

# REHAB IN REVIEW

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## FATIGUE AND RA

Rheumatoid arthritis (RA) is a multi-system, immune mediated, chronic disease. Pain and fatigue are common symptoms of RA, although only pain is included in the American College of Rheumatology's (ACR) core set of outcome measures. This study examined the reliability and sensitivity of changes in fatigue as an outcome measure for RA.

Successive patients referred to a rheumatology clinic with a diagnosis of RA were studied. All subjects who were prescribed anti-tumor necrosis factor alpha therapy were evaluated prospectively according to a predetermined protocol, which included the ACR core set of outcome measures and a quantitative assessment of fatigue. Fatigue severity was quantified using a unidimensional, 11-point numeric rating scale. Multiple regression analysis was used to examine the relationship between fatigue and the core set of outcome measures.

Forty-nine, successive patients were evaluated. Mean baseline measures included a pain visual analogue scale score of 5.79 mm, a tender joint count of 11.71, a swollen joint count of 13.46, a global health score of 5.84, an HAQ score of 1.37, a C reactive protein of 34, and a fatigue score of 6.65. At three months, the mean fatigue score had fallen to 4.3 ( $p < 0.001$ ). Multiple regression analysis was used to explain the variation in fatigue and to compare the independent contributions of fatigue to the six core set measures of RA. The relative independent contribution of fatigue was 22%, higher than that of the core set variables; i.e., tender joint count 20%; pain 19%, swollen joint count 16%, global health 8%, CRP 8 %, and HAQ 7 %.

**Conclusion:** This study of patients with rheumatoid arthritis (RA) suggests that measures of fatigue are reliable and sensitive to change. The

authors propose that these factors be considered for inclusion as core outcome measures when evaluating patients with RA.

Minnock, P., et al. Fatigue Is a Reliable, Sensitive, and Unique Outcome Measure in Rheumatoid Arthritis. *Rheum.* 2009, December; 48(11): 1533-1536.

## BLOOD PRESSURE AND HEMORRHAGIC TRANSFORMATION

The most common complication following the administration of tissue plasminogen activator (t-PA) for acute ischemic stroke is the development of hemorrhagic transformation (HT). Based upon neuroimaging, transformation can be classified as involving hemorrhagic infarction (HI), which is limited to petechial bleeding, or parenchymal hemorrhage (PH). Even when classified as "asymptomatic," PH is associated with poor outcome, whereas HI generally has not been found to be clinically significant. Previous studies have not identified reliable predictors of which patients are at risk for developing HT. This randomized, controlled trial sought to determine whether elevated blood pressure or increased diffusion weighted imaging (DWI) lesion volume is greater among patients with HT.

A total of 97 acute, ischemic stroke patients were included in this study. Forty-nine were randomized to receive t-PA and 48 to receive a placebo. The subjects underwent MRI before treatment and again at three and 90 days after treatment. DWI was used for pre-treatment MRI studies. Post-treatment MRIs were assessed for evidence of petechiae or parenchymal hemorrhage. The participants underwent continuous cardiac and blood pressure monitoring for 24 hours after randomization, with heart rate and

blood pressure recorded at regular intervals thereafter.

Approximately 50% of patients in both the t-PA and placebo treatment groups developed HT. PH occurred more frequently among those patients receiving t-PA than among controls ( $p = 0.049$ ). Subjects with HT had higher systolic and diastolic blood pressure readings during the 24 hours post-treatment than did those without HT. Multinomial logistic regression indicated that PH was predicted by DWI lesion volume, atrial fibrillation and 24-hour systolic blood pressure.

**Conclusion:** This study of patients with acute ischemic stroke found that pretreatment DWI lesion volume and post-thrombolysis blood-pressure are both predictors of hemorrhagic transformation.

Butcher, K., et al. Post-Thrombolysis Blood Pressure Elevation is Associated with Hemorrhagic Transformation. *Stroke.* 2010, January; 41(1): 72-77.

## VITAMIN C FOR THE PREVENTION OF CRPS AFTER ANKLE SURGERY

The pathophysiology of complex regional pain syndrome, type I (CRPS I) remains unclear. The syndrome includes joint pain, trophic disturbance, and bone demineralization. In 1999, one study found vitamin C effective in preventing CRPS I following distal radial fracture. This prospective study further investigated the role of vitamin C in preventing that syndrome among those undergoing foot or ankle surgery.

This quasi-experimental study compared two chronologically successive groups without and with prophylactic vitamin C treatment. All patients scheduled for ankle surgery by a single senior surgeon from July 2002 through July 2004 were

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included. From July 2002 to June 2003 (Group 1) the patients underwent surgery without receiving vitamin C post-surgery. The treatment group, undergoing surgery between July of 2003 and June of 2004, received 1 g of vitamin C on the first postoperative day, and then each morning for 45 days. Data were harvested from medical records and surgical reports. Several factors were analyzed, including gender, age, injury type, history of CRPS I, psychological context, tourniquet time, and cast immobilization time.

CRPS I occurred in 9.6% of group 1 patients and in 1.7% in group 2 patients ( $p < 0.0001$ ). In reviewing associated factors, 36.3% of patients with CRPS I demonstrated a psychological presentation suggestive of an anxiety-depressive state, compared to 14.3% of patients free of CRPS I ( $p < 0.001$ ). In addition, 31.8% of the patients presenting with CRPS I had a history of the syndrome, as compared to 3.2% of those without postoperative CRPS I ( $p < 0.0001$ ). A logistic regression analysis determined that the risk of presenting with CRPS I was five times lower in patients receiving vitamin C and 10 and times greater in those with a history of CRPS I.

**Conclusion:** This study demonstrates that vitamin C may be effective in preventing CRPS I, after foot and ankle surgeries.

Besse, J., et al. Effect of Vitamin C on Prevention of Complex Regional Pain Syndrome, Type I, in Foot and Ankle Surgery. **Foot Ankle Surg.** 2009, December; 15: 179-182.

### **FUNCTIONAL AND PSYCHOSOCIAL OUTCOMES ONE YEAR AFTER MILD STROKE**

The World Health Organization reports that 15 million people experience a stroke annually. Of those, five million die, while another five million are left permanently disabled. This study examined and described the biopsychosocial transitions of male patients and their wife caregivers during the first 12 months after stroke.

This prospective, cohort study recruited subjects from among consecutive couples admitted to a tertiary care stroke center in western Canada. All patients were seen by a stroke neurologist at the time of

admission, underwent standard stroke diagnostic imaging, and received care in an inpatient stroke department. All were males older than 45 years of age, residing with a wife caregiver in an independent living situation. Data were collected for 12 months post-discharge concerning quality of life, depression, caregiver strain, and marital function.

Further functional data were acquired using the Stroke Impact Scale (SIS)-16. Additional assessments included quality of life (using the Stroke Specific (SS)-QOL Scale for the patient and the Short Form (SF) for the wife-caregivers), depression [using the Beck Depression Inventory (BDI-II)], caregiver burden [using the Bakas Caregiver Outcome Scale (BCOS)], and marital function [using the Family Assessment Device (FAD) General Functioning Subscale (GFS)]. Logistic regression was used to determine which baseline demographic and biopsychosocial variables influenced marital functioning one year after discharge.

A total of 38 couples provided informed consent and completed the study. The average length of hospital stay for the patients was 4.5 days. No patients were referred to outpatient rehabilitation services at the time of discharge home. The patients' modified Rankin scale scores reflecting function and quality of life improved significantly over the 12-month study period. However, at 12 months post-discharge, 45% of the patients (17 of 38) rated their functional status as worse than at hospital discharge. The caregivers' quality of life scores did not change significantly during the first year. Multivariate analysis demonstrated worsening depression for both the patients and the caregivers ( $p = .017$ ), as well as deterioration of patients' marital function over time ( $p = .004$ ). Conversely, the caregivers' perceptions of caregiver strain improved over the 12 months of the study.

**Conclusion:** This study found that, despite improvement in a patient's functional status, measures of affect and of marital function deteriorate over the first year after a mild stroke.

Green, T., et al. Functional and Psychosocial Outcomes One Year after Mild Stroke. **J Stroke**

**Cerebrovasc Dis.** 2010, January; 19 (1): 10-16.

### **HYPOALBUMINEMIA PREDICTS ACUTE STROKE MORTALITY**

Stroke remains the third leading cause of death in the United States. The identification of factors that influence in-hospital mortality due to stroke may help in the early identification of patients at high risk. This study sought to identify factors that influence stroke mortality among patients admitted for acute stroke in a representative sample of hospitals in the state of Georgia.

The Paul Coverdell Georgia Stroke registry was one of four sites initially funded by the Centers for Disease Control and Prevention in 2001. Hospital selection was intended to create a representative sample from the state. The eight, largest hospitals in the state in terms of stroke volume were selected. Among the remaining hospitals, 52 were randomly selected for participation. Of those, two out of three agreed to participate.

Data were collected retrospectively by identifying all patients' charts after discharge during a three-month period between December 2001 and February 2002. Centrally abstracted information included demographic and clinical variables suggested by an expert external panel. Abstracted information included age, gender, race, smoking status, atrial fibrillation on admission and coexisting disease, serum albumin, creatinine, and hemoglobin blood glucose levels. Stroke type, initial Glasgow Coma Scale (GCS) score, and in-hospital death were also documented.

A total of 1,477, consecutively admitted patients from 34 hospitals were identified with an acute cerebrovascular accident meeting the entry criteria. A univariate analysis found that independent risk factors for mortality included age ( $p < 0.008$ ), stroke type ( $p < 0.051$ ), GCS scores ( $p < 0.0001$ ), creatinine levels ( $p < 0.067$ ), blood glucose levels ( $p < 0.0063$ ), and serum albumin levels ( $p < 0.001$ ). Multivariate analysis revealed that factors distinguishing survivors from non-survivors during hospitalization were age ( $p < 0.004$ ), stroke type ( $p < 0.0007$ ), and serum albumin ( $p = 0.0003$ ).

**Conclusion:** This large, representative sample of patients admitted to hospitals in Georgia found that decreased serum albumin is an independent predictor of mortality in patients admitted for acute stroke. Older age and hemorrhagic stroke were also found to be independent predictors of mortality.

Famakin, B., et al. Hypoalbuminemia Predicts Acute Stroke Mortality: Paul Coverdell Georgia Stroke Registry. **J Stroke Cerebrovascular Diseases.** 2010, January-February; 19(1): 17-22.

### **FUNCTIONAL ELECTRICAL STIMULATION AND GAIT AFTER STROKE**

The combination of functional electrical stimulation (FES) and treadmill training is a novel and effective intervention for post-stroke gait rehabilitation. This study compared walking patterns with FES delivered to both ankle plantarflexors (PFs) and dorsiflexors (DFs) to those with FES delivered only to the DFs.

A total of 13 patients with chronic hemiparetic stroke were recruited for study. Program timing logics were used to standardize FPS firing to both the ankle DF and PF. Three walking trials, lasting 20 to 40 seconds each, were tested at the subject's self-selected speed. The trial included walking with FES at the DF during the swing phase, walking with FES to both DF and PF at the swing phase and terminal stance phases, and walking without FES.

FES delivered to both ankle DF and PF, compared to that delivered to DF alone, provided advantages of greater for propulsion contribution of the paretic leg, greater swing phase knee flexion, and greater ankle PF at paretic toe off. Improvement of the ankle DF angle at swing phase was noted with FES to both DF and PF, but not as much with FES to DF alone.

**Conclusion:** This study found that delivering functional electrical stimulation to both plantarflexors and dorsiflexors of the ankle improved post-stroke gait deficits at the ankle and knee joints during the swing and stance phases of gait.

Kesar, T., et al. Functional Electrical Stimulation of Ankle Plantarflexor and

Dorsiflexor Muscles: Effects on Post-Stroke Gait. **Stroke.** 2009, December; 40: 3821-3827.

### **PHYSICAL THERAPY FOR LOW BACK PAIN**

Low back pain (LBP) is a common and costly condition. "Manual therapy" refers to a broad category of procedures designed to impact musculoskeletal structures for the purpose of reducing pain and improving function. The authors previously identified a clinical prediction rule (CPR) defining a set of clinical parameters that can accurately identify a subgroup of patients with LBP likely to enjoy reductions in pain and disability following thrust manipulation. This study examined the generalizability of three manual therapy techniques with patients that satisfy that CPR.

This randomized, single blind study included 112 patients with LBP for patients to be eligible, subjects had to have a modified Oswestry Disability Questionnaire (ODQ) score of  $>25\%$ , be between 18 and 60 years of age, and be positive for the spinal manipulation CPR, which required the presence of at least 4 of the 5 findings. Subjects had to have at least 4 of the following criterion in the CPR including: duration of current episode of LBP of less than 16 days, no symptoms distal to the knee, more than one hypomobile segment in the lumbar spine, at least one hip with at least 35 degrees of internal range of motion. The participants were randomized to receive one of three techniques, two high velocity, low amplitude thrust techniques and one non-thrust low velocity high amplitude technique.

Treatments differed only during the first two sessions. During those sessions, patients received the manual therapy technique to which they had been randomized and a spinal range of motion (ROM) exercise that was common to all groups. Following the first two sessions, all patients received the same standardized exercise regimen for three additional sessions (once weekly for three weeks), for a total of five treatment sessions over a four-week period. Outcome measures included side effects of therapy, a 50% decrease in Oswestry Disability Questionnaire (ODQ) scores, and

Numeric Pain Rating Scale (NPRS) scores.

Repeat measures analysis revealed significant group by time interactions for ODQ ( $P < 0.001$ ) and NPRS ( $P = 0.001$ ) scores. Pair-wise comparisons of ODQ scores by group revealed no differences between the supine thrust manipulation and side-lying thrust manipulation at any follow-up period. At each follow-up period, significantly more patients achieved a successful outcome (at least 50% reduction in ODQ scores) in the supine thrust and side-lying thrust manipulation groups than in the nonthrust group. After one week, success rates were 54.1%, 52.6%, and 8.1% for the supine thrust, side-lying thrust, and non-thrust manipulation groups, respectively ( $p < 0.01$ ).

**Conclusion:** This study of patients with low back pain found that the authors' clinical prediction rule generalized to another thrust manipulation technique, but not to the nonthrust manipulation technique used in this study.

Cleland, J., et al. Comparison of the Effectiveness of Three Manual Physical Therapy Techniques in a Subgroup of Patients with Low Back Pain to Satisfy a Clinical Prediction Rule. *Spine*. 2009, December 1; 34 (25): 2720-2729.

### BIOFEEDBACK FOR CHRONIC LOW BACK PAIN

Several interventions, such as biofeedback, are thought to be helpful for the rehabilitation of patients with chronic lower back pain (LBP). This study sought to better clarify the impact of a biofeedback program on pain and quality of life among patients with LBP.

Chronic LBP was defined as mechanical pain between the twelfth rib and the lower gluteal folds, persisting for more than three months. Sixty patients with chronic LBP were randomly assigned to a control or a treatment group. The control group received no further intervention during a two-month period. The treatment group participated in a 16-session program that included global muscular relaxation, exercises to strengthen the abdominal muscles, and cognitive restructuring techniques. All exercises were initially performed

using biofeedback. The biofeedback electrodes were placed over the abdominal muscles, as well as over the paraspinal muscles at L2-L4. As the patient improved, the use of biofeedback was reduced, and the patient then performed the exercises at home without the use of biofeedback. Assessment instruments included a visual analogue scale of pain (VAS), the Shober Index, the Roland-Morris Disability Questionnaire (RMDQ), the Beck Depression Inventory (BDI), and the State-Trait Anxiety Inventory (STAI). Those measures were administered at the beginning and at the end of the treatment period.

The mean VAS scores decreased from 5.88 to 4.76 in the control group, and from 4.79 to 3.35 in the treatment group. That difference did not reach statistical significance. The mean scores on the RMDQ improved from 12.57 to 8.16 in the control group, and from 9.97 to 5.31 in the treatment group. This difference was also statistically nonsignificant. In addition, no significant differences between the groups were found in changes on the BDI and the STAI.

**Conclusion:** This study did not find that biofeedback lessens pain or improves quality of life or anxiety among patients with chronic low back pain.

De Sousa, D., et al. Assessment of a Biofeedback Program to Treat Chronic Low Back Pain. *J Musculoskel Pain*. 2009; 17(4): 369-377.

### ACTIVE VERSUS STATIC STRETCHING FOR HAMSTRINGS

Poor hamstring flexibility has been associated with low back pain in both adolescents and adults. This study compared passive and active stretching techniques, in an effort to determine which is more effective in producing and maintaining flexibility of the hamstrings.

Fifty, healthy university students volunteered to participate, and completed the study. The subjects included 21 women and 29 men with established, poor hamstring flexibility and no history of significant lower extremity or spinal disease. All participants underwent a baseline measurement of right knee active extension range of motion. The subjects were then randomly

assigned to either a static or passive stretching group. All performed the assigned exercises twice per day, four days per week, for a total of six weeks. Active knee extension range of motion was again measured after three and six weeks of stretching, and once again four weeks after stretching cessation. Sixteen subjects were able to complete the entire protocol.

At each time interval, the mean gain of range of motion was significantly higher with active stretching. At three weeks, the mean gains with active and static stretching were  $5.7^\circ$  and  $3^\circ$ , respectively ( $p = 0.015$ ). At six weeks, the mean gains with active and static stretching were  $8.7^\circ$  and  $5.3^\circ$ , respectively ( $p = 0.006$ ). Finally, at four weeks after cessation of the stretching program, the active stretching program participants had a mean gain in range of motion of  $6.3^\circ$ , as compared to  $0.1^\circ$  in the passive group ( $p = 0.003$ ).

**Conclusion:** This study of subjects with pre-existing, poor hamstring flexibility suggests that active stretching produces greater gain in hamstring range of motion and maintenance of flexibility than does static stretching.

Meroni, R., et al. Comparison of Active Stretching Technique and Static Stretching Technique on Hamstring Flexibility. *Clin J Sp Med*. 2010, January; 20(1): 8-14.

### MAGNETIC RESONANCE IMAGING AND DEPRESSION

The vascular depression hypothesis suggests a strong vascular basis for the depression that sometimes develops in elderly individuals. This study investigated the relationship of several magnetic resonance imaging (MRI) markers of subclinical vascular brain disease with prevalent and incident depression.

This study employed an age stratified sample of 563 participants from the population-based Rotterdam study. All participants underwent multi-sequence brain MRI in 1995 to 1996. A depression assessment was completed at baseline and during three follow-up visits between 1997 and 2001. Patients were initially screened and, if positive, also underwent a Present State

Examination to diagnose major depression, dysthymia, or minor depression. Covariates included education, smoking status, blood pressure, diabetes, body mass index, and intimal-media thickness. MRI results for 479 persons ages 60 to 90 at baseline were available for evaluation.

Of the 479 participants, 36 had depressive symptoms at baseline. At follow-up, 92 had developed depressive symptoms or syndromes. The smaller the brain volume, the more likely persons were to have depressive symptoms according to a cross-sectional analysis. Parietal and temporal atrophy were significantly associated with depressive symptoms. The likelihood of depressive symptoms increased with increasing volume of white matter lesions, especially in the frontal lobes and the deep central region. Longitudinal analysis revealed that neither global nor lobar brain tissue volumes were associated with incident depressive symptoms or syndromes. Further, neither white matter lesions nor brain infarcts were associated with incident depressive symptoms.

**Conclusion:** This population-based, cohort study of elderly persons found that structural markers of vascular brain disease are cross-sectionally related to the prevalence of depressive symptoms, although no association was found between those markers and incident depressive symptoms or syndromes.

Ikram, M., et al. Vascular Brain Disease and Depression in the Elderly. **Epidemiology**. 2010, January; 21(1): 78-81.

### RELATIONSHIP BETWEEN MYASTHENIA GRAVIS AND COGNITIVE IMPAIRMENT

Clinical studies investigating the relationship between myasthenia gravis (MG) and cognitive dysfunction have produced conflicting results. This study compared cognitive function in elderly patients with MG with that of matched controls, using a standardized neuropsychological test protocol.

This case control study included a sample of 100, consecutive patients with MG who were over the age of 60 and had disease duration of at least one year. A control sample of 31

subjects without MG were matched for age, gender, and education level. Duration of disease, symptom severity, modality and length of treatment, and associated diseases were recorded for each patient. A neuropsychological test battery was administered, including the Mini Mental State Examination and an extended version of the Mental Deterioration Battery, which explores multiple cognitive domains.

A general, one-way MANOVA of the neuropsychological test results did not reveal significant differences between the patients with MG and the control subjects ( $p=0.51$ ). However, those with severe MG were found to be impaired on tests of praxis ( $p=0.03$ ), attention ( $p=0.002$ ), and two measures of frontal control ( $p=0.02$  and  $p=0.03$ ). A logistic regression analysis demonstrated that diabetes, thyroid dysfunction, and increasing age were independently associated with cognitive dysfunction in patients with MG.

**Conclusion:** This study did not find that MG increases the risk of dementia. The data did demonstrate that impaired memory, attention, and executive functions are related to increasing age and associated diseases.

Marra, C., et al. Determinants of Chronic Impairment in Elderly Myasthenia Gravis Patients. **Musc Nerve**. 2009, December; 40(6):952-959.

### GANGLIOSIDE ANTIBODIES AND DIABETIC NEUROPATHY

The most common cause of peripheral neuropathy is diabetes. The most severe form of peripheral neuropathy occurs in diabetes type I, wherein autoantibodies are expressed and interact with pancreatic cells. Gangliosides are a common component of pancreatic cells, and are also found in peripheral nerves. This study sought to identify the relationship between neuropathy and anti-ganglioside antibodies among patients with type I diabetes.

Subjects were selected from among adult patients with diabetes who were followed at a metabolic disease clinic in Italy. Patients were consecutively recruited from among those with and those without conditions associated with neuropathy. Subjects were tested for

anti-ganglioside antibodies and also underwent neurologic evaluation. Each was assigned a Neurological Symptom Score, in order to determine the presence of peripheral neuropathy. Electrophysiological testing was used when available. Thirty patients with other identified autoimmune conditions (Celiac disease and Lupus) had serum drawn for anti-GAD and anti-IA-2 antibodies.

Fifty subjects with diabetes were enrolled. Sixteen of those were identified with peripheral neuropathy of the sensorimotor peripheral type. Patients with neuropathies were significantly older and had longer disease duration than did those without neuropathy. Twelve of the participants had ganglioside reactivity, which was independent of disease duration. Twenty had anti-glutamic acid decarboxylase (GAD65) antibodies, and 10 had IA<sub>2</sub> antibodies. Patients with those antibodies had a significantly shorter duration of diabetes than did those without antibodies. No significant relationship was found between the presence of antibodies and peripheral neuropathy ( $p=0.55$ ). Only three control patients expressed anti-ganglioside antibodies.

**Conclusion:** This study demonstrates that many patients with type I diabetes express anti-ganglioside antibodies, with disease duration shorter among patients with these antibodies. No significant relationship was found between the presence of anti-ganglioside antibodies and peripheral neuropathy.

Lucchetta, M., et al. Anti-Ganglioside Autoantibodies in Type I Diabetes. **Musc Nerve**. 2010, January; 41(1): 50-53.

### OBSESITY AND MIGRAINE

Migraine or probable migraine has been estimated to occur in 34.5% of adult women and 20.1% of adult men in the general population. Some have found that total body obesity is a risk factor for migraine. However, data conflict concerning whether obesity is associated with the prevalence of migraine. This study investigated the relationship between migraine/severe headache severity and body mass index.

Data for this study were obtained from the National Health and Nutrition Examination Survey (NHANES).

Data were collected concerning demographics, self-report of headaches, including migraine and severe headaches, and body mass indices, including height, weight, and waist circumference. Data for those between 20 and 55 years of age were reviewed by multivariate analysis using a logistic regression model.

A total of 21,783 participants were identified for this analysis. The analytic sample comprised 10,623 men and 11,160 nonpregnant women. The overall prevalence of migraine was 14.9% in men and 27.6% in women. The prevalence of migraine was greater among those with total body obesity than among those without ( $p < 0.001$ ). However, after 55 years of age, the prevalence of migraine in both men and women was no longer associated with total body obesity.

Interestingly, among women older than 55 years of age, the prevalence of migraine was lower in those with abdominal obesity than among those without ( $p < 0.05$ ). After adjusting for demographics, cardiovascular risk factors, and total body obesity, migraine prevalence was no longer associated with abdominal obesity in younger men, but remained associated with an increased risk of migraine in younger women, as well as with a decreased risk in older women.

**Conclusion:** This study found that, in men and women under 55 years of age, migraine prevalence is higher among those with total body obesity. In men over 55 years of age, migraine is not associated with obesity. However, in women over 55 years of age, migraine prevalence is lower among those with abdominal obesity, independently of total body obesity.

Peterlin, L., et al. Obesity and Migraine: The Effect of Age, Gender, and Adipose Tissue Distribution. *Headache*. 2010, January; 50: 52-62.

### URATE AS A PREDICTOR OF DECLINE IN PARKINSON'S DISEASE

Oxidative damage is suspected to contribute to the neurodegenerative process in Parkinson's disease (PD). Antioxidants such as urate may provide an endogenous defense against the development and progress of Parkinson's disease.

This study tested the hypothesis that higher urate concentrations in cerebral spinal fluid predict a slower rate of clinical disease risk among patients with PD.

This three-year, double-blind, randomized trial was originally designed to test the hypothesis that long-term treatment of early PD extends the time to the emergence of disability. All subjects had typical or early PD of less than five years' duration. After baseline examination, the subjects were randomized to one of four treatment assignments. Urate concentrations were measured in serum samples collected at baseline, prior to treatment assignment. Urate concentration was measured in serum samples collected at the baseline visit prior to treatment assignment. Serum was initially collected from 730 subjects, and then again at the end of the study from 486 subjects. Following the baseline visit and initiation of study medications, subjects were scheduled for visits every three months for two years. At each visit, the investigators evaluated the subject for disability sufficient to require levodopa therapy, the primary endpoint of the study, and for secondary response variables, including the Unified Parkinson's Disease Rating Scale (UPDRS) score.

Overall, 369 (47.7%) of the participants progressed to disability sufficient to require levodopa therapy. The hazard ratio of reaching this point declined with increasing concentrations of serum urate ( $p = 0.002$ ). This ratio was 36% lower among subjects in the top quintile compared to those in the bottom quintile of serum urate concentration. In the analysis stratified by alpha-tocopherol, a decrease in the hazard ratio for the primary endpoint was seen only among subjects *not* treated with alpha-tocopherol. Results were similar concerning the rate of change in UPDRS scores. Surgical spinal fluid urate concentrations were inversely related to the primary endpoint and to the rate of change in UPDRS scores. These associations were present only among subjects not treated with alpha tocopherol.

**Conclusion:** This study found that high serum concentrations of spinal fluid urate are associated with lower rates of clinical decline among patients with Parkinson's disease.

Asherio, A., et al. Urate as a Predictor of the Rate of Clinical Decline in Parkinson's Disease. *Arch Neur*. 2009, December; 66(12): 1460-1468.

### LOCOMOTOR TRAINING AFTER PLATEAU IN STROKE

Despite initial improvements in motor function after stroke, patients often reach a plateau, or a deceleration in motor recovery, after six months. The data suggest that the physiological substrates of stroke decline in the latter stages after insult, and could contribute to this apparent plateau. Numerous studies, however, have demonstrated that improvements in motor function can occur when individuals are provided intensive practice of motor tasks after the plateau. As locomotor training (LT) can provide up to 4,000 steps per minute, this study sought to determine whether locomotor training might also facilitate improved walking ability among patients with chronic stroke.

Participants were patients with stroke induced hemiparesis of at least six months' duration. To be eligible subjects were required to walk at least 10 meters over ground without physical assistance. The patients were assigned to either four weeks of LT training or four weeks without therapy. The immediate LT group was provided four weeks of intensive LT after discharge from clinical PT, which consisted of high intensity stepping practice on a motorized treadmill.

LT was performed at the same frequency as PT (two to five days per week) at the highest tolerable speed, with velocity increased in 0.5-kmph increments until the subject's heart rate reached 80% to 85% of the age-predicted maximum. In the final four weeks of the study, the delayed therapy group received locomotor training and the immediate LT group received no therapy. Outcome measures included clinical and metabolic measures of walking over ground and on a treadmill, and measures of daily stepping activity in the home and community, including that performed during clinical PT and subsequent LT sessions.

Average, daily stepping was significantly higher during locomotor training than during physical therapy training ( $p < 0.0$ ). Significant

improvements in clinical measures of walking performance (self-selected velocity, fastest possible velocity, and a 12-minute walk) were observed at each assessment. No further improvement was seen after LT completion. Further analysis revealed that the average stepping dosage (# steps/session) provided to subjects was significantly related to improved daily stepping in the home and community ( $p < 0.001$ ).

**Conclusion:** This study of patients with chronic stroke demonstrates that intensive locomotor training can improve ambulatory function in those who have been discharged from physical therapy due to a perceived plateau in motor recovery.

Moore, J., et al. Locomotor Training Improves Daily Stepping and Everyday Efficiency in Individuals Post-Stroke Who Have Reached a Plateau in Recovery. *Stroke*. 2010, January; 41(1): 129-135.

#### **HYLAN G-F 20 FOR SHOULDER OSTEOARTHRITIS**

Osteoarthritis (OA) of the shoulder is a rare condition that is often challenging to treat. Studies involving knee and hip OA have suggested that viscosupplementation may be a useful treatment intervention. This study evaluated the feasibility, safety, and efficacy of Hylan G-F 20 for patients with shoulder OA.

Patients were recruited from six centers in France and Germany. All were over 18 years of age and had an active lifestyle. Shoulder pain was assessed using a visual analogue scale, with scores ranging from 40 to 90 out of 100. The primary diagnosis was OA, with an osteophyte at the lower part of the humeral head measuring at least 2 mm. along the long axis on plain radiographs. After study inclusion, each patient was administered an intra-articular injection of 2 ml of Hylan G-F 20 into the study shoulder under aseptic conditions.

Each patient was reevaluated after seven days and at one, two, three, and six months post-injection. All subjects who experienced continued pain rated between 40 and 90 out of 100 were offered a second injection. The primary criterion was the visual analogue scale score for pain at three months. Secondary

measures included the Western Ontario Osteoarthritis of the Shoulder (WOOS) score, changes in the SF-36 Quality of Life score, and the patient's and physician's VAS scale ratings for shoulder OA related discomfort.

Included in the analysis were 33 patients who received a first, and 16 patients who received a second injection. The mean VAS pain score decreased from 61.2 at baseline to 37.1 at three months after the last injection ( $p < 0.001$ ). The mean WOOS scores were 45% at baseline, 61.7% after seven days ( $p < 0.001$ ), 63.1% after three months ( $p < 0.001$ ), and 62.4% after six months ( $p < 0.008$ ). The mean SF-36 scores were 38.6 points at baseline, 40.7 points at three months ( $p < 0.069$ ), and 43.3 points at six months ( $p < 0.007$ ). Finally, the mean patient and physician scores both decreased significantly ( $p < 0.001$ ).

**Conclusion:** This study of patients with osteoarthritis and intact rotator cuffs found that a single injection of Hylan G-F 20 can significantly reduce pain and disability, with minimal side effects.

Noel, E., et al. Efficacy and Safety of Hylan G-F 20 in Shoulder Osteoarthritis with an Intact Rotator Cuff. Open Label, Prospective, Multi-Center Study. *Joint Bone Spine*. 2009, December; 76(6): 670-673.

#### **SOCIAL FUNCTIONING AFTER TRAUMATIC BRAIN INJURY**

The Centers for Disease Control and Prevention estimates that, each year, 1.56 million Americans sustain a traumatic brain injury (TBI) for which they receive medical attention. Of those, 290,000 are hospitalized, 45% of whom remain disabled one year after injury. Nearly 20% of hospitalized survivors of TBI do not return to work by one year after injury. This literature review sought to clarify the relationship between adult onset TBI and social functioning six months or longer after the injury.

The authors searched the published biomedical literature for studies that examined the association between TBI and outcomes that reflect social functioning, observed at least six months after the injury. The outcomes of TBI cases were compared with those of matched controls without brain injury. Fourteen primary, and 25 secondary studies

were identified which allowed comparisons to controls for adults who were at least six months post-TBI.

A higher proportion of patients in each of the TBI severity groups, except for the most mildly injured, were rated as significantly disabled according to Glasgow Outcome Scale scores. Those with TBI had a decreased probability of employment after injury, an increased length of time to return to work after injury, and a decreased likelihood of return to the same position after injury. TBI was also found to adversely affect leisure and recreational pursuits and social relationships, as well as quality-of-life and independent living.

**Conclusion:** This literature review demonstrates that traumatic brain injury adversely affects social functioning in adults. TBI seem to have a greater effect on social function than do injuries to other parts of the body.

Temkin, N., et al. Social Functioning after Traumatic Brain Injury. *J Head Traum Rehab*. 2009, December; 24 (6): 460-467.

#### **SHOULDER EXAMINATION IN POLYMYALGIA RHEUMATICA**

Bilateral subacromial/subdeltoid bursitis and trochanteric bursitis are frequent lesions, found in almost all patients with polymyalgia rheumatica (PMR) who complain of shoulder pelvic girdle pain. As ultrasonography (US) has been used to detect inflammation in proximal joints and periarticular structures, this study sought to determine the usefulness of US and power Doppler US as predictors of relapses in patients with pure PMR.

Sixty-six, consecutive, untreated patients with pure PMR were prospectively assessed. Those with clinical manifestations of giant cell arthritis, or with positive, temporal artery biopsies, were excluded from the study. After the first visit, all patients were treated with prednisone at an initial dose of 12.5 mg per day. This dose was titrated up by 2.5-5 mg per day, in order to obtain an appropriate response. Participants were assessed by a rheumatologist with US once monthly for the first six months, and then every three months during follow-up. Relapses and recurrences were defined as the

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reappearance of clinical manifestations associated with elevated ESR or CRP after discontinuation of treatment. After the second US, the patients were followed for at least 12 months, with the number of disease relapses recorded.

At the time of the first US, at least one sign of inflammation was found in 98.2% of the patients. That finding was bilateral in 84.2%. The prevalence of at least one sign of inflammation at US was significantly reduced at the time of the second examination ( $p=0.0001$ ). At the time of the second US, a significant reduction was noted in the laboratory values reflecting inflammation, including ESR ( $p=0.0001$ ) and CRP ( $p=0.0001$ ) levels.

**Conclusion:** This study of patients with polymyalgia rheumatica demonstrates that the clinical inflammation of this disorder can be detected by ultrasound.

Macchioni, P., et al. Longitudinal Examination with Shoulder Ultrasound of Patients with Polymyalgia Rheumatica. *Rheum.* 2009, December; 48: 1566-1569.

*Rehab in Review* is a monthly publication produced by physicians in the field of Physical Medicine and Rehabilitation (PM&R). The summaries appearing in this publication are intended as an aid in reviewing the broad base of literature relevant to this field. These summaries are not intended for use as the sole basis for clinical treatment, or as a substitute for the reading of the original research.

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