

REHAB IN REVIEW

TM

WWW.REHABINREVIEW.COM

Volume 21 Number 11

Published by Physicians
In Physical Medicine and Rehabilitation

November 5, 2013

PITOLISANT FOR NARCOLEPSY

Narcolepsy is characterized by excessive daytime sleepiness, impaired ability to sustain attention and abnormal REM sleep manifestations. Available treatments include psychostimulants to treat excessive daytime sleepiness and sodium oxybate to alleviate cataplexy and excessive daytime sleepiness. Tuberomammillary histaminergic neurons, crucial for the maintenance of wakefulness, seem to be essential in the waking action of hypocretins. As pitolisant is an inverse agonist of the histamine H3 receptor, this study sought to determine whether this medication may be useful for the treatment of narcolepsy in humans.

Patients were 18 years of age or older with narcolepsy, with or without cataplexy, and with self-reported excessive daytime sleepiness of more than three months' duration. The subjects were randomized to receive either modafinil, at 100 mg daily, a placebo or pitolisant, at 10 or 20 mg. Treatment lasted eight weeks, and included three weeks of flexible dosing, followed by five weeks of stable dosing. The primary endpoint was the difference in change in Epworth Sleepiness Scale scores after the eight-week treatment period. Secondary endpoints included the Maintenance of Wakefulness Test, a sustained attention to response task, and modified clinical global impressions of change, targeting excessive daytime sleepiness and cataplexy.

The 94 patients included 81% with cataplexy, and 45% who had taken psychostimulants. The primary analysis revealed that pitolisant was superior to placebo in improvement on the Epworth Sleepiness Scale scores, though not significantly different from Modafinil. A *Post hoc* analysis revealed pitolisant to be superior to placebo, but not inferior to modafinil, for improvement in cataplexy from baseline. Adverse

events occurred in 22 patients receiving pitolisant, 26 receiving modafinil and 10 receiving placebo.

Conclusion: This study of patients with narcolepsy found that an H3 receptor inverse agonist is effective in treating narcolepsy.

Dauvilliers, Y., et al. Pitolisant versus Placebo or Modafinil in Patients with Narcolepsy: A Double-Blind, Randomized Trial. **Lancet Neurol** 2013, November; 12: 1068–1075.

TRANSDERMAL MYELIN PEPTIDES FOR MULTIPLE SCLEROSIS

The pathogenesis of multiple sclerosis (MS) is thought to result from antigen specific autoimmunity, wherein autoreactive immune cells directed at myelin specific peptides mediate the destruction of myelin within the central nervous system. Among the antigens linked with this autoimmunity, a prominent role has been proposed for peptides from three major myelin proteins, myelin basic protein (MBP), myelin oligodendrocytes glycoprotein (MOG) and proteolipid protein (PLP). This study assessed the effect of transdermally applied peptides on the disease activity of patients with relapsing/remitting MS.

Thirty patients, ages 18 to 55 years, all with a diagnosis of relapsing/remitting MS, were randomized to receive patches with placebo or with a mixture of 1 mg of each of the three myelin peptides, administered in either 1 mg or 10 mg doses. The patches were changed once per week for four weeks, and then once per month for 11 months. The primary efficacy outcome measure was the cumulative number of active gadolinium lesions per patient per scan during the year of the study.

Treatment with the 1 mg myelin peptides skin patch resulted in a

66.5% reduction in the cumulative number of lesions per patient per scan ($p=0.02$), as compared with placebo. The cumulative number of new lesions was reduced by 68.8% with the 1 mg patch, as compared with the placebo ($p=0.07$). The annual relapse rate in patients treated with peptides was lower than that of the placebo group.

Conclusion: This study of patients with relapsing/remitting multiple sclerosis found that a transdermal application of a mixture of three myelin peptides may be effective in improving the MRI and clinical outcomes of these patients.

Walczak, A., et al. Transdermal Application of Myelin Peptides in Multiple Sclerosis Treatment. **JAMA Neurol.** 2013, September; 70(9): 1105-1109.

ENDOVASCULAR THERAPY VERSUS INTRAVENOUS THROMBOLYSIS

Large vessel occlusions account for a large percentage of acute ischemic strokes in the United States. To date, no study has demonstrated a benefit of endovascular therapy in reducing infarct volumes of intracranial large vessel occlusions (ILVO). This study compared infarct volumes among patients with ILVO who received intrarterial therapy (IAT), intravenous thrombolysis (IVT) or no reperfusion therapy.

This retrospective, cohort analysis included patients with acute ischemic stroke presenting to an academic stroke center between 2009 and 2011. A total of 203 consecutive patients, all at least 18 years of age, and all with an anterior circulation ILVO, were studied. The cohort included IAT [penumbra (62.7%)], Mechanical Embolus Removal in Cerebral Ischemia (41.8%), and stent-retriever devices (13.4%), intravenous tPA therapy, and no

Editor-in-Chief

David T. Burke, M.D., M.A.
Emory University, Atlanta, GA

Executive Editor

Randolph L. Roig, M.D.
Emory University, Atlanta, GA

Copy Editor

Roberta Alysoun Bell, Ph.D.
Emory University, Atlanta, GA

Contributing Editors

*Amy Cao, M.D.
BCM/UT Alliance, Houston, TX

*Jennifer Knowlton, M.D.
East Carolina University, Greenville, NC

*Mikhail Zhukalin, D.O.
Anna Cruz, M.D.
Chukwuemeka Ibekwe, M.D.
Mitchel Leavitt, M.D.
Cleo D. Stafford II, M.D., M.S.
Donnie Staggs, M.D.
Christopher Williams, M.D.
Emory University, Atlanta, GA

*Cyrus Kao, M.D.
*Pablo Vazquez, M.D.
Rajat Mathur, M.D.
Georgetown/MedStar National Rehab,
Washington, DC

*Alexander Drakh, D.O.
LSU Medical Center, New Orleans, LA

*Joshua S. Sole, M.D.
Kristin Garlanger, D.O.
Bryndon B. Hatch, M.D.
Katherine Nano, M.D.
Mayo Clinic, Rochester, MN

*Richard Chang, M.D., MPH
Mount Sinai Med. Ctr., New York, NY

*Arpit A. Patel, D.O.
Nassau University Med Center

*Christina Marciniak, M.D.
Christine Eng, M.D.
Allison Kessler, M.D.
Steven Makovitch, D.O.
Ben Marchall, D.O.
Jaymin Patel, M.D.
Glória G. Rho, M.D.
N.W.U./R.I.C., Chicago, IL

*David Woznica, M.D.
NYP, Columbia-Cornell, NY, NY

*Samaira Khan, D.O.
Kevin Bernard, M.D.
NYU/Rusk Inst. of Rehab Med, NY, NY

*Craig Best, D.O.
*Kashif Saeed, M.D.
Rush University Medical Center, Chicago, IL

*Alice Hon, M.D.
Arpit Arora, M.D.
Lawrence P. Lai, M.D., MS
Victoria Lin, M.D.
Rui Zhang, M.D.
Jimmy Chen, BS
Rutgers/Kessler Rehab, Newark, NJ

*Alan Vo, D.O.
Sinai Hospital, UMD, Baltimore, MD

*Vikram Arora, D.O.
Reed Williams, M.D.
Temple Univ./UPenn., Philadelphia, PA

*Anupam Sinha, D.O.
Thomas Jefferson Univ/Rothman Inst.,
Philadelphia, PA

*Usman F. Ahmad, D.O.
University of Miami, Miami, FL

*Seth Swank, D.O.
University of Michigan, Ann Arbor, MI

*Chulhyun Ahn, M.D., MS

reperfusion therapy. The primary outcome measure was final infarct volume, as assessed with MRI or CT, with the secondary outcomes including the proportion of patients who achieved a final infarct volume of less than 70 cm³, mortality rates and final discharge disposition.

The majority of the patients in the IAT group received full dose intravenous tPA prior to endovascular therapy. The median, final infarct volume was significantly smaller in the IAT group (42 cm³) than in the IVT group (109 cm³) or the NRT group (110 cm³). No significant difference was seen between the medians of the IVT and NRT groups. In addition, the IAT group had a greater chance of achieving an infarct volume of 70 cm³ or less than did the other two groups (p=0.001). Patients with an NIHSS score of 14 or more had a greater chance of recovery.

Conclusion: This study of 203 patients with acute intracranial large vessel occlusions found that those who received intra-arterial therapy had a smaller, final infarct volume than did those who received intravenous thrombolysis or no reperfusion therapy.

Rangaraju, S., et al. Comparison of Final Infarct Thrombolysis Patients Who Received Endovascular Therapy or Intravenous Thrombolysis for Acute, Intracranial, Large Vessel Occlusions. **JAMA. Neurol.** 2013, July; 70(7): 831–836.

NEUROSIS AND THE RECALL OF PERSISTENT LOW BACK PAIN

As memory is a reconstructive process, recall is subject to the effects of a number of factors. Previous studies have suggested that higher levels of neuroticism are associated with reports of higher levels of acute experimental pain and persistent pain. As studies of low back pain (LBP) often rely on the subject's recall, this study was designed to determine the effects of neuroticism on the recall of back pain.

The participants were 70 men and women with an average age of 43.9 years, all with LBP averaging 10 years in duration. The patients underwent an orientation phase, a 15-day diary phase and a laboratory recall phase. During the orientation phase, demographic variables and baseline measures were collected,

including pain interference, neuroticism and depression. During the diary phase, the subjects completed a structured, daily diary at the end of each of the 15 days. During the recall phase, the participants were asked to recall their pain intensity, pain unpleasantness and activity interference due to pain. A regression analysis was used to assess the degree to which neuroticism or depression was related to the absolute difference between the recalled and actual pain measures.

Patients with greater severity of depressive symptoms showed worse recall accuracy on all three measures. Those with higher scores on neuroticism were significantly more accurate in their recall of the variability of pain unpleasantness over time.

Conclusion: This study of patients with chronic low back pain found that those with higher levels of neuroticism have better recall of pain unpleasantness, while those with higher levels of depressive symptoms have worse recall of pain in general.

Lefebvre, J., et al. The Effect of Neuroticism on the Recall of Persistent Low Back Pain and Perceived Activity Interference. **J of Pain.** 2013, September; 14(9): 948-956.

COMPLICATIONS FOLLOWING HIP OR KNEE ARTHROPLASTY IN THE MORBIDLY OBESE

Obesity has been identified as a risk factor for postoperative complications in patients undergoing total hip arthroplasty (THA) or total knee arthroplasty (TKA). This study was designed to determine whether morbid obesity is associated with significant post-operative complications after THA or TKA.

This retrospective analysis used data from the Regulation of Coagulation and Orthopedic Surgery to Prevent Deep Vein Thrombosis and Pulmonary Embolism (RECORD) program. This trial involved subjects 18 years of age or older, scheduled to undergo elective THA or TKA. From these data, patients with a BMI of at least 40 kg/m² were compared with those of lesser BMI for rates of DVT, pulmonary embolism, bleeding and other adverse events for up to eight weeks postoperatively.

The adjusted analysis revealed that the morbidly obese group had more frequent, serious adverse events than did the other BMI groups combined ($p=0.0014$), including device-related infection (0.67%), femur fracture (0.67%), hypoxia (0.45%), increased alanine aminotransferase (0.45%), infective arthritis (0.45%), nausea (0.45%), vomiting (0.45%) and wound dehiscence (0.45%). However, no significant differences were found between groups in the rates of DVT, PE or bleeding events.

Conclusion: This study of patients undergoing total hip or total knee arthroplasty found that, while morbid obesity does not increase the risk of DVT, PE, bleeding or other life-threatening complications, the rates of other adverse events, such as surgical infection and inflammation, are higher in this group.

Friedman, R., et al. Complication Rates after Hip or Knee Arthroplasty in Morbidly Obese Patients. *Clin Ortho Related Res.* 2013, October; 471(10): 3358-3366.

NEW ORAL ANTICOAGULANTS FOLLOWING JOINT REPLACEMENT

Novel oral anticoagulants (NOACs), including direct thrombin inhibitors and factor Xa inhibitors, have been introduced for thromboprophylaxis. Among the disadvantages of these treatments is increased cost and a lack of antidotes for timely reversal of bleeding. This study assessed the comparative effectiveness of NOACs and standard thrombosis prophylaxis regimens for patients undergoing total hip or total knee replacement.

A search of multiple databases for articles published between January 2009 and March 2013 was completed to identify systemic reviews comparing NOACs with low molecular weight heparin. The search revealed six studies thought to be of good quality, each of which directly compared NOACs with other types of thromboprophylaxis.

Compared with low molecular weight heparins, typically, enoxaparin, at 40 mg per day, the NOACs demonstrated similar effects on most major clinical outcomes. The risk for symptomatic deep vein thrombosis was reduced with factor

Xa inhibitors as compared with low molecular weight heparin, while the risks of nonfatal pulmonary embolism and death were not significantly different. The factor Xa inhibitors did demonstrate an increased risk of major bleeding.

Conclusion: This literature review demonstrates that, for patients undergoing total hip or total knee arthroplasty, the new oral anticoagulants are effective in reducing the risk of thromboembolism, although at an increased risk of bleeding.

Adam, S., et al. Comparative Effectiveness of New Oral Anticoagulants and Standard Thromboprophylaxis in Patients Having Total Hip or Knee Replacement. *Ann Intern Med.* 2013, August 20; 159: 275-284.

BILATERAL VERSUS UNILATERAL ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION OUTCOME

Patients undergoing anterior cruciate ligament (ACL) reconstruction enjoy a reasonably high rate of return to sports participation. As the risk of contralateral injury is relatively high in certain cutting and pivoting activities, this study was designed to assess the outcomes of patients with bilateral ACL injuries.

Patients were identified through hospital records at five orthopedic clinics in Sweden. All were diagnosed with bilateral ACL reconstruction, with a maximum 12 years between the surgeries. Patients with unilateral ACL reconstructions served as a control group. Outcome measures included patient reported knee measures (the Knee Injury and Osteoarthritis Outcome Score(KOOS) and the Lysholm knee score), quality-of-life (ACL deficiency quality-of-life (ACL-QOL)), EuroQol index, a study specific questionnaire, using a Likert scale and activity level, using the Tegner Activity Scale.

Of those with bilateral ACL repair, 85% had been active in contact sports before the first injury, 67% before the second injury and 18% at follow up. At follow up, 92% had changed their training habits due to their knee injuries. Compared with the unilateral ACL group, the bilateral group earned significantly lower scores on the ACL -QOL, KOOS and

return to sports/recreation. In addition, Tegner Activity Scale results were significantly higher than in those in the control group before the second injury ($p<0.05$).

Conclusion: This study of patients undergoing bilateral anterior cruciate ligament repair demonstrated impaired, patient-reported knee function, quality of life and activity levels for up to 12 years after the initial injury.

Faltstrom, A., et al. Patient Reported Knee Function, Quality of Life, and Activity Level after Bilateral Anterior Cruciate Ligament Injuries. *Am J Sports Med.* 2013, September. doi: 10.1177/0363546513502309.

ATRIAL FIBRILLATION WITH JOINT ARTHROPLASTY

Atrial fibrillation (a-fib) is the most common chronic cardiac arrhythmia in the United States, affecting more than three million people, and up to nine percent of those eighty years of age or older. Some have estimated that the economic and health care burden of patients with a-fib are significantly higher than those without. This study was designed to determine the effect of a-fib and chronic anti-coagulation therapy on the hospital burden for patients undergoing total joint arthroplasty.

An institutional electronic database was used to identify patients with a preexisting diagnosis of a-fib who were undergoing aseptic primary or revision total hip or total knee replacement. From these data, 161 patients with a-fib were matched with 161 controls without a-fib. The groups were compared by type of procedure, age, gender, length of hospital stay, laboratory values, transfusion requirements and readmissions.

The preoperative, postoperative and total lengths of stay were all significantly longer in patients with a-fib than among the control group ($p<0.0001$, $p=0.0002$, and $p<0.0001$, respectively). The mean hemoglobin levels did not significantly differ between the groups. The prevalences of blood transfusion were 15.5% for patients with a-fib and 3.7% for the controls ($p=0.0005$). Of those with a-fib, 25.5% had an unplanned readmission related to surgery, as compared to 6.2% of the control group ($p<0.0001$). The overall rates

of complications related to surgery were 30.5% in the a-fib group and 11.2% in the control group ($p < 0.0001$).

Conclusion: This retrospective study demonstrates that patients undergoing total joint arthroplasty who have atrial fibrillation have longer lengths of stay and more complications, including readmissions, than do those without a -fib.

Aggarwal, V., et al. Patients with Atrial Fibrillation Undergoing Total Joint Arthroplasty Increase Hospital Burden. *J Bone Joint Surg.* 2013, September 4; 95-A(17): 1606–1611.

DO WE UNDERESTIMATE ATRIAL FIBRILLATION IN STROKE PATIENTS?

Atrial fibrillation (a-fib) is frequently associated with ischemic stroke, with many documenting the association between the presence of a-fib and poor stroke outcome. This study was designed to better understand the frequency of a-fib among young patients with ischemic stroke.

This observational study included 157 consecutive patients, up to 50 years of age, admitted to a hospital stroke unit within 72 hours of symptom onset. All were hospitalized for least 72 hours and underwent daily electrocardiograms, echocardiograms and 24-hour cardiac monitoring. Atrial fibrillation was classified as associated with structural heart disease or non-structural heart disease. The severity of the stroke was measured with the National Institutes of Health Stroke Scale (NIHSS), with three-month outcomes measured using the modified Rankin scale.

Of the 157 patients, 14 presented with a-fib, with four of these newly diagnosed. The a-fib was found to be due to structural heart disease in 10 patients. A multivariate analyses found that a-fib was independently associated with moderate to severe strokes (odds ratio 3.771), with a greater NIHSS score compared to those without a-fib ($p = 0.018$). No significant relationship was found between the presence of a-fib and three-month outcomes.

Conclusion: This study of young patients admitted with ischemic stroke found that 8.9% presented with

a-fib, with this condition associated with poorer NIHSS scores on admission.

Prefasi, D., et al. Atrial Fibrillation in Young Stroke Patients: Do We Underestimate its Prevalence? *Euro J Neurol.* 2013, October; 20: 1367-1374.

VOIDING DYSFUNCTION AFTER BRAINSTEM INJURY

Urinary incontinence and urinary retention are common after acute stroke. This study evaluated the voiding patterns of patients with a history of stroke according to the site of brainstem lesion.

Between November of 2008 and December of 2011, 30 patients with acute brainstem infarction were identified. Each subject was evaluated by history, laboratory values and magnetic resonance imaging. On admission, the participants were assessed with the National Institutes of Health Stroke Scale (NIHSS) and by urodynamic study (UDS).

The subjects included 16 men and 14 women. Of those, 21 had pontine strokes and nine had medullary strokes. Urodynamic studies revealed that 46.7% had a bladder storage disorder 23.3% had a bladder emptying disorder, while 30% had normal bladder function. Bladder storage disorders were more frequent among those with pontine stroke than those with medullary stroke (61.9% versus 11.1%, $p = 0.017$). Bladder emptying disorders were more frequent among those with medullary stroke than in those with pontine stroke (55.6% versus 9.5%; $p = 0.014$).

Conclusion: This study of patients with brainstem stroke found that voiding dysfunction patterns are significantly different between patients who sustain a pontine infarction and those who sustain a medullary infarction.

Yum, K. Pattern of Voiding Dysfunction after Acute Brainstem Infarction. *Euro Neurol.* 2013; 70(6): 291–296.

STATIN USE SLOWS COGNITIVE DECLINE

While some studies have demonstrated that statin use is

associated with less cognitive decline, the results have been mixed. This study was designed to better understand the effects of statin use on cognitive abilities.

Data were obtained from the Uniform Data Set, a standardized assessment and data protocol maintained by the National Alzheimer's Coordinating Centers. Inclusion criteria required that participants have normal cognition or mild cognitive impairment (MCI) at baseline. All subjects were assessed with the Clinical Dementia Rating (CDR) with the Sum of Boxes (SOB) used to provide a composite of overall level of impairment. Variables assessed included memory, orientation, judgment, problem solving, community affairs, home and hobbies, and personal care, rated for level of impairment. Neuropsychological testing was performed and statin use documented.

From among the overall group, subjects' participation was restricted to those who always used statins at all visits (2,029) or never used statins at any visit (3,309). The subjects were evaluated an average of 3.9 times over 2.8 years. Among those individuals with no baseline cognitive impairment, a significantly slower rate of deterioration of cognitive function, as measured by the CDR-SOB, was found for statin users than for those not taking statins ($p = 0.006$). Scores on the Mini Mental State Exam (MMSE) also demonstrated a slower cognitive decline in the statin users, although this finding failed to reach statistical significance. No significant benefit from statin use was found for those with MCI at baseline, either on the MMSE or the CDR-SOB.

Conclusion: This study found that statin use can slow the rate of cognitive decline in patients with normal cognition at baseline.

Steenland, K., et al. Statins and Cognitive Decline in Older Adults with Normal Cognition or Mild Cognitive Impairment. *J Am Geriatr Soc.* 2013, September; 61(9): 1449-1455.

EYE MOVEMENT TRAINING FOR AUDITORY AND VISUAL NEGLECT

Of patients with stroke who present with neglect, approximately one third demonstrate chronic neglect one year after stroke. Recent studies

using optokinetic stimulation (OKS) with smooth pursuit eye movement training (SPT) have demonstrated improvements in visuospatial and tactile neglect. This randomized, controlled trial further explored the effects of SPT with visual scanning therapy (VST) on auditory and visual neglect in patients with chronic stroke sequelae.

Fifty consecutive patients, each with a diagnosis of right hemisphere stroke and left-sided neglect, were randomly assigned to receive treatment using SPT or VST. SPT stimuli were presented as computer-generated, random displays with dots moving coherently toward the left. The subjects were asked to make smooth pursuit movements in the direction of the motion. In the VST group, all visual stimuli were stationary, with the subjects asked to scan the array systematically. The patients were compared by performance on measures of visual and auditory neglect at baseline and at two-week follow-up.

For the auditory midline tests, a significant effect was found for SPT ($p < 0.001$), but not for VST ($p = 0.08$). For visual neglect tests, the main effect analysis was significant for all tests for SPT, but not for VST. Comparing by severity of neglect, the groups were divided by median splits into mild or severe neglect subgroups. Analysis revealed that the effect sizes were considerably higher for SPT than the VST therapy, both in the visual and auditory modalities, and for both severity subgroups.

Conclusion: This randomized, controlled study of patients with visual and auditory neglect found that smooth pursuit eye movement training can be effective for both visual and auditory neglect.

Kerkhoff, G., et al. Smooth Pursuit Eye Movement Training Promotes Recovery from Auditory and Visual Neglect: A Randomized, Controlled Study. *Neurorehab Neural Repair*. 2013, November/December; 27(9): 789–798.

EXERCISE FOR CARDIORESPIRATORY FITNESS AFTER STROKE

Adults who are highly or moderately active have a significantly reduced risk of stroke. However, little research has explored the effect of

physical activity after stroke for improving longitudinal, cardiovascular health outcomes. Given that 70% of stroke survivors are sedentary or have low levels of physical activity, this meta-analysis was designed to further clarify the effectiveness of exercise interventions for improving cardiorespiratory fitness after stroke.

The authors undertook a systematic search of studies published in multiple databases through December 27, 2011. Included were those which focused on individuals 18 years of age or older, post-stroke or post-transient ischemic attack. All included an intervention designed to improve cardiorespiratory fitness and peak oxygen consumption.

Of the 3,209 citations reviewed, 28 studies were included in the analysis. Among those, 16 used aerobic training, 11 used mixed intervention, including aerobic training, and one used knee flexion/extension isokinetic training. All programs ranged from two weeks to six months, with session durations ranging from 20 to 90 minutes. Of the 16 randomized, controlled trials, 12 were included in the meta-analysis. From these data, it was determined that, with aerobic training a 10% to 15% improvement occurred in the VO_{2peak} . In the subgroup analysis, aerobic and mixed interventions were equally effective, as were programs of three months' duration or longer, and those of shorter duration.

Conclusion: This meta-analysis found that post-stroke interventions with an aerobic component can improve fitness by 10% to 15%, even with moderate doses of exercise.

Marsden, D., et al. Characteristics of Exercise Training Interventions to Improve Cardiorespiratory Fitness after Stroke: A Systematic Review with Meta-Analysis. *Neurorehab Neural Repair*. 2013, November/December; 27(9): 775–788.

ULTRASOUND ASSESSMENT OF NERVES IN CHARCOT MARIE TOOTH

Demyelinating Charcot Marie tooth disease (CMT) and chronic inflammatory demyelinating polyneuropathy (CIDP) have been differentiated by a combination of clinical history, nerve conduction studies and genetic testing. Prior

research has demonstrated differences between CMT and CIDP in nerve enlargement, using MRI or ultrasound. It remains unclear however, whether the distribution patterns of this enlargement differ by disease. This study investigated the differences in the degree of nerve enlargement and the distribution of this enlargement in patients with demyelinating CMT and CIDP.

This study included 10 patients with CMT and 16 with CIDP. Ultrasound testing was performed by tracing the median and ulnar nerves, measuring the nerve cross-section at 24 sites bilaterally at distal, intermediate and cervical sites. In addition, the fifth and sixth cranial nerve roots were measured. A nerve size of at least two standard deviations above the mean reference value was defined as nerve enlargement.

In patients with CMT, nerve sizes were significantly larger at all sites along the peripheral nerves than in patients with CIDP. In addition, significantly more sites exhibited nerve size enlargement among patients with CMT than those with CIDP ($p < 0.001$). Using the number of sites of nerve enlargement to distinguish between the two disorders in the intermediate region resulted in a sensitivity of 0.9 and a specificity of 0.94.

Conclusion: This study found that nerve sizes, as measured by ultrasound along the median and ulnar nerves, were significantly larger in patients with demyelinating CMT than in those with CIDP.

Sugimoto, T., et al. Ultrasonographic Nerve Enlargement of the Median and Ulnar Nerves and the Cervical Nerve Roots in Patients with Demyelinating Charcot-Marie-Tooth Disease: Distinction from Patients with Chronic Inflammatory Demyelinating Polyneuropathy. *J Neuro*. 2013, October; 260: 2580–2587.

HETEROTOPIC OSSIFICATION AFTER CERVICAL SPINE SURGERY

Among the adverse outcomes of cervical arthroplasty, heterotopic ossification (HO) has been noted in previous literature. While the risk of HO is well known after total hip or total joint replacement, the

prevalence after cervical spine arthroplasty remains unknown. This study was designed to better understand the predisposing factors of HO in patients undergoing cervical arthroplasty.

Subjects were 170 patients who had undergone cervical arthroplasty beginning in 2003, all with a follow-up of at least 12 months. The patients received one of three devices, the Bryan Cervical Disc Prosthesis, the Mobi-C disc prosthesis or the ProDisc-C. These patients included 62 who underwent concurrent cervical fusion. Most received nonsteroidal anti-inflammatory drugs during the first four weeks after surgery. All subjects were assessed by radiographs for pre-existing degeneration and postsurgical HO. A logistic regression model was used to determine risk factors for the development of HO.

Among the 170 patients, HO was observed in 40.6%. The rates of HO were 47.6% in males and 29.2% in females ($p=0.0377$). The relative risk for Mobi-C was 5.262 ($p<.001$) and that for ProDisc-C was 7.449 ($p<.001$), compared with the Bryan disc. No other predisposing factors were correlated with HO grade.

Conclusion: This study of patients undergoing cervical artificial disc replacement found that the risk of heterotopic ossification is greatest among males and those who receive a MOBI-C or ProDisc-C prosthesis.

Yi, S., et al. The Predisposing Factors for the Heterotopic Ossification after Cervical Artificial Disc Replacement. *Spine J.* 2013, September; 70(5-6): 1048–1054.

LEPTIN CONCENTRATIONS IN SPINAL CORD INJURY

Leptin is known to play a key role in the balance between energy expenditure and consumption. Leptin is also thought to play a part in developing insulin resistance, glucose intolerance and increased cardiovascular disease risks. In patients with spinal cord injury (SCI), elevated levels of leptin have been reported, although controversy exists concerning the effect of injury level and body mass index (BMI) on leptin levels. This study was designed to better understand the changes in leptin concentration in patients with SCI.

This meta-analysis included several database review articles that investigated leptin levels among patients with SCI, published through February 2013. The inclusion criteria were a human study population, the use of a control group, appropriate measurement of leptin concentrations and a post injury duration of at least one year. Five studies were selected for inclusion in the meta-analysis.

A positive relationship was found between BMI and serum leptin concentrations ($p<0.00001$). Significantly higher levels of leptin were noted in patients with SCI than in able bodied individuals ($p<0.0001$). Higher leptin levels were also noted in tetraplegic compared to paraplegic subjects, although that difference was not statistically significant.

Conclusion: This meta-analysis demonstrated that serum concentrations of leptin are significantly increased in patients with spinal cord injury, with levels trending higher among those with tetraplegia than in those with paraplegia.

Latifi, S., et al. Changes of Leptin Concentration in Plasma in Patients with Spinal Cord Injury: A Meta-Analysis. *Spinal Cord.* 2013, October; 51(10):728-731.

INTRATHECAL BACLOFEN FOR SPASTICITY IN MOTOR NEURON DISEASE

Spasticity and painful spasms are common among patients with motor neuron diseases. Intrathecal baclofen (ITB) has been used in patients with stroke, spinal cord injury and brain injury with severe, functionally limiting, diffuse spasticity. However, few studies have shown the utility of ITB for patients with motor neuron disease (MND). This study was designed to determine the efficacy of ITB in a cohort of patients with upper motor neuron predominant MND (UMND).

A total of 44 patients diagnosed with amyotrophic lateral sclerosis (ALS), primary lateral sclerosis (PLS) or MND were referred to a spasticity clinic. Patients were considered for ITB therapy if they had severe diffuse spasticity in the lower extremities, with failure of oral medications. In this cohort, 20 patients were chosen to initiate ITB and 15 to begin conservative treatment.

The participants were assessed at baseline, within six months and after six months of follow-up. The late follow-up time period within the ITB group averaged 304 days, and that in the control group 297 days. Outcome measures included the Numerical Rating Scale (NRS) for Pain, the Modified Ashworth Scale (MAS), manual muscle testing and a timed, 25-foot walk test.

At long term follow up, there was a significant difference in change in MAS score ($p<0.0001$) and NRS pain score ($p=0.04$) in favor of the ITB group. A significant reduction in oral medication was also noted among the ITB patients. The non-ITB group demonstrated worsening of MAS scores and a decline in gait speed between baseline and late follow-up. Hip flexor strength remained similar between the two groups.

Conclusion: This study of patients with upper motor predominant, motor neuron disease found that intrathecal baclofen can effectively reduce spasticity and symptoms without compromising function.

Bethous, F., et al. Use of Intrathecal Baclofen for Treatment of Severe Spasticity in Selected Patients with Motor Neuron Disease. *Neurorehab Neural Repair.* 2013, Nov/Dec; 27 (9): 828–833.

VIGOROUS VERSUS MODERATE ACTIVITY AND HEALTH

Most physical activity guidelines recommend at least moderate intensity physical activity for general population health benefits. Recent literature suggests that vigorous physical activity may provide additional physical and mental health benefits. This study assessed whether vigorous physical activity provides additional benefits over those that accrue from moderate intensity physical activity.

Women were recruited from the Australian Longitudinal Study on Women's Health, a prospective study of factors shaping the health and well-being of three cohorts of Australian women recruited from the national Medicare health insurance database. The cohort for this study were those born between 1946 and 1951 who completed surveys through 2010. The surveys asked the women to report time spent in moderate physical

activity, as well as time spent in vigorous physical activity.

Physical activity was calculated and categorized into three groups: inactive, moderate only physical activities (MOPA) moderate and vigorous activity (MVPA). The main outcome variables included hypertension and depression, with the latter measured by the 10-item Centers for Epidemiological Studies-Depression Scale.

Of the 11,285 participants, 18% were classified as inactive, 65.3% as MOPA and 16.8% as MVPA. Compared with inactivity, the odds for hypertension declined with increasing physical activity. The decline was slightly greater in the MVPA group than in the MOPA group. For depression, the odds ratio values declined more markedly with increasing physical activity. The odds ratio values were lower in the MVPA group than in the MOPA group, although this finding only reached statistical significance for the highest physical activity volume.

Conclusion: This prospective study found that some vigorous activity, added to a routine exercise program, provides additional benefits by improving hypertension and depression.

Pavey, T., et al. Does Vigorous Physical Activity Provide Additional Benefits Beyond Those of Moderate? **Med Sci in Sports and Exer.** 2013, October; 45(10): 1948–1955.

BLOOD PRESSURE AND PROGRESSION OF BRAIN ATROPHY

It has long been known that hypertension increases the risk for vascular brain lesions. However, prospective data concerning the association between hypertension and the progression of brain atrophy in high vascular risk patients are scarce. This study examined the association between changes in blood pressure levels over time and the progression of brain atrophy.

Data were gathered from the Secondary Manifestations of Arterial Disease-Magnetic Resonance (SMART-MR) study. Between 2001 and 2005, all patients referred with manifest coronary artery disease, cerebrovascular disease, peripheral artery disease or abdominal aortic aneurysm, and without MR

contraindications, were invited to participate in the study.

The MRI investigations were performed on the 1.5 Tesla whole body system. These scans were reviewed to identify white matter lesions, total intracranial volume (ICV), brain parenchymal fraction (BPF), cortical gray matter fraction (GMF) and ventricular fraction (VF). Blood pressure was measured twice in a sitting position, with an average of the two measurements calculated. Pulse pressure and mean arterial pressure were calculated as measures of blood pressure and were categorized as low, normal or high.

In the total population, lower baseline diastolic blood pressure and mean arterial pressure, as well as a higher baseline pulse pressure, were significantly associated with a progression of subcortical brain atrophy as measured by increased VF. Declining diastolic pressure levels over time in patients with higher baseline BP were associated with less progression of subcortical atrophy.

Conclusion: This study found that, among patients with arterial disease, low baseline diastolic blood pressure was associated with more progression of subcortical atrophy. Further, in those with higher baseline blood pressure, declining blood-pressure levels over time were found to be associated with less progression of subcortical atrophy.

Jochemsen, H., et al. Blood Pressure and Progression of Brain Atrophy. The Smart-MR Study. **JAMA Neurol.** 2013, August; 70(8): 1046–1053.

PREVALENCE OF UNDIAGNOSED CONCUSSIONS IN ATHLETES

Previous studies have suggested that athletes tend to under report concussions. This study was designed to determine the rate of previously undiagnosed concussions.

This multicenter, cross-sectional study included patients seen at two sport concussion clinics between October 1, 2009, and September 30, 2010. Eligible participants included those with sport related concussions, as well as patients with injury mechanisms and forces similar to those observed in sports. Data collected included demographic information, clinical data and scores on the Post-Concussion Symptom

Scale (PCSS). In addition, the subjects were asked, "Have you ever sustained a blow to the head which was not diagnosed as a concussion, but was followed by one or more of the signs and symptoms listed in the Post-Concussion Symptom Scale?" Those who responded positively to this question were classified as having a previously undiagnosed concussion.

The final analysis included 486 patients. Of those, 148 reported that they had sustained a previous blow to the head, followed by one or more signs and symptoms listed on the PCSS, but had not been diagnosed previously with a concussion. Those with previously undiagnosed concussions had higher PCSS ($p < 0.004$) scores and were more likely to have lost consciousness ($p = 0.038$) with their current injury than were other subjects.

Conclusion: This study found that almost one third of athletes presenting to a concussion clinic had a previously undiagnosed concussion.

Meehan, W., et al. The Prevalence of Undiagnosed Concussions in Athletes. **Clin J Sport Med.** 2013, September; 23(5): 339-342.

ACTIVE VERSUS SUPINE EXERCISE RECOVERY

In sports, performance is based upon maintaining high-level physical outputs during repeated bouts. Recovery is significant for maintaining performance, as it increases the rate of energy regeneration, stabilizes acid-base balances and decreases fatigue. The importance of recovery has led researchers to investigate a variety of recovery strategies. This study compared active and passive recovery strategies with regard to their effects on performance variables.

Subjects were 14 males, averaging 21 years of age, and split into two groups to perform six sets of 10 second bicycle sprints, followed by two-minute recovery intervals. Each participant performed two counterbalanced trials. In the active trial, the subjects used active recovery for the first three sets, walking 1.5 mph on a treadmill at a 2.5% grade. The passive recovery trial consisted of lying supine on a trainer's table. The trials were

(Continued from page 2)

*Chulhyun Ahn, M.D., MS
UPenn Health System, Philadelphia, PA

*Thiru Annaswamy, M.D.
Trixy Syu, D.O.
UTSW Medical Center, Dallas TX

*Rachel Hallmark, M.D., Ph.D.
Joseph Amalfitano, D.O.
UVA, Charlottesville, VA

*Ryan Solinsky, M.D.
Jennifer Soo Hoo, M.D.
University of Washington, Seattle, WA

*Bonnie Weigert, M.D.
Lauren Schatzeder, D.O.
University of Wisconsin, Madison, WI

*William Robbins, M.D.
Wiam Ahmed, M.D.
Priya Chandon, M.D.
Greg Condie, M.D.
VCU, Richmond, VA

*Adam J. Schulte, M.D.
Shannon Dietzmann, M.D.
Prateek Grover, M.D., PhD
Ikram Malik, M.D.
Washington University, St. Louis, MO

Executive Editor Emeritus

Donald F. Langenbeck, Jr., M.D.

Subscription Manager

Michael P. Burke, M.S.

***Regional Managing Editors have attested that they have no financial conflict of interest when choosing articles that appear in Rehab in Review.**

separated by four to seven days. Heart rates were measured every 20 seconds during recovery, with calculations of peak power, average power and time to return to baseline active heart rate.

The return to baseline active heart rate was faster during passive recovery than during active recovery. Heart rates during active recovery remained more elevated than did those during passive recovery. However, peak and average power did not differ significantly between the two conditions.

Conclusion: This study found that passive, supine recovery between sprint exercise sessions results in a lower heart rate than does active recovery, but does not alter subsequent performance.

Larson, L., et al. The Effect of Active versus Supine Recovery of Heart Rate, Power Output, and Recovery Time. *Inter J Exer Sci.* 2013; 6(3): 180-187.

Rehab in Review (RIR) is produced monthly by physicians in the field of Physical Medicine and Rehabilitation (PM&R), with the cooperation and assistance of Emory University School of Medicine, Department of Rehabilitation Medicine. 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.

The Emory University School of Medicine designates this journal based activity for a maximum of 3 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity. The Emory University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

RIR is affiliated with the Association of Academic Physiatrists, the World Health Organization, and the Chinese and Indian Societies of PM&R and endorsed by the International Society of Physical and Rehabilitation Medicine.

Private subscriptions are available by email at rehabinreview@aol.com or by fax or phone at (800) 850-7388.

ISSN # 1081-1303

www.rehabinreview.com



REHAB IN REVIEW

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



EMORY
UNIVERSITY
SCHOOL OF
MEDICINE

Department of
Rehabilitation
Medicine

Expanding the frontier of rehabilitation sciences in research, teaching, and patient care