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BIHEMISPHERIC BRAIN STIMULATION AND MOTOR FUNCTION IN CHRONIC STROKE

Ischemic stroke is one of the leading causes of disability in adults. Recent developments, including noninvasive brain stimulation techniques such as repetitive transcranial magnetic stimulation and transcranial direct current stimulation (tDCS), have shown some promise for the treatment of chronic stroke. To date, however, no study has tested the efficacy of bihemispheric stimulation in combination with peripheral sensory motor activities among patients with chronic stroke. As this combination results in up-regulation of the ipsilesional, and down-regulation of the contralesional, motor regions, the authors of this study investigated the capacity of these techniques to improve motor function.

Twenty subjects participated in this double-blind, randomized trial. All patients had experienced middle cerebral artery ischemic strokes at least five months previously. The subjects were randomized to receive either real or sham tDCS for five sessions, 30 minutes each, completed in conjunction with their physical and occupational therapy activities. Real stimulation consisted of 30 minutes of 1.5 mA direct current, with the anode placed over the ipsilesional and the cathode over the contralesional motor cortex. Baseline motor assessments include the Fugl-Meyer and Wolf Motor Function Tests (WMFT). Follow-up motor assessments were performed at three and seven days after the last intervention.

Improvements in motor function among those in the tDCS group were greater than those of the sham group. These gains persisted for at least one week after intervention and were accompanied by greater activation of the ipsilateral motor cortex on functional MRI when upper limb

movements were performed. In the tDCS group, a significant relationship was seen between changes in the precentral gyrus LI (using the elbow movement task) and changes in WMFT scores ($p = 0.029$).

Conclusion: In this study, chronic stroke patients receiving bihemispheric brain stimulation in conjunction with therapy improved upper limb motor function more than did those receiving therapy alone.

Lidenburg, R., et al. Bi-hemispheric Brain Stimulation Facilitates Motor Recovery in Chronic Stroke Patients. *Neur.* 2010, December 14; 75(24): 2176-2184.

CORTICOSTEROID INJECTIONS AND BONE LOSS IN RHEUMATOID ARTHRITIS

The inflammatory disease process of rheumatoid arthritis (RA) can result in joint erosions and osteoporosis, resulting from increased osteoclast activation and formation. In daily clinical practice, intra-articular corticosteroid injections rapidly reduce symptoms in clinically inflamed joints. This study explored the effect of these injections on bone density and generalized bone loss among patients with RA.

This study included 40 patients with RA, each with disease duration of fewer than 12 months. For the first three-month period, the subjects were randomized to receive either methotrexate (MTX) alone or MTX and intra-articular methylprednisolone, injected into joints with clinically active RA (defined as both tender and swollen). From three to 12 months, both groups received the same treatment of MTX and steroid injections. The patients were seen at baseline and at one, two, three, six, nine and 12 months. An MRI of the dominant hand was performed at baseline and at three and 12 months. Standardized bone

mineral density measures were made of both hands at baseline and at three, six and 12 months' follow-ups. Results of these tests were compared by treatment group.

A significant loss in bone mineral density was seen in the hand at three, six and 12 months, and in the spine and femoral neck at 12 months. In the first three months, a lower rate of BMD loss occurred in the combination group than in the MTX group. In the three- to 12-month period, no statistically significant difference was seen between the two groups.

Conclusion: This study demonstrates that intra-articular corticosteroid injections may be helpful in reducing bone loss in inflamed finger joints in patients diagnosed with rheumatoid arthritis.

Haugeberg, G., et al. Effect of Intra-Articular Corticosteroid Injections and Inflammation on Periarticular and Generalized Bone Loss in Early Rheumatoid Arthritis. *Ann Rheum Dis.* 2011, January; 70(1):184-187.

A FOUR-POINT INJECTION TECHNIQUE FOR DE QUERVAIN TENOSYNOVITIS

De Quervain tenosynovitis (DQT) is a painful and often disabling condition of the first dorsal compartment of the wrist. This condition usually responds well to nonsurgical management, with data indicating that a corticosteroid injection alone may have an 80% cure rate. Previously described injection techniques often refer to either a one- or two-point injection. This study assessed the efficacy of a novel, four-point injection technique developed by the authors.

This three year, multicenter trial included a cohort of 48 men suffering from persistent DQT. In all cases, the patients had not responded well to treatment with oral nonsteroidal anti-

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inflammatory drugs and splinting. All individuals were involved in high resistance training regimens, with the subjects randomly allocated to receive corticosteroid injections using a two-point (group B) or a four-point (group A) injection technique. Follow-up was performed at two, four, eight and 52 weeks, using scores on the Disabilities of the Arm, Shoulder and Hand (DASH) measure. Treatment efficacy was defined as the absence of the pain and tenderness typically seen in DQT.

Two weeks after the first treatment, seven patients in group A were symptom free. All patients in group A scored better on the DASH than did their group B counterparts ($p < 0.05$). Four weeks after the first treatment, six more group A subjects were symptom free, in contrast to only three in group B. Two patients in group A received repeat injections, in contrast to 20 in group B. Eight weeks after the first treatment, 13 patients from group A were released from treatment as being symptom free, while one received repeat injections. At the final follow-up, 21 patients in group A were symptom free, one underwent surgery and two relapsed. In group B, 12 were symptom free, none underwent surgery and three relapsed.

Conclusion: This study of high resistance training athletes suggests that recalcitrant De Quervain tenosynovitis responds more favorably to a four-injection technique than to a standard, two-injection technique.

Pagonis, T., et al. Improved Corticosteroid Treatment of Recalcitrant De Quervain Tenosynovitis with a Novel, Four-Point Injection Technique. **Am J Sports Med.** 2011, Feb; 39(2): 398-403.

EFFECTS OF FOOT ORTHOSES ON PATELLOFEMORAL PAIN

Patellofemoral pain syndrome (PFPS) is a common diagnosis among those presenting to sports medicine clinics. Previous studies have identified foot orthoses as helpful in reducing pain in patients with PFPS. No prior study has investigated changes in functional performance resulting from these shoe modifications. This study sought to determine the immediate effects of

prefabricated foot orthoses on functional performance in individuals with PFPS.

Fifty-two patients diagnosed with PFPS were studied. All attended a data collection session for evaluation of baseline characteristics (using the motion control properties scale from the Footwear Assessment Tool) and clinical measurements of changes in functional performance with the addition of prefabricated foot orthoses footwear. Only the symptomatic or most symptomatic limb was assessed. Functional outcome measures included changes in pain, ease of a single leg squat on a five-point Likert scale, pain-free step downs and single leg rises from sitting.

The results indicated that prefabricated foot orthoses enhanced function during the step down ($p = 0.005$) and single-leg rises from sitting ($p = 0.04$) tasks, as well as improved pain ($p = 0.002$) and ease of task ($p < 0.001$) during the single-leg squat test.

Conclusion: This study found that patients with patellofemoral pain syndrome can experience significant, immediate functional benefits with the use of a prefabricated foot orthosis.

Barton, C., et al. Immediate Effects of Foot Orthoses on Functional Performance in Individuals with Patellofemoral Pain Syndrome. **Br J Sports Med.** 2011, March; 45: 193-197.

FOOT ORTHOSES AND PREVENTION OF OVERUSE INJURY

The origins of overuse lower limb injuries are multi-factorial. Abnormal gait mechanics are recognized as a critical factor. As foot orthoses have been commonly used in the treatment of these injuries, this study investigated whether a customized foot orthosis can reduce the overuse injury rate.

Four hundred military trainees were assessed with pressure plate recording. All were then placed in a high risk, medium risk or low risk, based upon the number of corrections needed at the plantar surface. The trainees were randomized to either a test group, receiving a customized foot orthosis, or to a control group. Both cohorts were followed for seven weeks. The

primary outcome measure was overuse lower limb injury requiring removal from physical training for two or more days.

By the end seven weeks of training, the orthotic intervention group had sustained only 21 injuries, while the control group had sustained 61 injuries ($p < 0.0001$). The absolute risk reduction due to use of a prosthesis was 0.49 ($p < 0.0001$).

Conclusion: This study of military officer trainees demonstrates that foot orthoses may prevent overuse lower limb injuries.

Franklyn-Miller, A., et al. Foot Orthoses in the Prevention of Injury in Initial Military Training. *Am J Sports Med.* 2011, January; 39: 30-37.

MEAT CONSUMPTION AND RISK OF JOINT REPLACEMENT

Current dietary recommendations are to consume moderate to small amounts of red meat and processed meat as a means of reducing the risk of a number of chronic diseases, including cardiovascular disease and cancer. However, consumption of those foods may benefit the musculoskeletal system, with evidence of high animal protein associated with high bone mineral density and low risk of fracture. This study sought to determine whether consumption of red meat or processed meat affects the risk of primary knee and hip joint replacement due to osteoarthritis (OA).

This prospective cohort study involved 35,331 people between 27 and 75 years of age at baseline, all of whom were participants of the Melbourne collaborative cohort study, recruiting during 1990 to 1994. Consumption of fresh red meat, processed meat, chicken and fish was assessed using a food frequency questionnaire. During follow-up in the years 2001 through 2005, the incidence of primary hip and knee replacement due to OA was determined by linking the cohort records to the Australian National Joint Replacement Registry.

The data revealed a beneficial dose response relationship between fresh red meat consumption and the risk of hip joint replacement, with the highest quartile of consumption associated with a decreased risk of hip joint replacement, as compared

with the bottom quartile. No dose response relationship was observed between the consumption of fresh red meat and knee joint replacement. Consumption of processed meat, chicken or fish had little to no association with the risk of either hip or knee replacement.

Conclusion: This prospective cohort study found that a high level of consumption of fresh red meat is associated with a decreased risk of hip, but not knee, joint replacement for osteoarthritis.

Wang, Y., et al. Meat Consumption and Risk of Primary Hip and Joint Replacement Due to Osteoarthritis: A Prospective Cohort Study. *BMC Musculoskel Dis.* 2011; 12: 17.

PHYSICAL ACTIVITY AS A RISK FACTOR FOR JOINT REPLACEMENT

While regular, moderate physical activity is recommended for improved general health and life expectancy, uncertainty persists concerning whether such activity is beneficial or detrimental to the health of weight bearing joints. Many studies examining the relationship between physical activity and the incidence and progression of osteoarthritis (OA) have been inconclusive. This study prospectively examined the associations between the frequency and intensity of physical activity and the risks of knee and hip replacement due to OA.

Participants were selected from the Melbourne collaborative cohort study between 1990 and 1994. A baseline interview was performed to obtain demographic information, including the amount and level of physical activity. The participants were followed with further questions regarding their physical activity and overall health. Data concerning primary joint replacements, including those of the hip and knee, were gathered between 2001 and 2005 from the National Joint Replacement Registry.

A total of 541 patients were identified with incident primary knee replacement, and 468 with incident primary hip replacement, resulting from OA. Participants exposed to high levels of physical activity were found to be at greater risk of primary knee replacement than were those with no physical activity. A positive

dose response relationship was seen between levels of total physical activity and the risk of primary knee replacement. The frequency of vigorous activity was also associated with an increased risk of primary knee replacement. No significant association was seen between the level of activity and risk of hip replacement.

Conclusion: This study found a positive association between frequent and vigorous physical activity and the risk of knee replacement due to osteoarthritis.

Wang, Y., et al. Is Physical Activity a Risk Factor for Primary Knee or Hip Replacement Due to Osteoarthritis? A Prospective, Cohort Study. *J Rheum.* 2011, February; 38(2): 350-357.

TELEREABILITATION AFTER TOTAL KNEE ARTHROPLASTY

Access to therapy may be limited for patients living in remote areas or for those who have time and cost barriers. One possible solution is the use of telerehabilitation technology to enhance rehabilitation service delivery from a distance. This study evaluated the efficacy of internet-based telerehabilitation for patients who had undergone total knee arthroplasty (TKA).

This single blind, prospective, randomized, controlled trial included patients who were at least 18 years of age and who had undergone TKA. The subjects were randomized to participate in a six-week rehabilitation program, either using standard care or performed remotely by means of a video linked telerehabilitation program. Intervention began one week after hospital discharge, and involved one, 45-minute treatment session, once per week. The primary outcome measure was the WOMAC scale, with secondary outcome measures including the patient's specific functional scale, the Spitzer Quality of Life Uniscale, the Timed Up and Go Test, and pain intensity, graded on a visual analogue scale (VAS).

Thirty-one participants were assigned to a telerehabilitation group and 34 to a control group. Both groups demonstrated significant clinical improvements from baseline ($p < 0.01$ for all). Non-significant differences were found for all primary

and secondary outcomes, except for the stiffness component of the WOMAC scale ($p=0.04$) and the patient specific functional scale ($p=0.04$), both favoring the telerehabilitation group. The subjects reported a higher level of satisfaction with the telerehabilitation process.

Conclusion: This study provides evidence for the effectiveness of telerehabilitation in providing postoperative rehabilitation after total knee arthroplasty.

Russell, T., et al. Internet-Based, Outpatient Telerehabilitation for Patients following Total Knee Arthroplasty: A Randomized, Controlled Trial. *JBJS* 2011, January 19; 93: 113-120.

PREDICTING GAINS BASED UPON TRACT SPECIFIC STROKE INJURY

Motor deficits are among the most common after stroke, and, thus, are a major contributor to disability. Brain mapping studies suggest that many of the effects of therapies to improve hand motor function in the chronic phase of stroke are mediated by the surviving motor system of the stroke affected hemisphere. This study explored whether the extent of damage to specific white matter tracts descending from the motor cortex predicts the benefit of therapy targeting hand function.

Subjects were 23 patients with right hemiparesis due to chronic stroke. Twelve normal subjects were studied to generate a template of each tract. To do this, diffusion weighted magnetic resonance imaging (MRI) scans of white matter tracts descending from the primary motor cortex (M1), supplementary motor area (SMA), dorsal motor cortex (PMd) and central premotor cortex (PMv) were obtained. Each subject's MRI was compared to the template, in order to estimate the extent of damage. Therapy comprised repeated grasp-release movements by the affected distal upper extremity, using a pneumatically actuated robot. Performances on the Arm Motor Fugl-Meyer scale, the Box and Blocks measure and the Action Research Arm Test (ARAT) were determined before and after completion of therapy. Relationships between tract-specific injury and behavioral gains from therapy were then examined.

Across the 23 stroke subjects, the range of tract injury was wide, with the extent of overlap between infarct and descending tracts ranging from 0% to 100% for M1, PMd, and PMv, and from zero percent to 93.8% for the SMA. The presence of injury to any of the four white matter tracts predicted change in performance after therapy better than did infarction volume, NIHSS score or pretherapy performance. Specifically, the presence of M1, PMd, and SMA tract damage was significantly related to post-therapy FM score ($p<0.005$, $p<0.05$ and $p<0.0167$, respectively). The presence of PMd damage was significantly related to post-therapy Box and Blocks scores ($p<0.005$).

Conclusion: This study of patients with chronic stroke found that damage to specific white matter tracts may be important in determining who will benefit from targeted motor therapy.

Riley, J., et al. Anatomy of Stroke Injury Predicts Gains from Therapy. *Stroke*. 2011, February; 42(2): 421-426.

BLOOD PRESSURE ONE YEAR AFTER STROKE

Approximately 25% of hospital admissions with acute stroke are due to recurrent stroke. As lowering blood pressure (BP) in stroke survivors has been found to reduce the risk of recurrent stroke, BP reduction is a key recommendation in clinical guidelines for secondary stroke prevention. This study tested the efficacy of a nurse led nonpharmacological intervention strategy for BP reduction among stroke survivors.

Patients were recruited from among those admitted to the Copenhagen University Hospital with a diagnosis of stroke. The subjects included 303 acute stroke or transient ischemic attack survivors, randomized to either an intervention group or a control group. Patients in the intervention group were visited by a nurse on four occasions during the year following hospitalization. During each meeting, BP was measured and individually tailored lifestyle counseling was provided. Patients in the control group received lifestyle counseling during hospitalization only. BPs were checked at baseline and again at one year for both

groups. Secondary endpoints included medication compliance, frequency of physician visits, and changes in blood pressure medications.

At follow-up, the mean systolic BP reading was 3 mm Hg lower and the mean diastolic BP 4 mm Hg lower in the intervention group than in the control group ($p=.007$). This difference resulted from an increase in the BP of the control group. BP at the point of randomization was the strongest predictor of BP one year later ($p<0.001$). The proportion of patients on antihypertensive medications in the intervention group increased from 60% at baseline to 70% at one-year follow-up ($p<0.002$).

Conclusion: This study of patients hospitalized with a first stroke found that nurse led home visits did not significantly decrease blood pressure, as measured in the year after discharge, although those visits seemed to prevent the increase in BP that was noted in the control group.

Hornnes, L., et al. Blood Pressure One Year after Stroke: The Need to Optimize Secondary Prevention. *J Stroke Cerebrovasc Dis*. 2011, January-February; 20(1): 16-23.

PLASMA BETA-AMYLOID LEVEL AND COGNITIVE DECLINE IN THE ELDERLY

Plasma β -amyloid has emerged as a promising biomarker to identify elderly persons at risk for developing Alzheimer's disease (AD) related dementia. Patients with lower β amyloid 42 and 42/40 levels are at increased risk of developing AD. This study investigated whether plasma β amyloid levels are associated with cognitive decline, and whether such an association can be modified by cognitive reserve.

Participants were enrolled in the Health, Aging and Body Composition Study. Subjects were 997 individuals who had undergone repeat cognitive testing and β amyloid 42 and 40 measurements. Cognitive function was measured with the Mini Mental State Examination (MMSE) at baseline and at years three, five, eight and 10, in order to screen for dementia. Cognitive reserve was defined by years of education and literacy. Apolipoprotein E (ApoE)

levels were determined as a function of genetic vulnerability.

A low β amyloid 42/40 level was associated with a greater MMSE loss per year ($p < 0.001$), and was similar after adjustment for race, age, education, diabetes, smoking and ApoE status. This association was modified by measures of cognitive reserve. In patients with high cognitive reserve, β amyloid 42/40 was less associated with cognitive decline ($p = 0.0004$ for high school diploma, $p = 0.005$ for greater than six grade, and $p = 0.02$ for ApoE allele).

Conclusion: This study demonstrates that elderly persons without dementia and with lower β amyloid 42/40 levels have an increased rate of cognitive decline as compared with those with higher amyloid 42/40 levels. This relationship is modified by cognitive reserve.

Yaffe, K., et al. Association of Plasma Beta-Amyloid Level and Cognitive Reserve with Subsequent Cognitive Decline. *JAMA*. 2011, January 19; 305: 261-266.

A PET STUDY OF PHOTOPHOBIA DURING MIGRAINE

Migraine attacks frequently involve sensitivity to sensory stimuli, such as light. The concept of central neuronal hyperexcitability is proposed as a pivotal physiologic disturbance in migraine. This study investigated the effects of photophobia during migraine attacks, and its associations with visual cortex hyperexcitability and trigeminal nociception.

Eight patients with episodic migraine, all without aura and with consistent complaints of photophobia during attacks, were selected from among patients at a French hospital. All subjects were studied during a spontaneous, acute migraine attack, and were instructed not to take any medications, including triptans or analgesics, prior to testing. PET scanning was performed during the migraine attack, after headache relief following sumatriptan injection and during an attack free interval.

Photophobia was induced using luminous stimulation through white, semi-opaque goggles. The subjects were scanned in six conditions, with two scans performed for each condition; migraine headache in darkness, migraine headache with

luminous stimulation, headache relief in darkness, headache relief with luminous stimulation, attack free interval in darkness and attack free interval with luminous stimulation.

Seven women and one man were studied. During migraine attack, luminous stimulation induced activation of the primary visual cortex. During headache relief, the same luminous stimulation induced activation of the visual cortex, although the subjects did not report pain or photophobia. During the attack free period, the same stimulation did not activate the primary visual cortex.

Conclusion: This study found that, among patients with migraine headaches, photophobia is linked to cortical hyperexcitability, which is absent during attack free periods.

Denuelle, M., et al. A PET Study of Photophobia during Spontaneous Migraine Attacks. *Neur*. 2011, January 18; 76(3): 213-218.

BALLOON KYPHOPLASTY VERSUS CONSERVATIVE TREATMENT FOR VERTEBRAL BODY COMPRESSION FRACTURE

Balloon kyphoplasty (BKP) is a well-known technique, used since 1998. As this procedure is relatively costly, an economic analysis of this treatment seemed warranted. This study compared the hospital costs of BKP with those of conservative care.

This retrospective analysis included patients with a primary osteoporotic fracture, all treated at the Orthopaedic Hospital Speising in Vienna with either BKP or conservative care. Each subject had been diagnosed with a collapse of the vertebral body of at least 30%, thoracic kyphosis of at least 15° or lumbar kyphosis of at least 10°. The number of readmissions, length of hospital stay and related costs were calculated separately for the conservative and the surgical groups.

Between 2002 and 2005, 135 patients were treated with BKP and 110 with nonsurgical methods. Within this sample, 194 spine relevant readmissions were noted for the nonsurgical group, and 109 for the surgical group ($p < 0.039$). No significant difference in mortality rate was seen between the two groups. In addition, the length of stay per

observation year was lower in the BKP group ($p < 0.046$).

Conclusion: This retrospective study of patients with osteoporotic vertebral compression fractures, found that those treated with kyphoplasty had a lower rate of hospital readmission, as well as a shorter length of hospital stay, following initial discharge, than did those treated conservatively.

Becker, S., et al. Comparison of Inpatient Costs after Balloon Kyphoplasty and Nonsurgical Treatment of Vertebral Body Compression Fractures. *Eur Spine J*. 2011. DOI: 10.1007/s00586-011-1692-y.

COGNITIVE REHABILITATION AND GROWTH HORMONE REPLACEMENT AFTER TRAUMATIC BRAIN INJURY

Previous studies have demonstrated that cognitive rehabilitation procedures can induce neuroplastic changes in brain structures responsible for the control of different cognitive functions. A number of hormones play an important role in recovery from brain injury, acting either on neurogenesis or neural plasticity. Among these, the growth hormone-insulin-like growth factor-1 (GH-IGF-1) seems to play an important role. This study assessed the effects of growth hormone replacement and cognitive rehabilitation on recovery in patients with adult growth hormone deficiency (GHD) secondary to traumatic brain injury (TBI).

Eleven male patients with TBI and GHD formed the study group, while eight adult males with TBI and without GHD formed a control group. The GHRH-arginine test was performed on patients to determine whether patients with TBI suffered from an acquired GHD. All patients were administered the Weschler Adult Intelligence Scale (WAIS). The subjects were treated with recombinant human growth hormone at 1 mg per day or a placebo. Daily cognitive rehabilitation therapy was provided to both groups for three months. The primary outcome measures were results of the GHRH-arginine test and the WAIS, performed at baseline and at three months.

The neuropsychological test results demonstrated that the control group realized improvements in digits and in the manipulative intelligence quotient as compared with baseline. The combined treatment group realized significant improvements in more cognitive parameters than did the control group, including in understanding digits, numbers and incomplete figures ($p < 0.05$) and similarities, vocabulary, verbal IQ, manipulative IQ, and total IQ ($p < 0.001$).

Conclusion: This study of patients with a traumatic brain injury demonstrated that administration of growth hormone can significantly improve the effect of cognitive rehabilitation among those patients with a growth hormone deficiency.

Reimude, P., et al. Effects Of Growth Hormone (GH) Replacement and Cognitive Rehabilitation in Patients with Cognitive Disorders after Traumatic Brain Injury. *Brain Inj.* 2011, January; 25(1): 65-73.

COMBAT STRESS AND POSTCONCUSSIVE SYMPTOMS

A high incidence of mild traumatic brain injury (mTBI) has been reported in service members returning from the conflicts in Iraq and Afghanistan. While most recover within three months, some experience post-concussive syndrome, wherein cognitive, affective, somatic and sensory symptoms persist for longer than six months. This study examined the relationship between combat stress symptoms and post-concussive symptoms in a large sample of post-deployment service members diagnosed with mTBI.

Active duty service members who had experienced combat deployment to Iraq or Afghanistan were screened for TBI. Four hundred seventy-two service members identified as possibly sustaining a TBI through a three-item screening questionnaire were recruited for participation. Following informed consent, the service members completed a structured clinical interview and self-report questionnaires concerning post-traumatic stress and post-concussive symptoms [The Neurobehavioral Symptom Inventory (NSI)]. The subjects were split into two groups based upon scores on a post-traumatic stress assessment, i.e., a

high combat stress group or a low combat stress group.

NSI scores were significantly higher for the high combat stress group than for the low combat stress group, with scores ranging from three to eight times higher in the high stress group ($p < 0.001$). These scores included cognitive, affective and physical symptoms. The low combat stress group complained of fewer symptoms which included primarily sleep difficulties, headaches and memory problems.

Conclusion: This study found that service members who sustained concussive injuries and were experiencing high levels of comorbid combat stress reported a three to eight-fold increase in post-concussive symptoms over concussed service members without a comorbid stress disorder.

Cooper, D., et al. Association Between Combat Stress and Postconcussive Symptom Reporting in OEF/OIF Service Members with Mild Traumatic Brain Injuries. *Brain Inj.* January, 2011; 25(1): 1-7.

COST-EFFECTIVENESS OF DABIGATRAN VERSUS WARFARIN

High-dose dabigatran, an oral thrombin inhibitor, has recently been approved in the United States for the prevention of stroke and systemic embolism in patients with atrial fibrillation. This study compared the quality adjusted survival period, cost and cost-effectiveness of dabigatran with warfarin for stroke prevention.

This study used a hypothetical cohort of patients, 65 years of age or older, with atrial fibrillation, all of whom were at increased risk for stroke and had no contraindications to anticoagulation. Using the Markov model, a decision analysis was performed, comparing three methods of treatment; adjusted dose warfarin with a targeted international normalized ratio of two to three, twice daily dabigatran at 110 mg or twice-daily dabigatran at 150 mg. The authors quantified quality adjusted life years expectancy (QALYs), risk for adverse events and net cost over 35 years or until death.

The quality-adjusted life expectancies were 10.28 with warfarin, 10.7 with low dose dabigatran and 10.84 with high-dose

dabigatran. Total costs were \$143,193 for warfarin, \$165,576 for low-dose dabigatran and \$168,398 for high-dose dabigatran. Low-dose dabigatran averted 1,300 intracranial hemorrhages, but resulted in 400 additional ischemic strokes and 400 additional myocardial infarctions. High-dose dabigatran averted an average of 1,000 ICHs and 600 ischemic strokes, but resulted in an additional 400 MIs. High-dose dabigatran was the most effective therapy, with 0.56 QALYs over warfarin according to the base-case analysis.

Conclusion: This study suggests that dabigatran can be a cost-effective alternative to warfarin for patients 65 years of age or older with atrial fibrillation.

Friedman, J., et al. Cost-Effectiveness of Dabigatran Compared with Warfarin for Stroke Prevention in Atrial Fibrillation. *Ann Intern Med.* 2011, January 4; 154(1): 1-11.

NATALIZUMAB CESSATION AND RECONSTITUTION INFLAMMATORY SYNDROME

Natalizumab, a monoclonal antibody against α_4 integrin has been found to significantly reduce the rate of clinical relapse and the progression of disability in patients with relapsing forms of multiple sclerosis (MS). As evidence suggests that the risk of developing progressive multifocal leukoencephalopathy (PML) is higher with prolonged periods of immunosuppression, the authors instituted a planned drug suspension holiday for patients who had received natalizumab. This study reports on the clinical outcomes of those with relapsing remitting and secondary progressive MS after the discontinuation of long-term natalizumab therapy.

All subjects were diagnosed with MS and had received at least 12, consecutive months of natalizumab. All agreed to a temporary cessation of therapy, intended to restore immune surveillance and decrease the risk of progressive, multifocal leukoencephalopathy (PML). A primary outcome measure was the recurrence of MS disease activity, defined as clinically documented activity with objective findings and/or the development of one or more

lesions on magnetic resonance imaging.

The mean duration of therapy interruption was 119 days. Clinically defined relapses occurred in 38% of the relapsing remitting group and in 25% of the secondary progressive group. Overall, relapses occurred more often in younger patients who had had fewer natalizumab treatments before interruption. The mean number of gadolinium-enhancing lesions after drug holiday was significantly greater than the mean number of gadolinium-enhancing lesions prior to starting natalizumab therapy in patients experiencing a relapse ($p < .001$). These findings suggest a new reconstitution inflammatory syndrome.

Conclusion: This study of patients with multiple sclerosis who had a good response to natalizumab found that, upon magnetic resonance imaging, clinical disease activity was seen to have returned, often aggressively, following the discontinuation of natalizumab therapy.

Miravalle, A., et al. Immune Reconstitution Inflammatory Syndrome in Patients with Multiple Sclerosis following Cessation of Natalizumab Therapy. *Arch Neurol*. 2011; 68(2): 186-191.

LOCATION OF LOW BACK PAIN AS A PREDICTOR OF ITS SOURCE

Evaluation of the structural sources of low back pain (LBP) can be a challenge for the clinician. Sources are thought to include internal disc disruption, facet joint pain and sacroiliac joint pain. The authors of this study evaluated the predictive utility of the distribution of LBP for the detection of the structural source of pain.

This retrospective review included consecutive patients with LBP presenting at a university spine center. All participants underwent a physical examination, as well as diagnostic procedures, including provocation discography, facet joint blocks and sacroiliac joint blocks. The exact location of each patient's LBP was then documented and compared to findings of the physical examination.

Among the patients with internal disc disruption, significantly more

reported midline pain, and significantly fewer reported paraspinal pain, as compared with those diagnosed with facet joint pain and sacroiliac joint pain ($p < 0.0001$ and $p = 0.0003$, respectively). The specificities of midline LBP for internal disc disruption, facet joint pain and sacroiliac joint pain were 74.8%, 28% and 36%, respectively.

The negative predictive values of paraspinal pain for internal disc disruption, facet joint pain and sacroiliac joint pain were 29%, 91.7% and 95.8%, respectively. The diagnostic accuracies of midline LBP for internal disc disruption, facet joint pain and sacroiliac joint pain were 83.5%, 24.1% and 31.8%, respectively.

Conclusion: This retrospective study found that the presence of midline low back pain increases the probability of lumbar internal disc disruption and reduces the probability of symptomatic facet joint pain and sacroiliac joint pain. The presence of isolated, paramidline LBP increases the probability of symptomatic facet joint pain and sacroiliac joint pain, but mildly reduces the likelihood of lumbar internal disc disruption

DePalma, M., et al. Does The Location of Low Back Pain Predict its Source? *PMR*. 2011, January; 3(1): 33-39.

NEUROLOGIC EXAMINATION RESULTS AS A PREDICTOR OF GLOBAL OUTCOME AFTER TRAUMATIC BRAIN INJURY

Traumatic brain injury (TBI) is a leading cause of disability worldwide. Previous research has demonstrated that severity of injury measurements, based upon clinical assessments of consciousness, are robust predictors of global outcome. This study assessed the influence of neurologic examination variables on one-year Glasgow Outcome Scale scores, as compared to the duration of post-traumatic amnesia.

This multi-center study included 210, active duty, veteran or military dependent patients in the Defense and Veterans Brain Injury Center (DVBIC), each diagnosed with moderate to severe, non-penetrating TBI. All subjects were admitted to the DVBIC for acute rehabilitation services within six months of injury. A structured neurological examination

was performed during inpatient rehabilitation, including manual motor testing, the Romberg test and the Kurtzke Expanded Disability Status Scale (EDSS). The participants were evaluated 12 months later, in order to obtain Glasgow Outcome Scale scores (GOSs).

The relationships among all predictor variables and the GOSs were significant, with the strongest found for the EDSS. In predicting the one year GOS, the duration of post-traumatic amnesia (PTA) accounted for 23% of the variance. The results of the addition of neurologic examination screening variables was significant, and accounted for an additional 19% of the variance (42% total), and yielded an overall accuracy of 76.7%.

Conclusion: This study of patients with non-penetrating traumatic brain injury found that the prediction of functional outcome can be enhanced by using a combination of post-traumatic amnesia, upper extremity motor weakness and balance problems.

Walker, W., et al. Does Neurologic Examination during Inpatient Rehabilitation Help Predict Global Outcome after Nonpenetrating Traumatic Brain Injury? *PMR*. 2011, January; 3: 6-12.

STROKE IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING

Stroke occurs in approximately 1.3% of patients undergoing coronary artery bypass grafting (CABG). While many studies have identified patient-related factors associated with post-CABG stroke, information concerning the timing and influence of different surgical techniques remains limited. This study sought to clarify these issues.

This single center, prospective study evaluated 45,432 consecutive patients with CABG. Perioperative stroke was defined as neurologic deficits not resolved after 24 hours. Four different CABG operative strategies were identified, including cardiopulmonary bypass (on pump), with arrested heart; on pump with beating heart; on pump with hypothermic circulatory arrest and off pump. Complications and survival rates of each group were assessed for comparison.

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Of the 45,432 patients studied, 1.6% experienced a stroke, with the peak incidence occurring in 1988, and with continued decline thereafter. Of all strokes, 40% occurred during surgery and 60% after. The stroke risk peaked at 40 hours post-surgery, and returned to baseline six days post-surgery. Among the techniques studied, the highest risk of stroke occurred in the group on pump with hypothermic circulatory arrest. The lowest risk was found in the off pump group. Patients sustaining a perioperative stroke had unadjusted survival rates of 70%, 37% and 12% at one, 10, and 20 years, respectively, as compared with 95.3%, 68% and 35% among those not experiencing a perioperative stroke ($p < .001$).

Conclusion: This study of patients undergoing coronary artery bypass grafting found that the risk of stroke was 1.6%, with this risk peaking 40 hours after surgery, and resulting in a significant reduction in long-term survival.

Tarakji, K., et al. Temporal Onset, Risk Factors and Outcomes Associated with Stroke after Coronary Artery Bypass Grafting. *JAMA*. 2011, Jan 26; 305(4): 381-390.

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