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## TRANSCRANIAL MAGNETIC STIMULATION FOR VISUAL NEGLECT

Unilateral visual spatial neglect (VSN) is common following a stroke or trauma to the brain. This seems related to a disruption of the posterior parietal cortex. Some studies have suggested that the dysfunction underlying VSN may be related to a relative hyperactivity of the unaffected hemisphere. Previous studies have demonstrated that the application of low frequency repetitive transcranial magnetic stimulation over the unaffected side might provide a transient reduction in the magnitude of the neglect. This study sought to determine whether this technique could be used to induce long-lasting improvement.

Fourteen patients with a history of right brain stroke and with a presentation of visual spatial neglect were included in the study. The subjects were divided into a treatment and a control group. The treatment group received 15 minutes of repetitive low frequency stimulation twice per day for two weeks. The coil was placed over the primary motor area of the left cerebral hemisphere. The stimulus intensity was gradually increase until five out of 10 consecutive stimuli elicited a motor evoked potential of approximately 50 microvolts. All participants performed line bisection and cancellation tests every two weeks to evaluate the effect of the treatment.

There was no difference between performance at two weeks before the treatment and at the beginning of treatment, demonstrating no progression prior to intervention. The treatment group demonstrated a significant improvement at the end of treatment ( $p=0.003$ ) with no significant change between that endpoint and two weeks posttreatment ( $p=0.261$ ). At the end of treatment, the treatment group scored significantly better than the

control group in cancellation ( $p=0.007$ ), but not in line bisection ( $p=0.065$ ).

**Conclusion:** This pilot study demonstrates that among stroke patients with visual neglect, low-frequency transcranial magnetic stimulation of the unimpaired hemisphere can significantly improve the symptoms within two weeks.

Song, W et al Low-Frequency Transcranial Magnetic Stimulation for Visual Spatial Neglect: a Pilot Study. *J Rehabil Med*; 2009, February: 41:162-165.

## FRACTURE HEALING FOLLOWING TBI

Patients who have sustained a severe traumatic brain injury (TBI) commonly demonstrate alterations in the normal process of bone healing. This study investigated the relationship between TBI and fracture healing.

Seventeen patients diagnosed with severe TBI and with long bone fractures were compared to 24 patients without TBI who had sustained similar fractures. Serum measures of C-reactive protein, alkaline phosphatase, adjusted calcium, and inorganic phosphate were collected from all patients four times during the first week after injury. The subjects' serum was added to well plates seeded with osteoprogenitor cells. Clinical and radiographic follow-up was conducted for all long bone fractures.

Patients with TBI had greater rates of proliferation of the osteoprogenitor cells at all points measured than did controls. Those with TBI also had twofold shorter times to union ( $p=0.01$ ) and increased callus ratios ( $p<0.01$ ). A negative relationship was found between Glasgow Coma Scale scores and callus ratios.

**Conclusion:** This study revealed that the presence and severity of traumatic brain injury is related to decreased fracture healing time, increased callus formation, and increased proliferation of osteoprogenitor cells.

Cadosch, D., et al. Humoral Factors Enhance Fracture Healing and Callus Formation in Patients with Traumatic Brain Injury. *JBJS*. 2009, February: 91(2):282-288.

## VISCOSUPPLEMENTATION FOR SYMPTOMATIC TIBIO-FEMORAL OA

Osteoarthritis (OA) is a common disease affecting synovial joints. OA is anatomically characterized by cartilage breakdown, osteophyte formation at the margins of the joint, and low-grade synovial inflammation. This study investigated the efficacy and safety of new dosing regimens of Hylan G-F 20 in patients with knee OA.

This prospective, multicenter, randomized, open trial included patients forty years of age or older presenting with OA pain involving one knee. All had x-rays confirming tibiofemoral OA. The subjects were assigned to one of five groups. Group one received one injection of six ML; group two received one injection of four ML; group three received two injections of four ML, administered two weeks apart; group four received three injections of four ML, administered one week apart; and group five received three injections of two ML, administered one week apart.

The primary endpoint was the leg pain score 24 weeks after the first injection. Secondary endpoints included knee pain at all time points, and improvement in pain, stiffness, and functional impairment, as measured by the Western Ontario and McMaster University OA Index.

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Treatment resulted in significant improvement from baseline to week 24 on all endpoints for all treatment regimens. The largest changes were observed in group five, with a mean change of -36.7 mm on the knee OA visual analogue scale from baseline to week 24. Groups one and four consistently showed similar mean improvements (-34.9mm and -32.6mm, respectively). Smaller changes were seen in groups two and three. Subjects in group four reported the highest percentage of adverse events, while those in group one reported the lowest percentage.

**Conclusion:** This study of patients with knee osteoarthritis found that a single, six ml injection of Hylan G. F 20 may be as efficacious and well-tolerated as three injections of two ml administered one week apart.

Conrozier, T., et al. Prospective, Multicenter, Randomized Evaluation of the Safety and Efficacy of Five Dosing Regimens of Viscosupplementation with Hylan G. F 20 in Patients with Symptomatic Tibio-Femoral Osteoarthritis: A Pilot Study. *Arch Ortho Traum Surg.* 2009, March; 129: 417-423.

### **U/S GUIDED INJECTION FOR LATERAL EPICONDYLITIS**

Lateral epicondylitis (LE) is a common tendinopathy resulting in pain within the common extensor origin site at the lateral epicondyle of the humerus. The differential diagnosis for pain in this region of the arm is broad. This study examined the advantage of using sonograms to guide injections when treating LE.

Eligible subjects included 52 patients with unilateral LE of at least three weeks' duration. Each was assessed with ultrasound for tendinopathy. The patients whose clinical diagnosis was confirmed with US received a sonographic-guided injection of methylprednisolone 20 mg and 0.5 ml one percent lidocaine. Those without visible tendinopathy by ultrasound were given injections of methylprednisolone combined with lidocaine, one percent, at the point of maximum tenderness over the lateral epicondyle. Outcome measures included a visual analogue scale for pain, physical functioning, and bodily pain scales of the Medical Outcomes Study 36-Item Short Form Health Survey.

At three months follow-up pain, tenderness, and function were significantly more improved in the ultrasound guided group than in the group that was not assessed or treated with the assistance of ultrasound ( $p < 0.000$ ).

**Conclusion:** This study demonstrates that ultrasound, used both for diagnosis and injection guidance, can improve outcome in patients with lateral epicondylitis.

Unlu, Z., et al. Sonographic Guided Injection of Corticosteroid in the Treatment of Lateral Epicondylitis. *J Musculoskel Pain.* 2009; 17(1): 48-58.

### **SYRINGE USE: DOES SIZE MATTER?**

Arthrocentesis is an important procedure in outpatient musculoskeletal medicine. For that procedure, the size of the syringe is left to the discretion of the physician, with that choice based upon the size of the joint and the estimated volume of the injectate. This study sought to better understand the effect of syringe size on the physician's ability to control the syringe and the needle.

This two-part study first assessed an operator's ability to control different sizes and kinds of syringe devices, with the second portion of the study designed to determine the effect of syringe size on clinical outcome. Operators were tested for their ability to control one, three, five, ten, and twenty ml syringes using a quantitative, needle-based placement method. All participants performed 100 procedures with one hand, 100 with two hands, and 100 with a reciprocating procedure device. A nonoperating observer queried the patients and the physician concerning satisfaction with the syringe used and pain during the procedure.

Unintended forward penetration or retraction worsened with increasing syringe size ( $p < 0.002$ ). In addition, two-handed operation resulted in greater control than did one-handed operation ( $p < 0.001$ ). When one-handed operation was required, the reciprocating procedure device reduced unintended penetration ( $p < 0.001$ ) and patient discomfort by over fifty percent ( $p < 0.001$ ).

**Conclusion:** This study of arthrocentesis procedures revealed

that better syringe control is achieved with smaller syringe sizes.

Michael, A., et al. Syringe Size: Does It Matter in Physician Performed Procedures? *J Clin Rheum.* 2009, March; 15(2): 56-60.

### ADVERSE OUTCOMES WITH CLOPIDOGREL AND PROTON PUMP INHIBITORS

Proton pump inhibitors (PPIs) are often prescribed prophylactically in order to reduce gastrointestinal bleeding among patients taking dual antiplatelet therapy. Recently, some mechanistic studies have found that PPIs can reduce the inhibitory effect of clopidogrel on platelet aggregation. Therefore, this study investigated the effect of combining these medications after hospitalization for acute coronary syndrome (ACS).

Data were compiled from a national database for the Veterans Health Administration from October 2003 through January 2006. Participants included any individuals discharged from a Veterans Administration hospital with acute myocardial infarction or unstable angina who were prescribed clopidogrel upon discharge. Of the 8,205 patients who filled a prescription for clopidogrel, 63% were also prescribed a PPI. Those groups were compared for the endpoints of all-cause mortality or re-hospitalization for acute coronary syndrome. Secondary outcomes included revascularization procedures and percutaneous cardiac intervention.

Death or rehospitalization due to ACS occurred in 29.8% of patients taking both medications, but in 20.8% of those taking clopidogrel alone. Multivariable analysis revealed that the use of clopidogrel plus PPI at any point in time was associated with a greater increase in risk of death or rehospitalization for ACS than was the use of clopidogrel without PPI (adjusted OR=1.25).

**Conclusion:** This study suggests that concurrent use of clopidogrel and a proton pump inhibitor after hospitalization for acute coronary syndrome is associated with a higher risk of adverse outcomes than is clopidogrel use alone.

Ho, P., et al. Risk of Adverse Outcomes Associated with

Concomitant Use of Clopidogrel and Proton Pump Inhibitors Following Acute Coronary Syndrome. *JAMA.* 2009, March 4; 301(9): 937-944.

### PHYSICAL FRAILTY AND ANTI-THROMBOTIC THERAPY

Atrial fibrillation (AF) is the most common arrhythmia seen in clinical practice. This condition predisposes the individual to cardioembolic stroke. Warfarin therapy significantly reduces the risk of such stroke in patients of all ages with AF. A major adverse effect of warfarin is hemorrhage, with that risk heightened in older adults. Current risk schemes have a limited ability to predict thromboembolism in patients with AF. Identification of those who are most vulnerable to hemorrhage and/or cardioembolic stroke may assist clinicians in their decision to prescribe warfarin. This study investigated the relationship between frailty and antithrombotic utilization among older patients with AF.

This prospective, observational study included all patients seventy years of age or older with AF admitted to a teaching hospital in Sydney, Australia. Baseline data were collected from inpatient interviews and medical records, and included demographics, clinical characteristics, antithrombotic therapy, and clinical outcome. At three and six months after enrollment, the participants or their caregivers were contacted by telephone and asked to report on hemorrhages, strokes, or death.

A total of 140 patients were characterized as frail. The frail patients were significantly less likely to utilize warfarin (compared with other antithrombotics or no antithrombotic therapy) than were the non-frail patients, both on admission ( $p=0.002$ ) and at discharge ( $p<0.001$ ). The incidence of major or severe hemorrhage over six months was 20.8%; including 23.0% in the frail group and 16.9% in the non-frail group ( $p=0.29$ ). Subgroup analysis by antithrombotic utilization found that the incidence of major/severe hemorrhage over six months was 30.0% in the frail and 18.9% in the non-frail participants prescribed warfarin, 25.0% for the frail and 13.6% for the non-frail participants receiving aspirin/other antithrombotic therapy, and 8.3% for frail and 0% for

non-frail participants receiving no antithrombotic therapy. Cardioembolic strokes occurred in 9.7% of participants overall, in 12.3% of the frail group and 3.9% of the non-frail group ( $p<0.05$ ).

**Conclusion:** This study of elderly patients with atrial fibrillation demonstrates that the frail are less likely to receive Coumadin, have more than twice the risk of cardioembolic stroke, and have a greater mortality rate in the six months after hospital discharge.

Perera, V., et al. The Impact of Frailty on the Utilization of Antithrombotic Therapy in Older Patients with Atrial Fibrillation. *Age Aging.* 2009, March; 38: 156-162.

### BRACES FOR ANKLE SPRAINS

Acute ankle sprain accounts for three to five percent of all emergency department visits in the UK. It is thought that early management, including ice, elevation, and controlled mobilization of the joint, promotes a speedy recovery and prevents chronic symptoms. However, systematic reviews have highlighted a lack of quality evidence to aid clinical decision making, including whether to mobilize or immobilize the joint, and, if immobilization is chosen, which types of supports are best. This study compared the relative effectiveness of various types of ankle supports with that of a tubular compression bandage for the promotion of recovery of function following a severe ankle sprain.

A total of 594 adults with a severe ankle sprain were randomized to one of three groups. The participants were placed in a tubular compression bandage for two to three days, and then randomized to be placed in a Bledsoe boot, an air cast, or a below the knee cast. Each supportive device remained in place for ten days. Outcomes included the Foot and Ankle Score, measured at one, three, and nine months.

Greater clinically important benefits were found at three months in quality of ankle function with the below-knee cast than with the tubular compression bandage [mean difference in quality of ankle function ( $p<0.007$ ), as well as in pain symptoms, and activities]. The Bledsoe boot offered no significant

advantage over the tubular compression bandage. Comparing all immobilization devices to the compression bandage, no significant difference was found at nine months.

**Conclusion:** This study found that immobilization with a below the knee cast for ten days may be the best option for enhancing rapid functional recovery after a severe ankle sprain.

Lamb, S., et al. Mechanical Supports for Acute, Severe Ankle Sprain: A Pragmatic, Multicentre, Randomized, Controlled Trial (CAST). *Lancet*. 2009, February 14; 373: 575-581.

### ATORVASTATIN FOR GERIATRIC STROKE PATIENTS

Most instances of strokes and coronary heart disease are seen in patients over the age of 65 years. Previous studies have established that geriatric patients with vascular disease or risk thereof can benefit from statin treatment. This study compared the benefits of atorvastatin use in geriatric patients with that in younger patients with recent stroke or transient ischemic attack (TIA).

This randomized, double-blind, prospective, cohort study included adult patients with stroke or TIA from 205 centers. Eligible patients received either a placebo or atorvastatin at 80 mg per day. The participants were then followed at one, three, and six months, and every six months thereafter. In the analysis, patients from the entire cohort were divided into elderly (age 65 years and over) and younger groups (age <65 years). The primary outcome variable was the occurrence of fatal or nonfatal stroke. Secondary outcomes included TIA, coronary events, and revascularization procedures. Of the 4,731 subjects, 2,249 were geriatric patients.

Baseline, low-density lipoprotein and total cholesterol levels were similar between the two groups. Among those receiving atorvastatin the relative risk of stroke was decreased by 10% in the geriatric patients and by 26% in the younger patients. The relative risk of secondary endpoints was also reduced in both groups.

**Conclusion:** This study found that, after a cerebrovascular accident, the introduction of atorvastatin can

reduce the rate of recurrent events in both elderly and younger individuals.

Chaturvedi, S., et al. Effect of Atorvastatin in Elderly Patients with a Recent Stroke or Transient Ischemic Attack. *Neurology*. 2009, February 24; 72 (8): 688-694.

### FUNCTIONAL STATUS IN PERSONS ADMITTED TO NURSING HOMES

It has been predicted that 44% of 65-year-old persons will be admitted to a nursing home during their lives. More than half of those will remain for more than one year. This study sought to characterize the functional trajectories of older persons admitted to a nursing home with disability after an acute hospitalization.

This prospective cohort study involved 754 community living persons over the age of seventy years who were initially nondisabled. Monthly phone interviews were conducted for nine years in order to gather information concerning nursing home admissions, hospitalizations, and disability, as it related to four types of activities of daily living: bathing, dressing, walking inside the home, and transferring from a chair. Data were ultimately obtained from 296 participants admitted to the nursing home with disability. Follow-up data were used to characterize the subjects' functional trajectories.

For this sample, the median time to nursing home admission was 46 months. Upon admission to the nursing home, the most common disabilities involved bathing (95%), followed by dressing (75.3%), walking (68.6%), and transferring (60.5%). The mean duration of each admission was 12.4 months. Over 53% of the nursing home admissions involved a duration of two months or longer. When the duration of admission was one month, most were discharged to home with disability (54.7%). When the duration was two months or more, the most common outcomes were continuous disability in the nursing home (42.1%) or discharge home with disability (39%). Overall, nearly half of the index nursing home admissions were discharged to home with disability. More than 25% had continuous disability in the nursing home. Only one in five was discharged home without a disability.

**Conclusion:** This study outlines the functional trajectories of older persons admitted to a nursing home with disability after an acute hospitalization. Fewer than twenty percent returned home without disability, as measured by four essential activities of daily living.

Gill, T., et al. Functional Trajectories in Older Persons Admitted to a Nursing Home with Disability after an Acute Hospitalization. *J Am Ger Soc*. 2009, February; 57(2): 195-201.

### DEFICIT AWARENESS IN SEVERE TBI

Impaired awareness of deficits is common after traumatic brain injury (TBI). This phenomenon is associated with poor compliance with rehabilitation, longer length of stay, higher caregiver distress, and poorer functional outcome. This study examined changes in awareness of deficits in the first year post-injury.

Data for the study were obtained from the National Institute on Disability and Rehabilitation Research (NIDDR) funded TBI model systems. All subjects had been admitted to a level I trauma center within 24 hours of injury, and all had received follow-up care at an acute rehabilitation hospital. Each subject was assessed with awareness questionnaires (AQs), patient competency rating scales (PCRSs), time to follow commands, and disability rating scales. Baseline AQs and PCRSs were collected after posttraumatic amnesia had resolved, with those measures repeated at one year post-injury.

Of the 176 participants originally recruited for the study, 123 had usable data. Awareness of deficits was operationalized as the discrepancy between patients' and family members' ratings on the AQs and PCRSs. At follow-up, all correlations were significant, ranging from moderate (.33) to large (.53). In each instance the patients rated themselves as higher in functioning than did their relatives. Awareness was more improved at one year when smaller discrepancy scores and stronger correlations were noted between participants' and family members' ratings. The change in awareness was most pronounced for the behavioral and affective domains,

and least pronounced for the motor and sensory domains.

**Conclusion:** This prospective study of patients with traumatic brain injury found that, at one year post-injury, the patients rated themselves as significantly higher in functioning than did their significant others. The greatest improvements in self-awareness involved behavioral and affective issues.

Hart, T., et al. A Longitudinal Study of Awareness of Deficit after Moderate to Severe Traumatic Brain Injury. **Neuropsych Rehab.** 2009;April 19(2): 161-176.

### **PREDICTORS OF LONG-TERM POST CONCUSSIVE SYNDROME**

Although most individuals with Mild Traumatic Brain Injury (mTBI) recover within three to six months, some developed persistent neuropsychiatric symptoms, frequently referred to as post concussive syndrome (PCS). Common symptoms include persistent behavioral, cognitive, emotional, and physical problems. This study sought to determine which initial symptoms of mTBI are useful in predicting the development of PCS.

One hundred ten patients, each admitted to a level I trauma center with a diagnosis of mTBI, were evaluated. The subjects completed a baseline assessment during the initial trauma center admission, which included biochemical markers, balance measures, clinical findings, and neurometric tests. Follow-up testing was completed at three to five days, seven to ten days, three months, six months, and twelve months post-injury. Symptom frequency and intensity were graded on a scale of one to ten.

The data revealed that early anxiety ( $p=0.001$ ), depression ( $p=0.04$ ), memory dysfunction ( $p=0.02$ ), difficulty thinking ( $p=0.007$ ), irritability ( $p=0.03$ ), and light and noise sensitivity ( $p=0.03$  and  $p=0.008$ , respectively) were significant predictors of persistent PCS. The greatest predictors were early anxiety and noise sensitivity. Additional, independent risk factors for persistent PCS included female gender and baseline depression.

**Conclusion:** This study found that early anxiety and noise sensitivity are the two greatest risk factors for

developing post concussive syndrome after mild traumatic brain injury.

Dischinger, P., et al. Early Predictors of Post-Concussive Syndrome in a Population of Trauma Patients with Mild TBI. **J Traum Inj Inf, Crit Care.** 2009, February; 66(2): 289-297.

### **NEUROTROPHIC FACTORS AND NEURON SPECIFIC ENOLASE LEVELS AND BRAIN INJURY OUTCOME**

Secondary brain damage due to neuroinflammatory mechanisms is a known complication of traumatic brain injury (TBI). Neuron specific enolase (NSE) and many neurotrophic factors, including doublecortin (DCX), nerve growth factor (NGF), brain derived neurotrophic factor (BDNF), and glial derived neurotrophic factor (GDNF), are released following brain injury. Neurotrophic factors, which stimulate growth and differentiation, play a protective role, while NSE is associated with neuronal damage. The relationships of those neurotrophic factors and NSE to the severity of TBI remain unclear. This study compared levels of NGF, BDNF, GDNF, DCX, and NSE in the CSF of children with TBI with the clinical severity of the brain injury.

Thirty-two children with severe brain injury, defined as a Glasgow Coma Scale score of eight or below, were compared with 32 matched controls. The children ranged in age from 1.3 to 15.6 years. Cerebral spinal fluid samples were collected at two and 48 hours after TBI admission. Neurologic outcome was measured using the Glasgow Outcome Scale at six months post-TBI.

At two hours after admission, NGF, NSE, and DCX had increased significantly more in the subjects with TBI than among the control subjects ( $p=0.01$ ). BDNF was also significantly increased. No significant difference was found in levels of GDNF between patients and controls. Patients with better neurologic outcomes had lower NSE levels ( $p<0.01$ ), but also had significantly stronger NGF and DCX upregulation ( $p<0.01$ ).

**Conclusion:** This study of children with severe traumatic brain injury suggests that the nerve growth factor, doublecortin, and neuron

specific enolase concentrations in the CSF may be useful markers of brain damage following a TBI.

Chiaretti, A., et al. NGF, NSE, and DCX Upregulation Correlates with Severity and Outcome of the Head Trauma in Children. **Neurology.** 2009, February 17; 72: 609-616.

### **VISUAL IMPAIRMENT FOLLOWING STROKE**

Although many patients suffer visual disability as a result of stroke, data are lacking concerning the prevalence of that disability, its extent, and the trajectory of recovery. This study explored the extent of visual impairment within the stroke population.

This prospective, multi-center trial included stroke survivors with a suspected visual impairment. Referrals were made from inpatient wards, rehabilitation units, community services, and outpatient clinics. Standardized screening and investigation forms were employed to document visual impairments, specifically assessing visual acuity, ocular pathology, extra-ocular muscle movement, visual perception, and visual field deficits. Stroke details were recorded for stroke type and area involved.

Three hundred twenty-three patients were recruited. The median duration from onset of stroke to initial eye examination was 22 days. Sixty-eight percent were found to have eye alignment or movement impairment, 49% visual field impairment, 27% low vision, and 21% perceptual difficulties. Overall 92% of the stroke survivors with a suspected visual difficulty had a visual impairment.

**Conclusion:** This study of patients referred for a suspected visual difficulty found that nearly seventy percent had eye movement deficits and fifty percent had visual field impairment.

Rowe, F., et al. Visual Impairment Following Stroke: Do Stroke Patients Require Visual Assessment? **Age Aging.** 2009; 38: 188-193.

### **VISUAL SPEECH PERCEPTION AND BROCA'S APHASIA**

Behavioral treatment of non-fluent aphasia has traditionally focused on

speech production. Impaired speech production is associated with damage to both Broca's area and the left anterior insula. Several neuroimaging studies have suggested that the same areas implicated in impaired speech production are also recruited during speech perception. This study examined the utility of targeting visual speech perception to improve the speech production in nonfluent aphasia.

Ten patients with stroke and subsequent nonfluent aphasia, all at least one year post-stroke, were studied. Each was provided a laptop and headphones that played a program presenting various colored pictures divided into two treatment phases: one with audio and visual stimuli (AV), depicting a mouth pronouncing the word along with auditory stimuli, and one with auditory stimuli alone (AO). Half the participants began with AV stimuli and then were switched to AO, while the other half did the reverse. All received one treatment per day, lasting thirty minutes, five days per week. Outcome measures included a 36-item naming task and the Philadelphia Naming Test.

More items were named correctly after treatment with AV than at baseline ( $p < 0.0001$ ). Importantly, participants were able to name more items after treatment with AV than with AO ( $p = 0.0006$ ). While treatment with AO improved naming of items compared with baseline, that finding failed to reach statistical significance.

**Conclusion:** This study found that adding visual speech perception tasks can significantly improve speech production in nonfluent aphasia.

Fridriksson, J., et al. Treating Visual Speech Perception to Improve Speech Production in Nonfluent Aphasia. *Stroke*. 2009, March 1; 40: 853-858.

### REDUCING ATHEROSCLEROSIS WITH VITAMIN B SUPPLEMENTATION

Total homocysteine plasma level (tHcy) is a strong, independent risk factor for cardiovascular disease. However, it is unclear whether tHcy is a cause or a marker of such disease. This study sought to determine whether tHcy reduction through high

dose supplementation of vitamin B could reduce the progression of atherosclerosis.

This double-blind, randomly controlled trial included 506 patients between the ages of forty and 89 years. All had an initial tHcy of  $> 8.5$  micromole/liter and no history of diabetes or cardiovascular disease. The test patients received high dose vitamin supplementation, including 5 mg of folic acid, 0.4 mg of vitamin B12, and 50 mg of vitamin B6. The supplementation continued for 3.1 years. Placebo patients received a similar appearing inert tablet.

Treatment adherence was assessed at each visit by pill compliance and every six months by measuring tHcy and B vitamin levels. Every six months, oral methionine loading and fasting blood samples were also obtained. Subclinical atherosclerosis progression was assessed using high-resolution B-mode ultrasonography, in order to measure the carotid artery intima media thickness. A multidetector spiral CT was used to measure aortic and coronary artery calcium.

The carotid artery intima media thickness progression was lower in the treatment than in the control subjects, although that difference did not reach statistical significance. Patients with a baseline tHcy of 9.1 micromole/liter or more had significantly lower rate of carotid artery intima media thickness progression than did controls.

**Conclusion:** High dose supplementation of vitamin B may reduce the progression of subclinical atherosclerosis in healthy individuals especially among those with a fasting total homocysteine plasma level of 9.1 micromole/liter or more.

Hodis, H., et al. High-Dose Vitamin D Supplementation and Progression of Subclinical Atherosclerosis: A Randomized, Controlled Trial. *Stroke*. 2009, March; 40(3): 730-736.

### LARGE ARTERY STENOSIS AND POST-STROKE DEPRESSION

Post-stroke depression is a common disabling outcome thought to be associated with cerebral perfusion. This study compared the rate of depression among those patients small, subcortical infarctions resulting from large artery disease

with those resulting from small vessel disease.

Subjects were patients at least 18 years of age with ischemic stroke. A total of 127 such participants were recruited, 44 of whom had large artery disease 83 with small vessel disease. At three months, depressive symptoms were assessed by a fifteen-item Geriatric Depression Scale. The Barthel index and an instrumental activities of daily living scale were used to assess functional deficits stemming from depression.

Diabetes mellitus and multiple acute infarctions were more prevalent among the large artery disease group ( $p = 0.002$  and  $p < 0.001$ , respectively). More depressive symptoms were observed in those with large artery disease than among those with small vessel disease ( $p = 0.014$ ). Of the 44 patients with large artery disease, 52.3% had post-stroke depression, as compared to 25% of those with small vessel disease.

**Conclusion:** This study found that post-stroke depression is more common among patients with small, subcortical infarcts resulting from large artery disease than among those with infarcts resulting from small vessel disease

Chen, Y., et al. Post-Stroke Depression in Patients with Small Subcortical Infarcts. *Clin Neur Neurosur*. 2009;April; 111(3): 256-260.

### LONG-TERM RISK OF SEIZURE DISORDER AFTER TBI AMONG CHILDREN

Traumatic brain injury (TBI) increases the risk of epilepsy. However, little is known concerning the duration of the increased risk or factors that modify that risk, especially among children and young adults. This study investigated these issues.

Data concerning TBI and epilepsy were collected from records of individuals born in Denmark from 1977 to 2002, using the Danish National Hospital Register. Cohort members, their parents and siblings were classified with epilepsy if they had been hospitalized or in outpatient care with a diagnosis of epilepsy. Cohort members were classified with mild brain injury, severe brain injury, or skull fracture respectively, if they had been admitted or been in

outpatient care with the relevant diagnosis. Time of onset of epilepsy and brain injury was defined as the first day of the first contact with the hospital for the relevant diagnosis. The subjects were followed until the development of epilepsy, death, or emigration from Denmark.

A total of 1,605,216 individuals were followed. During the study period, 78,572 individuals had a least one TBI. A total of 17,470 developed epilepsy, among whom 1,017 had a history of prior TBI. Relative to no brain injury, the risk of epilepsy was two times higher after mild brain injury, seven times higher after severe brain injury, and two times higher after skull fracture. The risk of epilepsy after mild and severe brain injury was highest during the first years after injury, but remained high for more than ten years, as compared to those without a brain injury. The risk of epilepsy was increased in all age groups, but was highest among those older than fifteen years of age at the time of injury. Women had a relatively higher risk of epilepsy with mild injury than did men, although that did not occur in the case of skull fracture or severe brain injury.

**Conclusion:** This study of children and adolescents found that, after brain injury, the risk of seizures is increased for ten years, with that risk greatest among those who are least fifteen years of age at the time of injury.

Christiansen, J., et al. Long-Term Risk of Epilepsy after Traumatic Brain Injury in Children and Young Adults: A Population-Based, Cohort Study. *Lancet*. 2009, 373 (9669):1105-1110

### OA OF THE KNEE AFTER THA

Total hip arthroplasty (THA) results in disturbed kinetics in adjacent joints and in the pelvis. It is thought that progression of knee osteoarthritis (OA) is associated with a progression of hip OA. This study investigated the course of knee OA among patients undergoing long-term follow-up after THA.

Between 1986 and 1995, 411 primary, total hip arthroplasties were performed. Among those, 279 were unilateral, with 48 of those having undergone preoperative radiographs of the lower extremities. Patients who had sustained knee injuries or who had undergone knee surgery

prior to THA were excluded from analysis. The subject pool included thirty patients who were followed for a minimum of ten years after THA. The Japanese Orthopedic Association Hip Score was used for the clinical evaluation at follow-up. For grading of knee OA, a modified Kellgren-Lawrence (KL) scale was used

At follow up, distribution of modified KL scales in the medial compartment revealed significantly more severe knee OA on the non-THA side than on the THA side ( $p=0.044$ ). The severity in the lateral compartment did not significantly differ ( $p=0.12$ ) between each side. Reviewing medial tibiofemoral OA, 11 patients (33%) showed progression on the non-THA side, while 3 (10%) showed progression on the THA side. This difference was significant ( $p=0.033$ ). At follow-up, pain was almost completely relieved by the surgery

**Conclusion:** This ten-year follow-up of patients undergoing total hip arthroplasty found that the contralateral knee demonstrates accelerated OA when compared to the ipsilateral knee.

Umeda, N., et al. Progression of Osteoarthritis of the Knee after Unilateral Total Hip Arthroplasty: Minimum Ten-Year Follow-Up Study. *Arch Orth Traum Surg*. 2009;February 129(2): 149-154.

### TOPICAL ANESTHESIA FOR BOWEL PROGRAMS AFTER SPINAL CORD INJURY

Spinal cord injury (SCI) above the fifth thoracic level is sometimes complicated by autonomic dysreflexia (AD). The most common causes of AD are bladder distention, bowel distention, and defecation. The most widely used bowel programs are manual evacuation programs, used regularly by 67% of patients with complete SCI. As this maneuver can induce a rise in blood pressure and autonomic dysreflexia, this study investigated whether topical anesthesia could reduce that effect.

Twenty-five patients with cervical SCI were randomly divided into two groups, one receiving a local anesthetic lubricant and the other a non-anesthetic lubricant. At fifteen minutes prior to each bowel program, the subjects emptied their bladders and then had their vital signs taken.

The lubricant was then administered. After five minutes, the bowel program was completed, with blood pressure and heart rate monitored every minute until completion of stool flow.

Systolic blood pressure values were significantly lower in the lidocaine treatment group during insertion of medication, digital stimulation, beginning of stool flow, manual stool removal, end of stool flow, and five minutes after completion. The maximum rise in systolic blood pressure in the lidocaine group was significantly lower than that with placebo (33 mmHg versus 50 mmHg, respectively;  $p<0.001$ ).

**Conclusion:** This study of patients with cervical spinal cord injury found that anorectal lidocaine, used prior to manual stool removal, minimizes the rise in blood pressure and decreases autonomic dysreflexia incidence and severity.

Furusawa, K., et al. Topical Anesthesia Blunts the Pressor Response Induced by Bowel Manipulation in Subjects with Cervical Spinal Cord Injury. *Spinal Cord*. 2009, February; 47(2): 144-148.

### MODAFINIL FOR ALS

Fatigue is a common problem among patients with amyotrophic lateral sclerosis (ALS). This study sought to determine whether modafinil could alleviate fatigue among patients with ALS.

This four-week, double-blind trial included 32 patients with probable or definite ALS. All had clinically meaningful fatigue. The subjects were randomized to receive either modafinil or placebo. Modafinil doses began at 100 mg per day, increased to 300 mg per day, based upon clinical improvements. The subjects were followed weekly by telephone or personal visit. Outcome measures were collected at baseline and at two-week intervals. The primary endpoint measure was the Clinical Global Impressions Improvement Scale (CGI). Secondary endpoints included the Fatigue Severity Scale, the Epworth Sleepiness Scale, the Beck Depression Inventory, the Role Function Scale, and the Visual Analogue Scale for energy depression and stamina.

In the intention to treat analysis, the response to modafinil was 86%,

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and the response to placebo fourteen percent. Modafinil produced significantly more improvement than did placebo on measures of fatigue and sleepiness, as well as on measures of energy and stamina. In an open label extension phase of the study, the response was maintained for the twelve weeks of follow-up.

**Conclusion:** This study of patients with amyotrophic lateral sclerosis who complain of fatigue found modafinil to be effective in reducing those fatigue complaints for the twelve weeks of the study.

Rabkin, J., et al. Modafinil Treatment of Fatigue in Patients with ALS: A Placebo-Controlled Study. **Musc Nerve**. 2009, March; 39: 297-303.

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