength in healthy adults.

This single-blind, placebo-controlled, repeated measure study included 36 healthy volunteers, ranging in age from 18 to 47 years. All subjects participated in nonprofessional sports activity at least twice a week. The participants were tested across three different sessions, randomly receiving one of three kinesiotaping interventions. These included facilitatory or inhibitory taping, designed to enhance or inhibit strength, respectively. The third group underwent sham kinesiotaping. The outcome measures included the isokinetic peak torque test (IPTT), the single leg triple hop and a global rating of change. Data were analyzed to determine whether torque differed among the three conditions.

No significant differences were noted between baseline and the various taping conditions for IPTT at 60° or 180° per second, or for the single leg triple hop test (all  $p > 0.05$ ). At an individual level, very few subjects showed positive or negative changes of more than the minimal detectable change (MDC) at the 95% confidence level.

**Conclusion:** This study found no

significant change in muscle strength after kinesiotaping.

Vercelli, S., et al. Immediate Effects of Kinesiotaping on Quadriceps Muscle Strength: A Single Blind, Placebo-Controlled, Crossover Trial. *Clin J Sport Med.* 2012, July; 22: 319-326.

### KINESIOTAPING FOR MEDIAL EPICONDYLITIS

Medial epicondylitis is a common overuse injury among athletes that can result in pain and reduced performance. Standard nonoperative therapy often includes kinesiotaping, though no formal studies have examined the effects of this intervention on injured athletes. This study therefore investigated the effect of kinesiotaping on strength, force sense and pain among baseball pitchers with medial epicondylitis.

Ten baseball pitchers with medial epicondylitis and ten healthy subjects were enrolled in this study. Three conditions were tested, including no taping, placebo taping, and kinesiotaping taping of the forearm. These conditions were separated by one-week intervals. Outcome measures included maximal wrist flexor isometric strength, force sense of wrist flexor measurements, and pressure pain assessment. Pressure pain threshold and 4-kg pressure pain tolerance were tested using a pressure algometer, with the results scored on a visual analogue scale.

The maximal wrist flexion strength was not different in the three taping conditions for either the healthy group or the medial epicondylitis group. For absolute force sense error, there were significant results among the three taping conditions for the medial epicondylitis group ( $p=0.023$ ), but not in the control group. Placebo taping demonstrated similar effects on force sense and pain thresholds. For the 4-kg pressure pain tolerance, both taping groups had decreased the VAS compared with the no tape group.

**Conclusion:** This study of patients with medial epicondylitis found that both sham taping and kinesiotaping may reduce pain and improve wrist force control without improving wrist flexor strength.

Chang, H et al. Could Forearm Kinesiotaping Improve Strength, Force Sense And Pain In Baseball

Pitchers With Medial Epicondylitis? *Clin J Sport Med.* 2012, July; 22:327-333

### TREATMENT OF POOR RANGE OF MOTION AFTER KNEE ARTHROPLASTY

Stiff knee with reduced range of motion is a common complication after total knee arthroplasty (TKA). Among the nonsurgical approaches for treating the stiffness, mobilization under anesthesia is commonly used. This study evaluated the efficacy of this intervention as compared with stretching using a mechanized, low load stretch device. Fifty-four patients with reduced range of motion after TKA were studied. Knee stiffness was defined as active flexion of less than 90° and/or a flexion contracture that negatively impacts function as reported by the patient. The subjects were randomized to either a group undergoing manipulation under anesthesia or a group treated with a low load stretch device.

After manipulation under anesthesia, those in the anesthesia group received active assisted physiotherapy to maintain the range of motion daily for two weeks, followed by twice a week for another four weeks. Those in the low load stretch group used a computer-controlled motion technology device to perform repetitive stretching over a preset range of motion. This range was set such that a preset maximum resistance would not be violated. This device was used for 80 minutes per day for six weeks. Range of motion at week six was compared between groups.

Both groups showed a significant increase in the flexion and extension range of motion ( $p < 0.05$  for both). No significant difference was found between groups in flexion or extension range of motion or on any of the pain, function or stiffness measures.

**Conclusion:** This study of patients with stiff knee after total knee arthroplasty found that a low load stretch device can achieve similar increases in range of motion as those realized by manipulation under anesthesia.

Witvrouw, E., et al. Manipulation under Anesthesia versus Closed Stretch Device in Poor Range of Motion after TKA. *Knee Surg Sports Traumatol Arthrosc.* 2012, DOI

### STATIN THERAPY FOR LOW RISK PATIENTS

In previous studies, the reduction of low-density lipoprotein (LDL) cholesterol using statins has been found to reduce the risk of major vascular events. However, uncertainty persists concerning whether statin therapy is of overall net benefit as a primary prevention. This meta-analysis was designed to clarify whether people at low risk of vascular disease can benefit from the LDL cholesterol lowering effect of statins.

The cholesterol treatment trialists (CTT) collaboration is a meta-analysis of individual data from 170,000 patients within 21 trials of standard statin regimens. In all studies, the intervention's main effect was to lower LDL cholesterol, with the main outcomes of interest including major vascular events, major coronary events, stroke, coronary revascularization procedures, cancer and cause specific mortality. For this meta-analysis, the participants were separated into five baseline categories of 5-year risk of a major vascular event. The effects of statin use were analyzed within each risk category.

Among all 27 trials, statins reduced the risk of major vascular events by 21% per 1.0mmol/L LDL cholesterol reduction ( $p < 0.0001$ ). There were significant reductions in major vascular event risk in each of the two lowest risk categories, including the  $< 5\%$ , and the  $\geq 5\%$  to  $< 10\%$  groups (both  $p < 0.0001$ ).

**Conclusion:** This meta-analysis demonstrates that statins may be effective in lowering the risk of cardiovascular events, even among those in the lowest risk category.

Cholesterol Treatment Trialists Collaboration. The Effects of Lowering LDL Cholesterol with Statin Therapy in People at Low Risk of Vascular Disease: Meta-Analyses of Individual Data From 27 Randomized Trials. *Lancet*. 2012, August 11; 380 (9841): 581-590.

### LEPTIN LEVELS AND KNEE OSTEOARTHRITIS

Leptin is a peptide molecule, synthesized by adipocytes, which

regulates appetite and energy expenditure at the hypothalamic level. In addition, this molecule modulates the immune response affecting bone and cartilage metabolism. As exercise and glucosamine sulfate are common interventions for osteoarthritis (OA) of the knee, this study assessed the effects of these interventions on serum leptin levels.

Thirty-seven women diagnosed with knee OA were enrolled in this study. OA severity was rated using radiographs of both knees. Leptin levels were measured at baseline and after 12 weeks of treatment. Patients were randomized into two groups. Group 1 participated in an exercise program only, while group 2 additionally received glucosamine sulfate at 1,500 mg per day. The subjects performed isometric and isotonic exercises for 45 minutes, three days per week for twelve weeks. Both groups were assessed for level of pain, disability, walking performance, muscle strength, quality of life and level of depression.

Leptin levels were positively correlated with body mass index and negatively correlated with duration of symptoms. With treatment, both groups demonstrated significant improvements in pain, physical function, muscle strength, walking distance and decreases in leptin levels. No difference was seen between the two groups on any of these measures after glucosamine therapy.

**Conclusion:** This study demonstrates that exercise alone can improve leptin levels and clinical parameters of osteoarthritis, with no additional benefit realized through the use of glucosamine sulfate.

Durmus, D., et al. Effects of Glucosamine Sulfate and Exercise Therapy on Serum Leptin Levels in Patients with Knee Osteoarthritis: Preliminary Results of Randomized, Controlled Clinical Trial. *Rheum Inter*. 2012; DOI: 10.1007/s00296-012-2401-9.

### PREVENTING FRICTION INDUCED CHONDROCYTE APOPTOSIS IN OSTEOARTHRITIS

Most patients treated conservatively for osteoarthritis (OA) receive physical therapy, nonsteroidal anti-inflammatory drugs, or joint injections of corticosteroids or hyaluronic acid. Prior to injection,

arthrocentesis is advised by the manufacturer of Synvisc (a hyaluronic acid). However, this process may remove important components of the synovial fluid, including Lubricin, a glycoprotein important for joint lubrication. This study investigated the effectiveness of Hylan G-F 20 for reducing the coefficient of friction and preventing chondrocyte apoptosis in OA.

This in-vitro comparison study employed bovine cartilage explants from load bearing regions of the femoral condyle. A disc on disc bovine cartilage bearing model was employed, using a material testing system to apply axial loading with axial rotations. The static and kinetic coefficients of friction were measured under three conditions. These included lubrication with Hylan G-F 20, human synovial fluid (HSF) and phosphate buffered saline (PBS). After the tests of friction, the fluid was analyzed for markers of apoptosis.

The mean static coefficient of friction (COF) was significantly lower for the HSF group than for the PBS group ( $p = 0.006$ ). The Hylan G-F 20 group did not differ significantly from those receiving PBS or HSF. The mean kinetic COF was significantly lower when the explants were lubricated with HSF than with Hylan G-F 20 ( $p = 0.022$ ) or PBS ( $p = 0.003$ .) Bearings lubricated with Hylan G-F 20 had a significantly higher percentage of cells positive for activated caspase-3 compared to unloaded control bearings or bearings lubricated with HSF. This indicates that Hylan GF-20 is less chondroprotective than HSF.

**Conclusion:** This study suggests that arthrocentesis prior to injections with a Hylan G-F 20 may not adequately protect cartilage from friction and other sources of chondrocyte apoptosis.

Waller, K., et al. Preventing Friction-Induced Chondrocyte Apoptosis: Comparison of Human Synovial Fluid and Hylan G-F 20. *J Rheum*. 2012, July; 39(7): 1473-14.

### PROACTIVE COUNSELING AND RETURN TO WORK FOR BACK PAIN PATIENTS

Nonspecific low back pain (LBP), although often a self-limiting condition, frequently results in a disappointing return to work rate. In Belgium, LBP accounts for 25% of all

claimants with a lifetime disability benefit. Evidence is increasing regarding the importance of encouraging claimants with LBP to stay active, with medical reassurance often a key component of such an intervention strategy. This study reviewed the impact of purposeful advice from medical professionals on return to work and subsequent absenteeism.

Five hundred six patients who applied for a sick leave benefit as a result of LBP were randomized to receive either a standardized disability evaluation or a disability evaluation with additional information and counseling designed to encourage return to work. The primary outcome variable was the rate of return to work at three and 12 months, assessed through administrative databases. Secondary outcomes included the number of days of sick leave taken, subsequent return to sick leave and subsequent surgery for LBP.

The percentage of claimants who did not resume professional activity at three months was higher in the control group, although this finding did not reach statistical significance. At one year, eight percent of the control group and four percent of the intervention group had not returned to work ( $p=0.03$ ). During the follow-up period, the mean number of days on full benefits, due to LBP, were 75.9 days in the control group and 63.9 days in the intervention group. Repeat sick leave was taken by 15% of the intervention group and 23% of the control group ( $p=0.02$ ).

**Conclusion:** This Belgian study of patients on medical leave for low back pain found that proactive counseling concerning return to work can decrease time out of work and episodes of repeat sick leave.

Dubois, M., et al. Guiding Low Backed Claimants to Work: A Randomized, Controlled Trial. *Spine*. 2012, August; 37(17): 1425-1431.

### EFFECT OF PILATES ON ABDOMINAL MUSCLES

Pilates is a fast-growing rehabilitation and fitness intervention, designed to provide symmetric strengthening of the muscles of the abdominal wall and the spine. This study was designed to assess the effect of Pilates on the symmetry and volume of abdominal muscles in

active, healthy women.

Twelve healthy, sedentary women were recruited for this study. For 36 weeks, each attended biweekly Pilates sessions of 55 minutes' duration. Before and after intervention, MRI was used to determine the area and volume of the bilateral rectus abdominus (RA) muscles and bilateral oblique and transverse abdominus (OT) complex. The dominant abdominal side was defined as ipsilateral to the dominant arm.

No significant change in body mass or total body fat was found after the program. Before training, the total volume of the nondominant OT complex was eight percent greater compared to the dominant side ( $p<0.01$ ). After training, this volume difference was reduced to two percent ( $p=0.43$ ). The volume of the RA increased by 21% after Pilates ( $p<0.05$ ). Dominant and nondominant RA volumes increased by 21% and 20%, respectively, after Pilates.

**Conclusion:** This study demonstrates that Pilates, 55 minutes twice per week, can increase the muscle volume in the rectus abdominus and the oblique and transverse abdominal complex while reducing asymmetries.

Dorado, C., et al. Marked Effects of Pilates on the Abdominal Muscles: A Longitudinal Magnetic Resonance Imaging Study. *Med Sci Sports Exerc*. 2012, August; 44(8): 1589-1594.

### GAIT AND NEUROMUSCULAR ASYMMETRY AFTER ANTERIOR CRUCIATE LIGAMENT TEAR

Previous studies have demonstrated that patients with anterior cruciate ligament (ACL) tears have reduced dynamic knee stability, and often adopt an asymmetric gait that includes less knee flexion and decreased internal knee extensor moment of the injured limb. This study further explored the gait and neuromuscular asymmetries among patients with ACL tears.

Subjects included 31 athletes with unilateral ACL deficiency who were functionally classified as non-copers (demonstrated knee instability). A gait analysis was performed to determine knee extensor moment, with muscle forces estimated using an EMG-driven musculoskeletal model approach. Comparisons were made

between the injured and the contralateral limb.

The peak knee flexion angle during the first half of stance was significantly lower for the injured limb than for the uninjured limb ( $p=0.028$ ). The gait analysis also demonstrated a decreased internal knee peak extensor moment ( $p=0.0004$ ) in the injured, as compared to the uninjured, knee. In addition, extensor muscle force was significantly lower ( $p=0.0001$ ) for the injured limb, as compared with the uninjured limb.

**Conclusion:** This study demonstrates neuromuscular asymmetries in anterior cruciate ligament deficient individuals, which results in a gait strategy requiring less global muscle force from the injured limb.

Gardinier, E., et al. Gait and Neuromuscular Asymmetries after Acute Anterior Cruciate Ligament Rupture. *Med Sci Sports Exerc*. 2012, August; 44(8): 1490-1496.

### ENERGY DRINKS

It has been estimated that energy drinks are consumed on a regular basis by 30% of American male and female adolescents and young adults. Consumption of these drinks is purported to increase alertness, energy and sports performance. This study examined the effects of one popular energy drink on cardiovascular performance.

Subjects were seven university kinesiology students, 18 to 30 years of age. Baseline data included height, weight, EKG results and blood pressure. The students were randomized to treatment (RL) or placebo control (PL) groups. In the RL group, subjects drank 240 mL of Redline, 40 minutes before exercise. This drink contains 250 mg of caffeine anhydrous, Vit-C, Ascorbic Acid, Potassium and Beta-Alanine. The control subjects drank a similar volume of wild Berry Crystal Lite. All participants completed two maximal aerobic stress tests on a treadmill. Differences in estimated  $VO_{2max}$ , HR, ectopic beats, blood pressure, rate pressure product (SBP x HR) and RPE between the two groups were evaluated.

Maximal oxygen consumption was significantly lower in the RL group than in the PL group ( $p=0.02$ ). Rate pressure product and diastolic blood pressure were higher in the RL group

after exercise. The RL group reported an increase in side effects, including lightheadedness, extreme nausea and pale skin. A slightly higher, though insignificant, increase in ectopic heartbeats was noted in the treatment group.

**Conclusion:** This study of healthy subjects found that ingesting the energy drink, Redline, after a 12-hour fast and immediately before exercise, resulted in a decrease in performance.

Sillivent, J., et al. Energy Drinks: Ergolytic or Ergogenic? *Inter J Exer Sci.* 2012; 5(3): 214-222.

### **INTRINSIC FACTORS OF NONCONTACT ANKLE SPRAINS**

Several studies have proposed potential extrinsic and intrinsic factors of ankle sprain susceptibility. Suggested intrinsic factors include anatomic characteristics, functional deficits in strength, flexibility, joint position sense, balance (posture sway and gait mechanics), limb dominance, previous ankle sprains and increased weight and body mass index (BMI). This study was designed to determine the extent to which these and other characteristics are related to an increased risk of noncontact ankle sprains in professional soccer players.

A cohort of 115 players was recruited from among third division professional soccer teams. A preseason evaluation of the ankle joint was conducted for isokinetic muscle strength, flexibility, joint stability, neuromuscular coordination and anthropometric characteristics. Of the subjects, 74 were right-footed, 16 left-footed and 10 mixed. Any noncontact ankle sprain that forced the player to be absent from at least one scheduled practice or game was recorded by each club's medical staff for a period of 10 months. The side and severity of injury were recorded.

Of the 100 players, 37 had concentric and 34 had eccentric, clinically important ankle asymmetries, (>15%). Twenty-four players sustained one or more ankle sprains, both contact and noncontact. The noncontact sprains were associated with incorrect foot positioning at landing in 13 cases and cutting movements in four cases. Of the 17 noncontact sprains, nine occurred in the nondominant extremity, three in the dominant

extremity and five in the mixed foot group. Logistic regression analysis revealed three significant predictors of noncontact ankle sprains. These included eccentric isokinetic strength asymmetries of ankle dorsal and plantar flexors, increased body mass index and increased weight. Those with eccentric strength asymmetry of at least 15% had 8.8 times the odds of sustaining a noncontact sprain than did those with no strength asymmetry. In addition, those with a BMI of greater than 23.1 and a weight of greater than 72.6 kg had six times and eight times greater odds, respectively, of sustaining an ankle sprain, as compared to those with less weight and lower BMI.

**Conclusion:** This study of professional soccer players found that those with significant ankle flexion strength asymmetry, a body mass index of greater than 23 and increased body weight are at increased risk for noncontact ankle sprains.

Fousekis, K., et al. Intrinsic Risk Factors of Noncontact Ankle Sprains in Soccer. A Prospective Study on 100 Professional Players. *Am J Sports Med.* 2012, August; 40(8): 1842-1850.

### **REPETITIVE MAGNETIC STIMULATION AND HAND FUNCTION AFTER ISCHEMIC STROKE**

Following stroke, the lesioned hemisphere is inhibited by the contralesional hemisphere and may contribute to motor impairments. Low frequency, repetitive transcranial magnetic stimulation (LF-rTMS) over the motor cortex downgrades excitability, which may improve motor function when applied to the contralesional hemisphere. Few studies have explored the effect of this intervention for patients with moderate to severe hand motor impairment within the first months after stroke. This study evaluated the effect of LF-rTMS on improvement of hand function when applied within 45 days of ischemic stroke.

This pilot, randomized, double-blind clinical trial included subjects ages 18 to 80 years of age with an ischemic stroke. All were within five to 45 days of stroke and demonstrated hand paresis. Patients were randomized to receive either active or sham LF-rTMS, undergoing treatment

five times per week for a total of 10 sessions. In the active group, the coil was tangentially positioned while in the sham group it was perpendicularly placed. The primary outcome measures were compliance and adverse events. Secondary outcomes included time required to perform activities resembling daily life, as measured by the Jobson-Taylor Test (JTT). Other secondary outcomes included force of the lateral pinch of the paretic hand, sensorimotor recovery of the hand, the Ashworth scale and the modified Rankin scale.

Of the 29 subjects, 15 were placed in the active group and 14 in the sham group. Compliance was 100% in the active group and 94% in the sham group. No significant group differences were seen in adverse events, including sleepiness and headache. Performance on the JTT improved in the active group, but not in the sham group, as measured at one month ( $p=0.03$ ). Lateral pinch force improved in the active group and not in the sham group at one month ( $p=0.008$  and  $p=0.44$ , respectively). No significant difference was seen between groups in the other measures.

**Conclusion:** This pilot study of patients with recent ischemic stroke found that low-frequency repetitive magnetic stimulation is safe and may improve hand function when applied in the acute rehabilitation setting.

Conforto, A., et al. Transcranial Magnetic Stimulation in Mild to Severe Hemiparesis Early after Stroke: A Proof of Principle and Novel Approach to Improve Motor Function. *J Neurol.* 2012, July; 259(7): 1399-1405.

### **RESTORING HAND SENSATION AFTER BRACHIAL PLEXUS INJURY**

Complete brachial plexus palsies can occur during sports injuries and motor vehicle accidents, resulting in paralysis and loss of sensation of the upper extremity. Surgery of the brachial plexus has been shown to restore elbow flexion, although the effect on hand sensation restoration has not been well explored. This study reviewed the progression of hand sensation following a C-5 to musculocutaneous nerve graft after complete brachial plexus injury.

This study enrolled 11 patients

who had suffered a complete brachial plexus injury and had undergone subsequent C-5 to musculocutaneous nerve graft at least three years prior to the study. Six patients with complete brachial plexus injury without surgery served as controls. The participants were assessed using nociception, warm and cold discrimination, monofilament testing and two-point discrimination.

In all of the grafted patients, nociception and warm and cold discrimination had returned to at least a portion of the hand. Seven of the 11 patients were able to detect a 2 g monofilament. None of the grafted patients recovered two-point discrimination. The control group experienced no noticeable return in hand sensation.

**Conclusion:** This study of patients with a brachial plexus injury found that a C-5 to musculocutaneous nerve graft often results in a return of sensation to the lateral forearm, palm and dorsal radial portion of the hand.

Bertelli, J., et al. Grafting the C-5 Route to the Musculocutaneous Nerve Partially Restores Hand Sensation in Complete Palsies of the Brachial Plexus. *Neurosurg.* 2012, August; 71 (2): 259-263.

### BRAIN DAMAGE AND PLASTICITY IN MULTIPLE SCLEROSIS

While remyelination is an important mechanism of repair after acute inflammatory demyelination, clinical recovery for patients with multiple sclerosis (MS) is facilitated by adaptive functional reorganization. The integrity of the extralosomal brain tissue explains part of the potential for network plasticity, which underlies clinical recovery. This study investigated the relationship between microstructural damage and brain plasticity in patients with MS.

Subjects included 23 patients with MS and 12 healthy controls. Only patients who had been free of relapse for the six months prior to screening were included in the study. All subjects were assessed with an initial functional MRI scan during short-term practice of a visuomotor task. A structural MRI analysis was used to measure normalized brain volume (NBV) and to calculate mean fractional anisotropy (FA). The subjects were then asked to perform an isometric visuomotor tracking task

daily for two weeks. At the end of two weeks a functional MRI and a structural MRI were completed.

Patients with MS performed worse on the visuomotor task than did controls at baseline, although both groups demonstrated similar improvements over the course of the study. Brain region activation for visuomotor tasks differed significantly between the two groups. Greater short-term practice improvements were associated with smaller task related signal changes in various brain regions in patients with MS, but not in controls. Greater long-term practice improvements were associated with smaller signal changes in the occipital cortex for controls, but not for MS patients.

**Conclusion:** This study of patients with multiple sclerosis demonstrates that, despite diffuse microstructural damage, brain plasticity can be preserved through motor practice.

Tomassini, V., et al. Relating Brain Damage to Brain Plasticity in Patients with Multiple Sclerosis. *Neurorehabil Neural Repair.* 2012, July/August; 26 (6): 581-593.

### STEM CELL PROLIFERATION THROUGH EXERCISE

Previous studies have demonstrated the positive effects of exercise on cell proliferation in muscles, tendons, and the central nervous system. However, much less data exist concerning the effects of exercise on cartilage tissue, including intervertebral discs. This study was designed to determine the effects of exercise on stem cell proliferation within intervertebral discs.

Thirty rats were administered 5-bromo-2-deoxyuridine (BrdU), which is incorporated into proliferating cells. Of those, 15 rats were subjected to an exercise program and 15 served as controls. At various time points after BrdU administration, the rats were sacrificed and their lumbar intervertebral discs examined histologically. The number of BrdU positive cells was assessed, with comparison made between the two groups. The areas assessed included the stem cell niche, a special microenvironment for stem cells. Cells from these areas are responsible for the growth homeostasis and repair of many tissues.

The exercise group demonstrated a greater number of BrdU positive cells in the stem cell niche, outer annulus fibrosis and peripheral epiphyseal cartilage areas at 14 days ( $p < 0.01$ ). At 105 days, the exercise group demonstrated a greater number of BrdU positive cells than did the control group in the stem cell niche and outer annulus fibrosis areas ( $p < 0.05$ ).

**Conclusion:** This animal study demonstrates that exercise can increase stem cell proliferation in the intervertebral disc, suggesting ongoing cell regeneration capacity in mammals, which can be affected by exercise.

Sasaki, N., et al. Physical Exercise Affects Cell Proliferation in Lumbar Intervertebral Disc Regions in Rats. *Spine.* 2012, August 1; 37(17): 1440-1447.

### TOFACITINIB FOR RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammation and destruction of joints. Tofacitinib is a Janus kinase inhibitor that inhibits signaling through heterodimeric receptors, blocking signaling for several cytokines which are integral to lymphocyte function. This study evaluated the efficacy and safety of Tofacitinib as a monotherapy for the treatment of RA.

Subjects include patients at least 18 years of age, all diagnosed with RA. Each had experienced an inadequate response to at least one non-biologic or biologic disease modifying drug. The subjects were randomized to groups receiving five mg of Tofacitinib twice-daily, 10 mg of Tofacitinib twice-daily or placebo twice daily for three months, followed by five mg of Tofacitinib twice-daily or placebo for three months followed by 10 mg of Tofacitinib twice-daily. The three primary endpoints were, the percentage of patients who met the criteria for an ACR 20 response, a change in baseline physical function as measured by the Health Assessment Questionnaire-Disability Index (HAQ-DI), and the percentage of patients with a disease activity score of 28 joint counts, based upon an erythrocyte sedimentation rate of below 2.6.

A total of 555 patients completed the six-month study. At month three,

(Continued from page 2)

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59.8% of the participants in the five mg group and 65.7% of those in the 10 mg group, as compared to 26.7% in the placebo group, met the criteria for ACR 20 response ( $p < 0.001$  for both comparisons). The corresponding percentages of patients who met the criteria for ACR 70 response were 15.4%, 20.3% and 5.8% ( $p = 0.003$  and  $p < 0.001$  for the five mg and 10 mg dose, respectively, as compared with placebo). In addition, the reductions from baseline HAQ-DI scores were greater in both treatment groups than in the placebo group ( $p < 0.001$ ).

**Conclusion:** This study demonstrates that Tofacitinib, at a dose of 5 mg or 10 mg twice daily, is associated with decreased signs and symptoms of rheumatoid arthritis, as well as improved physical function.

Fleishmann, R., et al. Placebo-Controlled Trial of Tofacitinib Monotherapy in Rheumatoid Arthritis. *N Eng J Med.* 2012, August 9; 367 (6): 495-507.

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