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AMANTADINE TO TREAT BRAIN INJURY

For patients with traumatic brain injury (TBI), neuropharmacological therapies are commonly used off-label to improve functional outcome. Amantadine hydrochloride is a commonly prescribed medication for the treatment of brain injury, with preliminary studies suggesting a positive role for this medication. This study was designed to better clarify the effectiveness of amantadine in promoting recovery from a post-traumatic vegetative or minimally conscious state.

This prospective, double-blind, placebo-controlled trial included subjects 16 to 65 years of age who had sustained a non-penetrating TBI four to 16 weeks prior to enrollment. All were receiving inpatient rehabilitation and were in a minimally conscious or vegetative state. The participants were randomized to receive either amantadine or placebo. The amantadine was initiated at 100 mg twice per day, and titrated to a maximum of 200 mg twice per day, based on their response. The primary outcome measure was the rate of improvement on the Disability Rating Score (DRS) during the four weeks of treatment. During the study, clinically relevant behavioral benchmarks were assessed using the Coma Recovery Scale-Revised (CRS- R). After treatment, the patients were followed for response during a two-week washout period.

A total of 184 patients were enrolled, with patients matched with respect to major demographic variables and prognostic factors. Both the treatment group and the placebo group improved over the four weeks of the trial, although the amantadine group enjoyed significantly faster recovery, with fewer dose increases at weeks two and three. The positive benefits of amantadine seemed to be greater among those who were enrolled earlier after injury than among those enrolled later. More patients in the amantadine group had favorable outcomes on the DRS, with fewer remaining in a vegetative state. No significant difference was seen in adverse events between the two groups

Conclusion: This double-blind, placebo-controlled study of patients with severe brain injury, all enrolled at a rehabilitation unit, demonstrated that amantadine can enhance their functional recovery.

Giacino, J., et al. Placebo-Controlled Trial of Amantadine for Severe Traumatic Brain Injury. **N Eng J Med**. 2012, March 1: 819-826.

HYPOXIA TO TREAT INCOMPLETE SPINAL CORD INJURY

In patients with motor incomplete spinal cord injury (SCI), the extent of recovery is often limited. Acute intermittent hypoxia (AIH)has been shown to induce spinal plasticity, strengthening synaptic pathways to respiratory motor neurons by a mechanism known as respiratory long -term facilitation. This study tested the hypothesis that AIH may induce brain derived neurotrophic factor dependent plasticity in non-respiratory motor pathways.

Thirteen adults were included in this study, all with chronic SCI classified as American Spinal Cord Injury Association Impairment Scale C or D. All had retained ankle plantar flexion strength in at least one leg. The subjects were exposed to two different protocols of AIH, which differed in duration of the episodic, intermittent exposures to hypoxia. Sham control studies were completed with patients receiving continuous normal oxygen. Maximum voluntary ankle plantar flexion torque strength was tested, and surface EMG recorded from the medial head of the gastrocnemius.

In both ischemic protocols, when compared to baseline, isometric ankle plantar flexion strength increased immediately after AIH. Depending upon the protocol, this effect was also seen at 30, 60, 90, 45 and 270 minutes after AIH. These results were not seen in the sham studies, and were correlated at all intervals with increased medial gastrocnemius activation on EMG.

Conclusion: This study of patients with chronic, incomplete spinal cord injury demonstrates that exposure to intermittent hypoxia increases sustained ankle plantar flexion strength.

Trumbower, R., et al. Exposure to Acute Intermittent Hypoxia Augmented Somatic Motor Function in Humans with Incomplete Spinal Cord Injury. **Neurorehab Neural Repair.** 2012, Feb; 26(2): 163-172.

INTRANASAL INSULIN FOR PATIENTS WITH ALZHEIMER DISEASE

Insulin serves a number of important functions in the central nervous system. Insulin modulates glucose utilization in the hippocampus and other brain regions, and facilitates memory at optimal levels in normal metabolism. Some have produced evidence that insulin dysregulation contributes to the pathophysiology of Alzheimer disease (AD). This study examined the effect of long-term insulin administration on cognition in patients with AD and amnestic mild cognitive impairment (aMCI).

This study included 104 older adults, each diagnosed with aMCI or probable AD. The patients were randomized to groups to receive either intranasal insulin at 10 or 20 IU or placebo, administered twice daily for four months. Blood glucose levels were measured daily for the first week and weekly thereafter. The

primary outcome measures were the Delayed Story Recall (DSR) and the Dementia Severity Rating Scale (DSRS). Secondary outcome measures included the Alzheimer Disease Assessment Scale - Cognitive Subscale (ADAS-Cog) score, and the ADAS Activities Of Daily Living Scale test, administered at baseline and at two, four and six months. In addition, a subset underwent PET scan (n=40), and lumbar puncture to measure AD biomarkers including Aβ1-42, tau protein, and P181-tau (n=23).

Treatment with insulin was significantly related to improved memory, preserved caregiver rated functional ability, and preserved general cognitive ability. A significant treatment by time interaction was found for DSRS as compared to the control group (p=0.01). A treatment effect was also found for the partner rated DSRS scores (p=0.008) and the ADAS-cog (p=0.004). Changes in memory and function were associated with changes in the cerebral spinal fluid Aβ42 level and in the tau protein to Aβ42 ratio. PET scans revealed a reduced progression of hypometabolism in the bilateral frontal, right temporal, bilateral occipital and right precuneus and/or cuneus regions during the study period. No changes in blood sugar levels were noted in any of the treatment groups.

Conclusion: This pilot trial suggests that intranasal insulin can potentially stabilize and/or improve the cognition and function of patients with amnesic mild cognitive impairment or Alzheimer disease.

Craft, S., et al. Intranasal Insulin Therapy for Alzheimer Disease and Amnesic Mild Cognitive Impairment: A Pilot Clinical Trial. **Arch Neurol.** 2012, January; 69(1): 29-38.

BRAIN NATRIURETIC PEPTIDE AND FUNCTIONAL OUTCOME AFTER STROKE

Elevated serum levels of brain natriuretic peptide (BNP) can be a powerful predictor of outcome in patients with cardiovascular disease, and have been associated with atrial fibrillation, cardioembolic stroke and higher post-stroke mortality. This study was designed to determine whether admission serum BNP levels predict functional outcome after ischemic stroke.

This prospective, cohort study included 569 consecutive patients, admitted with an ischemic stroke. Serum BNP was collected at enrollment and within 48 hours of admission. Patients and caregivers were interviewed by telephone at three and six months after stroke, in order to assess functional outcome using the Modified Rankin Scale.
A multivariate analysis indicated that only age, NIHSS score and higher BNP levels independently predicted functional outcome. In addition, NIHSS score and higher BNP levels were independent predictors of mortality. In stroke subtypes, BNP was an independent predictor of functional outcome and mortality in patients with cardioembolic stroke subtypes, but not in those with non-cardioembolic stroke.

Conclusion: This study suggests that an elevated brain natriuretic peptide at hospital admission for ischemic stroke is independently associated with poorer functional outcome at six months.

Rost, N., et al. Brain Natriuretic Peptide Predicts Functional Outcome in Ischemic Stroke. **Stroke.** 2012, February; 43: 441-445.

MNEMONIC STRATEGIES IMPROVE HIPPOCAMPAL ACTIVITY IN MILD COGNITIVE IMPAIRMENT

Mild cognitive impairment (MCI) is widely recognized as a pre-dementia state, with the majority of patients converting to Alzheimer disease (AD) within a few years of diagnosis. Due to the relatively specific memory deficits involved, considerable emphasis has been placed on examining the pattern of structural and functional abnormalities within the medial temporal lobes, especially the hippocampus. However, few attempts have been made to identify interventions that facilitate the function of the hippocampus. This study sought to determine whether mnemonic strategy training might facilitate hippocampal functioning among patients with MCI using an ecologically relevant task that required participants to remember the location of objects.

This randomized, controlled, single-blind study included a total of

51 individuals (results of the larger study are *in press* with the journal *Neuropsychology*), though the current study examined fMRI-related changes in a subset of 34 individuals (18 MCI patients). Participants were randomized to either a group undergoing three sessions of mnemonic strategy training or an exposure matched control group. All participants underwent pre-and post-training fMRI as they encoded and retrieved object location associations. Findings revealed that participants who received mnemonic strategy training remembered significantly more information than those in the control group. Although MCI patients showed less hippocampal activity than healthy controls at the start of the study, memory strategy training partially restored activation in the left hippocampal body. No significant increases were found in the MCI control group.

Conclusion: This study demonstrated that mnemonic strategy training may help improve memory functioning and mitigate hippocampal dysfunction in patients with MCI.

Hampstead, B.M., et al. Mnemonic Strategy Training Partially Restores Hippocampal Activity in Patients with Mild Cognitive Impairment. **Hippocampus**. 2012.DOI: 10.1002/ hipo.22006.

POSITRON EMISSION TOMOGRAPHY AND MOTOR RECOVERY AFTER STROKE

Functional imaging and brain mapping have provided insight into the dynamic reorganization and adaptive changes which occur during recovery from stroke. This study used positron emission tomography (PET) to assess cerebral reorganization over time in patients with hemiplegia after stroke, comparing those with and those without good motor recovery.

Ten patients with a first subcortical stroke underwent a PET scan within four weeks of stroke, repeated eight weeks later. These scans were compared to those of five, healthy controls. At the time of the second scan, patients obtaining at least 20 points on the Fugl-Meyer motor scale were designated as having good motor recovery, while those with lower scores were placed in a low recovery group. At the baseline PET scan, regional cerebral blood flow (rCBF) was measured at rest and during passive elbow movements of the affected arm. This procedure was repeated at the second scan.

At baseline, healthy controls demonstrated significant increases in rCBF, with passive elbow movement, in the contralateral sensorimotor cortex, with little change in activation pattern at follow-up. At eight weeks after baseline PET, different patterns of brain activity were seen between those with good recovery and those without good recovery. The patients with good recovery showed greater recruitment of additional areas in the contralateral parietal somatosensory cortex, than did those with poor or no recovery.

Conclusion: This study of patients with ischemic stroke found that good recovery is associated with more contralateral activation of the primary somatosensory cortex.

Nelles, G., et al. Neural Substrates of Good and Poor Recovery after Hemiplegic Stroke: A Serial PET Study. **J Neurol.** 2011, December; 258(12): 2168-2175.

EFFECT OF IBUDILAST ON NEUROPATHIC PAIN

A number of pro-inflammatory substances are released from immune cells, recruited to the site of pathology. The release of tumor necrosis factor alpha (TNF-α) and other inflammatory mediators sensitize primary afferent sensory neurons, leading to exaggerated responses to cutaneous stimuli. Through these processes, primary afferent activity is abnormally prolonged, leading to persistent changes in the physiology and phenotype of both primary afferent and dorsal neurons. As ibudilast is thought to inhibit the release of cytokine TNF-α from activated spinal microglia, this animal study assessed the ability of this drug to treat neuropathic pain.

Two groups of male rats were studied. In one group, a sciatic nerve injury was created, while a second group underwent a spinal cord compression injury. After injury, the rats were treated with either ibudilast or placebo. The sciatic group was treated for 14 to 16 days, and the spinal cord injury group for 30 to 32 days.

In each group, the animals were tested for hypersensitivity.

In both the sciatic and a spinal cord injury groups, ibudilast treatment reduced hindpaw hypersensitivity as compared to the placebo group. Repeated treatment led to increased baseline threshold, beyond the half-life of the medication, suggesting persistent changes in neuropathic pain processing.

Conclusion: This animal study demonstrates that ibudilast, an asthma drug, may be useful as an analgesic medication for neuropathic pain.

Harna, A., et al. The Antinociceptive Effect of the Asthma Drug Ibudilast in Rat Models of Peripheral and Central Neuropathic Pain. **J Neurotrauma.** 2012, February; 29(3): 600 - 610.

FIBRONECTIN FOR PAIN DEVELOPMENT AFTER SPINAL CORD INJURY

Chronic pain is a major challenge in the treatment of patients with spinal cord injury (SCI). Often, chronic pain cannot be eliminated, leading to continuous administration and potential abuse of pain medications. A complicated and interactive central injury cascade can lead to conditions beyond those produced by the initial injury. This seems caused by an exaggerated interruption of a variety of descending systems, including those that modulate pain. Integrins physically connect cells to the extracellular matrix and stimulate a variety of signaling cascades. After injury, different integrins have been identified in primary afferent neurons that mediate pain via the spinothalamic system. This animal study used a dorsal column crush injury as a model to test the effect of fibronectin for the treatment of chronic pain.

Adult, male rats underwent cervical level spinal crush injuries. Immediately after the lesion, the subjects received an injection into the spinal fluid of full length fibronectin or fragments thereof. To test the influence of the serotonergic system, additional rats received two doses of a five HT synthesis inhibitor, a five HT receptor blocker or placebo at two and five weeks after crush injury. After surgery, all animals were tested

for mechanical allodynia and thermal hyperalgesia. At designated time points, groups of rats were sacrificed and assessed for signs of inflammation and blood spinal cord barrier permeability.

The use of various fibronectin fragments, as well as competitive inhibitors, was found to inhibit the development of mechanical allodynia over an eight-month observation period. The use of serotonergic antagonists resulted in a reversal of the therapeutic effects of fibronectin.

Conclusion: This animal study found that a one-time injection of fibronectin can dramatically inhibit the development of chronic allodynia after a spinal cord injury.

Lin, C., et al. Fibronectin Inhibits Chronic Pain Development after Spinal Cord Injury**. J Neurotrauma**. 2012, February; 29(3); 10: 589-599.

BODY MASS INDEX TRENDS IN THE PAST DECADE

Based on national survey data, the prevalence of obesity in the United States changed little between 1960 and 1980. However, its prevalence increased by almost eight percent through 1994, and again by a similar amount through 2000. This study examined the latest results concerning body mass index (BMI) from the National Health and Nutrition Examination Survey (NHANES) from 2009 to 2010.

The NHANES program of the National Center for Health Statistics, Centers for Disease Control and Prevention, includes a series of cross -sectional, nationally representative health examinations surveys beginning in 1960. In these, weight and height were measured, with BMI calculated. Following current recommendations, overweight was defined as a BMI of 25 to 29.9 kg/m^2, and obesity as a BMI of 30 kg/m^2 or higher.

The sample included in this report comprised 2,889 adult men and 3,037, non-pregnant, adult women. Overall, the age-adjusted obesity prevalence was 35.7%, including 35.5% of men and 35.8% of women. The age-adjusted prevalence of overweight and obesity combined was 68.8% overall, including 73.9% of the men and 63.7% of the women. Comparing the 1999 to 2000 and 2009 to 2010 reporting periods, the median BMI for men increased from 26.8 to 27.8 kg/m^2, and for women from 26.8 to 27.3 kg/m^2. The changes in the past two years, however, were not significant as compared to the previous six.

Conclusion: This 2009 to 2010 survey of American adults found the prevalence of obesity to be 35.7%, with no significant change as compared with the period of 2003 to 2008.

Flegal, K., et al. Prevalence of Obesity and Trends in the Distribution of Body Mass Index among U.S. Adults, 1999 to 2010. **JAMA.** 2012, February 1; 307(5): 491-497.

OBESITY AND FALLS

In the United States, more than 33% of adults age 65 or older will fall each year. In 2005, it was estimated that falls resulted in nearly 16,000 deaths in the United States. As the population moves toward a greater percentage of obesity, conflicting evidence has emerged concerning the relationship between obesity and the risk of falling. This study assessed the relationship between the risk of falling and body mass index (BMI).

This longitudinal, population-based study included 10,755 respondents to the Health and Retirement Study. The study included self-report surveys administered to individuals 65 years of age or older. From these were determined the occurrence of falls, falls with serious injury requiring medical treatment and falls with reduced activities of daily living disability. Data were also obtained concerning BMI, dividing individuals into those underweight (BMI <18.5 kg/m^2), normal weight (BMI 18.5-29.9 kg/m^2), obesity category I (BMI 30-34.9 kg/m^2), obese category II (BMI 35-39.0 kg/m^2) or obesity category III (BMI > 40 kg/m^2). The incidence of falls was compared with the BMI.

Compared with normal weight individuals, those in obesity classes I, II, and III had increases in the incidence of falling by 12%, 26% and 50%, respectively. That relationship was not seen between BMI and the risk of injury with falls, with the exception being that those in obesity class III were significantly less likely to be injured by a fall. Obesity classes I and II were associated with 17% and 39% increased risks of fall with disability, respectively, as compared to normal weight.

Conclusion: This study of patients 65 years or older found that, compared to normal weight individuals, the risk of falling increases with increasing obesity. However, those with a body mass index of greater than 40 kg/m^2 were found to have a reduced risk of injury due to the fall.

Himes, C., et al. Effect of Obesity on Falls, Injury and Disability. **JAGS.** 2012, January:60(1); 124-129.

ETHYL CHLORIDE SPRAY AND SKIN STERILITY

Ethyl chloride is widely used as a topical anesthetic spray to decrease pain due to needle puncture. Ethyl chloride is labeled as being non-sterile, with little information published regarding its safety from an infectious disease perspective. As sterility during an intra-articular injection is critical, the use of ethyl chloride has potential, negative consequences. This study sought to determine the change in the skin's sterility resulting from the application of ethyl chloride topical spray.

This prospective, blinded, controlled study included 15, healthy, adult subjects who were prepared for mock injections of both shoulders and both knees. No injections were actually performed. Skin culture samples were obtained before skin preparation, after skin preparation and immediately before the application of the spray. A final culture was obtained immediately after an ethyl chloride spray.

To prepare the skin, three, complete circles of increasing size were cleaned with alcohol swabs. A second culture was obtained immediately after this preparation. The ethyl chloride was then sprayed for three to seven seconds. The final culture was obtained after the spray. In a second arm of the study, the ethyl chloride was sprayed directly into agar plates.

Thirty knees and 30 shoulders were tested, with a total of 180 cultures. Bacterial growth was noted in 70% of the samples before skin preparation, with the most common organism identified as coagulase negative staphylococci. Growth was observed in three percent of the

samples immediately before spraying, and in five percent of the samples immediately after spraying (p=0.65). Spraying methyl chloride on agar plates resulted in bacterial growth in 13% of the treated plates as compared to 11% of the control plates (p=0.8).

Conclusion: This randomized trial found that, while ethyl chloride is nonsterile, its application does not seem to significantly change the sterility of injection site at the shoulder or the knee.

Pilischuck, D., et al. Skin Sterility after Application of Ethyl Chloride Spray. **J Bone Joint Surg (Am)**. 2012, January 18; 94(2): 118-120.

PAIN THRESHOLD AND RHEUMATOID ARTHRITIS

As central pain sensitization is likely in long-standing rheumatoid arthritis (RA), it is possible that disease duration affects pain threshold. This study examined the variability of pain thresholds in RA and the factors that influence them.

This cross-sectional study included 105 patients with RA. Pain thresholds were measured with a visual analogue scale using a digital algometer. This information was analyzed with regard to age, disease duration, race, mental health, disease activity, fatigue, disability and the presence of tender points suggestive of fibromyalgia (FM).

Subjects were 80 women and 25 men with a mean disease duration of 13 years. Of these, 89% were receiving disease modifying treatment, including 20 patients receiving biologic therapies. Seventeen percent met the criteria for FM. Pain thresholds were highly correlated with tender point counts, tender joint counts, fatigue and disease activity scores. Pain thresholds were moderately correlated with depression/anxiety scores, age and disease duration. Finally, pain thresholds were lower in patients with tender point scores of at least 11 (p<0.001), as well as among those with RA disease duration of at least 10 years (p=0.027).

Conclusion: This study of patients with rheumatoid arthritis shows an association between pain thresholds and disease activity. The authors recommend investigation of treatments focusing on central pain sensitization.

Pollard, L., et al. Pain Thresholds and Rheumatoid Arthritis: The Effect of Tender Point Counts and Disease Duration. **J Rheumatol.** 2012, January; 39: 28-31.

HETEROTOPIC OSSIFICATION AFTER CERVICAL DISC REPLACEMENT

Cervical total disc replacement has become a popular alternative to anterior cervical discectomy with fusion (ACDF) for the treatment of degenerative disc disease. While several authors have reported on the occurrence of heterotopic ossification (HO) after lumbar disc replacement, its effects on spinal range of motion have not been well studied. This study was designed to determine the incidence of HO following cervical total disc replacement (TDR).

The subjects included 28 consecutive patients who had undergone cervical TDR between September of 2006 and October of 2008. The subjects were diagnosed with radiculopathy and or myelopathy due to disc herniation. All underwent TDR with a Mobic-C artificial disc. Imaging was obtained at one, three, six, 12 and 24 months postoperatively. The occurrence of HO was determined on lateral radiographs, with angular motion measured with flexion and extension radiographs. A visual analogue scale and the Neck Disability Index value were obtained for each patient before surgery and at the time of each radiograph.

Twenty-eight patients with a mean age of 44 years were included in the follow-up data. The mean follow-up period was 21.6 months. Nineteen patients underwent a single level TDR, and nine underwent a hybrid surgery consisting of a cervical TDR and ACDF. Sixty-four percent of the subjects developed HO during the course of the study. However, only three developed grade III HO, and one developed grade IV HO. Progression of HO continued throughout the study. There was no significant loss of range of motion overall, except among those with grade III or IV HO. In this group two to three degrees of range were lost segmentally.

Conclusion: This study of patients undergoing total disc replacement found that HO developed in most, although this development did not significantly reduce segmental range of motion.

Lee, S., et al. Early Development and Progression of Heterotopic Classification in Cervical Total Disc Replacement. **J Neurosurg Spine**. 2012, January; 16(1): 31-36.

INTENSIVE INPATIENT REHABILITATION AND PARKINSON'S DISEASE

Parkinson's disease (PD), even when treated with medication, leads to major disability and reduces quality of life. The positive effects of rehabilitation have been established, although it is unknown whether these effects persist over time. This study was designed to determine the effect of intensive rehabilitation treatment on the functional ability of patients with PD.

Fifty patients diagnosed with PD were studied. Those subjects were randomized to either admission to the Rehabilitation Institute of Montesano for a four-week treatment, to be repeated one year later, or to follow usual care. Patients in the usual care control group underwent pharmacologic treatment and were instructed to practice generic physical exercises at home and to walk. Those randomized to the treatment group received a four-week cycle of physiotherapy, including three daily sessions five days per week. The therapy sessions included cardiovascular exercise, stretching, balance training, treadmill training and occupational therapy. The primary outcome measure was the Unified Parkinson's Disease Rating Scale (UPDRS), with the secondary outcome measure being the intake of levodopa.

At one-year follow-up, the treatment group obtained scores on the UPDRS similar to those at baseline, while the control group obtained increased scores, indicating a worsening of function (p<0.0001). A second cycle of intensive rehabilitation treatment at one year produced effects similar to those of the first cycle. At the end of the study, daily medication dosage was reduced in the rehabilitation treatment

patients, and significantly increased in the control group.

Conclusion: This randomized, controlled trial of patients with Parkinson's disease found that multidisciplinary therapy treatment can reduce the worsening of symptoms and reduce therapeutic drug usage.

Giuseppe, F., et al. Effectiveness of Intensive Inpatient Rehabilitation Treatment on Disease Progression in Parkinsonian Patients: A Randomized, Controlled Trial with One-Year Follow-Up. **Neurorehab Neural Repair**. 2012, February; 26 (2): 144-150.

TAI CHI AND PARKINSON'S DISEASE

Movement impairments adversely affect function and quality of life in patients with Parkinson's disease (PD). As this disease progresses, the patient loses postural stability and develops gait dysfunction, with frequent falls. As tai chi has been shown to improve strength, balance and physical function, this study examined whether a tailored tai chi program could improve postural stability in patients with PD.

This randomized, clinical trial included persons ages 40 to 85 years with PD, with a disease severity rating of stage I to IV. The subjects were assigned to one of three groups, including tai chi, resistance training or stretching. The tai chi protocol consisted of six tai chi movements integrated into an eight form routine. This program was designed to tax balance and gait by having participants perform symmetric and diagonal movements. Those in the resistance training group focused on strengthening the muscles important for posture, balance and gait. Finally, those in the stretching group engaged in a low intensity exercise program involving various stretches of the upper body and lower extremities. The primary outcome measures were two indicators of postural stability.

A total of 176 participants completed their assigned interventions, and 185 provided complete data on the outcome measures at follow-up. On the primary outcomes, the participants in the tai chi group performed significantly better than did those in the resistance training or stretching groups in maximum excursion ($p=0.01$) and in directional control ($p=0.002$). The tai chi group also performed better than did the stretching group in secondary outcome measures. These included measures of gait and strength, functional reach and timed get up and go tests, and better United Parkinson's Disease Rating Scores (UPDRS) III scores than did the stretching group ($p<0.001$ for all comparisons). The tai chi group further performed better than did the resistance training group in stride length and functional reach ($p=0.01$).

Conclusion: This study of patients with PD demonstrates that tai chi training can improve balance impairments, with additional benefits including improved functional capacity and reduced falls.

Li, F., et al. Tai Chi and Postural Stability in Patients with Parkinson's Disease. **N Engl J Med.** 2012, February 9: 366(6): 511-519

ACUTE MYOCARDIAL INFARCTION AND HEART FAILURE IN ACUTE STROKE

Cerebrovascular and coronary artery disease share several risk factors. Coronary artery diseases are a major cause of morbidity and mortality in the long-term follow-up of patients with ischemic stroke. This study was designed to evaluate the rate of acute myocardial infarction (AMI) and acute heart failure (AHF), the effects of AMI and AHF on mortality and the risk factors for AMI and/or AHF after stroke.

This prospective, observational study enrolled consecutive patients admitted to a stroke unit with acute ischemic or hemorrhagic stroke. In the acute care setting, risk factors for stroke, history of prior cardiac events and in-hospital occurrence of AMI or AHF were documented. At three months after the index stroke, neurologists, blinded to the in-hospital occurrence of AMI or AHF collected outcomes measures including death and cause of death.

Of the 814 participants, 84.2% experienced an ischemic stroke. Fifty-three patients developed an in-hospital AMI or AHF, all among the ischemic stroke patients. Independent predictors of these events included prior angina, AMI within three months prior to admission, hyperglycemia, and high NIH stroke scale scores. Subjects with cardioembolic stroke had a higher incidence of AMI or AHF (13.1%), than did patients with large vessel disease (5.5%) and small vessel disease (1.9%). The mortality rate at three months was higher among the group who experienced an in-hospital AMI and/or AHF (60.4%) than among those who did not (15.9%).

Conclusion: This study of patients hospitalized with an acute stroke found that 6.5% developed an acute myocardial infarction or heart failure while hospitalized, with this group experiencing significantly greater mortality at three months.

Micheli, S., et al. Acute Myocardial Infarction and Heart Failure in Acute Stroke Patients: Frequency and Influence on Clinical Outcome. **J Neurol.** 2012, January; 259: 106-110.

APIXABAN VERSUS ENOXAPARIN AFTER JOINT REPLACEMENT

Apixaban is an oral factor Xa inhibitor, developed for the prevention and treatment of thromboembolism. In previous phase III studies, the primary efficacy outcome measure was the occurrence of any postoperative venous thromboembolism, including isolated calf vein thrombosis. This study was designed to provide a better estimate of major venous thromboembolism and estimates of clinically relevant bleeding rates.

The authors conducted a pooled analysis of two previously reported double-blind, randomized studies involving 8,464 patients undergoing hip or knee arthroplasty. The subjects were randomized to receive either apixaban, 2.5 mg twice per day, starting 12 to 24 hours after surgery, or enoxaparin, 40 mg subcutaneously once per day, starting 12 hours before surgery. Each was continued for 12 days after knee, and 35 days after hip surgery.

Bilateral venography was scheduled at the end of the treatment to assess for asymptomatic deep vein thrombosis (DVT). Clinically suspected DVT was confirmed or excluded with ultrasound or venography, and suspected pulmonary embolism with CT, ventilation -perfusion lung scanning or pulmonary angiography. The prespecified outcome measure for

this pooled analysis was major venous thromboembolism, including symptomatic or asymptomatic proximal DVT, nonfatal pulmonary embolism or death from venous thromboembolism.

Major venous thromboembolism occurred in 0.7% of the patients in the apixaban group and 1.5% of those in the enoxaparin group (p=0.001). Major bleeding occurred in 0.7% of the apixaban group and 0.8% of the enoxaparin group.

Conclusion: This pooled analysis of studies involving patients undergoing hip and knee arthroplasty found that apixaban, 2.5 mg twice per day is more effective than enoxaparin, 40 mg once per day, without increasing the risk of bleeding

Raskob, G., et al. Apixaban versus Enoxaparin for Thromboprophylaxis after Hip or Knee Replacement. **J Bone Joint Surg (BR).** 2012, February; 94B (2): 257-264.

LONG-TERM EFFECT OF CORTICOSTEROID INJECTIONS IN THE ACROMIOCLAVICULAR JOINT

Primary osteoarthritis (OA) is a common source of pain arising from the acromioclavicular (AC) joint. If conservative treatment fails, a common treatment is a corticosteroid injection into the joint. As data concerning these injections is limited, this study sought to determine the long-term effects of injecting corticosteroid, combined with a local anesthetic, into the AC joint.

This prospective study included 58 patients with isolated AC joint symptoms. A physical examination was performed, including five, specific AC compression tests. All subjects had at least one positive response to AC joint compression testing. The patients received injections of one mL of lidocaine and one mL of corticosteroid. Five minutes after the injection, the AC joint compression tests were repeated, to verify that the pain had been eliminated. The patients were seen in clinic one month after the injection and were asked about the effects of the injection on pain and function.

At one month after the injection, 64% of the patients had failed to improve sufficiently, with arthroscopic surgery offered at that time. One patient reported a severe increase in symptoms at 10 days following the injection. Symptoms had satisfactorily resolved in 16 patients, accounting for 28% of the sample. At final follow-up, an average of 42 months after injection, one subject experienced a recurrence of pain, four reported occasional mild pain and 11 reported no residual joint symptoms.

Conclusion: This study of patients with isolated acromioclavicular joint pain found that injections with corticosteroids can provide long-term pain relief in approximate 25% of these patients.

Van Riet, R., et al. The Long-Term Effect of an Intra-Articular Injection of Corticosteroids in the Acromioclavicular Joint. **J Shoulder Elbow Surg.** 2012, March; 21: 376-379.

MAGNETIC RESONANCE IMAGING'S INFLUENCE ON THE DECISION TO TREAT RADICULOPATHY

The use of radiological testing has not been shown to improve outcomes in patients with low back pain. Widespread use of magnetic resonance imaging (MRI) has been found to account for some of the increasing costs of treatment and the increases in rates of spine surgery. This randomized, controlled trial was designed to determine whether MRI improves outcome or affects decisión making in patients with lumbosacral radiculopathy

Participants were 132 patients with signs and symptoms of lumbosacral radiculopathy, referred or scheduled for epidural steroid injections (ESI). All had undergone recent MRI or were willing to undergo MRI. The subjects were randomized to two groups. Group 1 received epidural steroid injections, with the type and level determined solely by history and physical examination. In group 2, treatment was determined by clinical findings and imaging results. For group 1 patients, an independent physician proposed a treatment plan after reviewing the MRI, which was compared to the treatment plan the patient had received. The primary outcome measure was leg pain, as assessed on a numerical rating scale at one month. Function was assessed with the Oswestry Disability index.

In group 1, independent evaluators agreed with the treating doctor in 66% of the cases. In group 2, the physician opted not to perform an epidural steroid injection after reviewing the MRI in five cases. In group 1, patients who received a different injection than that proposed by the independent physician had inferior responses with regard to both pain (p=0.01), and function (p=0.04), as compared to those who had injections correlated with imaging results. Overall, slightly lower leg pain scores were noted in group 2 at one month, as compared with group 1 (p=0.12)

Conclusion: This study found that magnetic resonance imaging does not significantly improve the outcomes of patients who receive epidural steroid injections.

Cohen, S., et al. Effect of MRI on Treatment Results or Decision-Making in Patients with Lumbosacral Radiculopathy Referred for Epidural Steroid Injections. **Arch Intern Med**. 2012, January 23; 172(2): 134-142.

RISK FACTORS FOR MEDICATION OVERUSE HEADACHE

In the general population, two to five percent of adults suffer from chronic, daily headache, while one to two percent experience medication overuse headaches (MOHs). This prospective, longitudinal, population-based, cohort study evaluated the incidence of, and risk factors for developing MOH.

The Nord-Trondelag Health Survey is a longitudinal cohort study, in which all inhabitants of Nord-Trondelag , 20 years of age or older were invited to participate. The subjects were surveyed, with data including a large number of health-related items covering a wide range of topics. The surveys were performed from 1995 to 1997 and from 2006 to 2008. The International Classification of Headache Disorders was used, with chronic headache defined as headaches occurring for 15 or more days per month. MOH was defined as chronic, daily headache, associated with daily medication use for over one month.

A total of 26,197 people responded to the headache questionnaire. Among these, chronic, daily headache was reported in 2.3%, and MOH was found in 0.8%.

(Continued from page 2)

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Chronic, daily headache without medication use was found in one percent. There was a fivefold increase for developing MOH among individuals who, at baseline, reported regular use of tranquilizers, had a history of migraine or had a combination of chronic musculoskeletal and gastrointestinal complaints and had Hospital Anxiety and Depression Scale Scores of at least 11. Smoking and physical inactivity more than doubled the risk of MOH. However, these factors did not increase the risk of chronic, daily headaches without medication overuse.

Conclusion: This population-based study found several risk factors for medication overuse headaches, which did not increase the risk for chronic, daily headache without medication overuse.

Hagen, K., et al. Risk Factors for Medication Overuse Headache: An 11-Year Follow-Up Study. The Nord-Trondelag Health Studies. **Pain.** 2012, January; 153(1): 56-61.

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