

# REHAB IN REVIEW

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## ENDOGENOUS ADENOSINE A<sub>3</sub> RECEPTOR ACTIVATION AND PAIN

The most successful approaches to the treatment of chronic pain rely on engagement of endogenous circuits involving opioid, adrenergic and calcium channel mechanisms. While adenosine has been found to provide potent and long-lasting pain suppression in both animal and humans studies, targeting this endogenous pathway for pain management has not yet been achieved. This animal study explored the analgesic effects of increasing endogenous adenosine through the use of a selective A<sub>3</sub>AR agonist.

Male Sprague Dawley rats and female mice were studied. Persistent neuropathic pain models were produced through chronic constriction injury (CCI), spared nerve injury, spinal nerve ligation, chemotherapy induced peripheral neuropathy (CIPN) and cancer induced bone pain. The animals then received intrathecal injections of a selective non-nucleoside adenosine kinase inhibitor, ABT-702. Mechano-allodynia was assessed using calibrated von Frey filaments. Neurologic function and motor coordination were evaluated by a Rotarod motor test. Nociception was assessed by tail flick and hotplate latency tests. Spontaneous and affective aspects of spinal nerve ligation-induced pain were assessed using conditioned place preference.

Administration of ABT-702 at peak CCI-induced pain reversed mechano-allodynia. These effects were partially attenuated by pretreatment with selective A<sub>3</sub>AR antagonists. In addition, in the model of CIPN, ABT-702 reversed mechano-allodynia and mechano-hyperalgesia. ABT-702 did not alter paw withdrawal thresholds in the unaffected contralateral paws.

**Conclusion:** This animal study found that an A<sub>3</sub>AR agonist can be

effective in treating several types of persistent pain.

Little, J., et al. Endogenous Adenosine A<sub>3</sub> Receptor Activation Selectively Alleviates Persistent Pain States. *Brain*. 2015, January; 138(1): 28-35.

## SINGLE SPORT SPECIALIZATION AND ADOLESCENT INJURY

Both the American Academy of Pediatrics and The American Medical Society for Sports Medicine have discouraged single sport specialization in youth. However, this recommendation has been made with limited data concerning the relationship between such specialization and the risk of injury. This study sought to clarify the relative impact of sports specialization on adolescent injury.

This case control study included athletes seven to 18 years of age seen in primary care sports medicine clinics. All participants completed surveys at enrollment, including demographics and current sports specialization, as well as self-assessment of pubertal maturation. Sports specialization was defined as year-round, intensive training in a single sport at the exclusion of other sports. Using this definition, sports specialization was categorized as low, moderate or high. Injuries were classified by clinical diagnoses obtained from medical records, characterized as acute or overuse.

Of the injuries noted, 67.4% were overuse, with patellofemoral pain the most common. Independent and dose dependent risks for injury, and for serious overuse injury were found for sports specialized training, after accounting for age and time spent in sports activity ( $p < 0.01$  for all). There was no difference in the growth rate between the two groups.

**Conclusion:** This study found that sports specialization in young

athletes increases the risk of acute and overuse injury.

Jayanthi, N., et al. Sports-Specialized Intensive Training and the Risk of Injury in Young Athletes. A Clinical Case Control Study. *Am J Sports Med*. 2015, February. doi:10.1177/0363546514567298

## MEMANTINE FOR FIBROMYALGIA

Pain is the most common and disabling symptom of fibromyalgia (FM). Glutamate, a central nervous system excitatory neurotransmitter, has been thought to play a role in the pathophysiology of FM. Given the glutamate blocking role of memantine, this study was designed to determine the efficacy of this medication for the treatment of FM.

This controlled, double-blind, randomized trial involved 63 patients diagnosed with FM, randomized to one of two groups. A treatment group received memantine, titrated to 20 mg per day, while a control group received a similar appearing placebo. The main outcome measure was the change in pain threshold and pain perception, evaluated using the Pain Visual Analogue Scale (PVAS), with assessments at baseline, and then at three and six months' follow-up.

Compared with placebo, patients treated with memantine showed significant improvements in PVAS scores at one, three and six months follow-up ( $p = 0.001$  for all comparisons). For secondary outcomes, at six months, significant improvements in favor of the memantine group were found in assessments of global function ( $p = 0.000$ ), clinical global impression ( $p = 0.000$ ), quality-of-life ( $p = 0.001$ ), cognitive function ( $p = 0.001$ ) and depression ( $p = 0.002$ ).

**Conclusion:** This study of patients with fibromyalgia found treatment with memantine to be

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effective for the treatment of pain and improvement in quality-of-life.

Olivan-Blazquez, B., et al. Efficacy of Memantine in the Treatment of Fibromyalgia: A Double-Blind, Randomized, Controlled Trial with Six -Month Follow-Up. **Pain.** 2014, December; 155(12): 2517-2525.

### **CATHETERIZATION PRACTICES AMONG ELITE ATHLETES WITH SPINAL CORD INJURIES**

The guidelines of the European Association of Urology recommend anticholinergic drugs and clean intermittent catheterization (CIC) as first-line management for patients with spinal cord injury (SCI). This study examined the primary modes of bladder management among elite athletes with SCI and the factors contributing to urinary tract infections (UTIs) in athletes who use the CIC method.

All participants in the London 2012 Paralympic Games and the 2013 Paracycling World Championship were reviewed for participation. Those with SCI of at least one year's duration and who reported using intermittent catheterization for bladder management were invited. Patients were queried concerning frequency of urinary tract infections and catheter reuse, and were assessed by age, chronicity of injury, country of origin and level of injury.

Athletes catheterized an average of six times per day, with this frequency unrelated to the development of UTIs ( $p=0.07$ ). Thirty one percent reported reuse of catheters. Those who reused catheters had an average of four UTIs per year, compared to one among those who never reused ( $p<0.001$ ). Patients from developing countries were more likely to reuse catheters than were those from developed countries, correlating to a higher frequency of UTIs among those from developing nations ( $p=0.027$ ).

**Conclusion:** This study of elite athletes with spinal cord injuries found that reuse of catheters is common among these athletes, and is associated with an increased risk of urinary tract infection.

Krassioukov, A., et al. The Good, the Bad and the Ugly of Catheterization

Practices among Elite Athletes with Spinal Cord Injury: A Global Perspective. **Spinal Cord.** 2015, January; 53(1): 78-82.

### **LASTING IMPAIRMENT FOLLOWING HAMSTRING INJURY**

Previous studies have shown that neuromuscular maladaptations associated with previous hamstring strain injuries may be related to an elevated risk of future injuries. This study assessed eccentric hamstring strength changes among athletes with a history of hamstring injury.

A cohort of 99 elite Australian footballers, 17 of whom had sustained unilateral hamstring injuries in the prior 12 months, were recruited for this study. All injured had completed rehabilitation, ranging from 19 to 79 days, and had completed preseason exercise training from November through February. Hamstring eccentric strength was measured at the first and final weeks of each month of preseason training, using an instrumented Nordic hamstring device.

By averaging strength daily, it was discovered that previously injured athletes had a significantly reduced improvement in muscle strength over the course of preseason training, as compared to the uninjured athletes ( $p<0.001$ ). This diminished response was not confined to the previously injured limb, but was also observed in the contralateral uninjured limb.

**Conclusion:** This study of elite Australian footballers with hamstring injuries found that, despite completing rehabilitation, these athletes have a reduced response to eccentric strengthening, as compared to those without such an injury history.

Opar, D., et al. The Effect of Previous Hamstring Strain Injuries on the Change in Eccentric Hamstring Strength during Preseason Training in Elite Australian Footballers. **Am J Sport Med.** 2015, February; 43(2): 377-384

### **ORAL HYALURONIC ACID FOR KNEE OSTEOARTHRITIS IN OBESE PATIENTS**

Osteoarthritis (OA) is a major cause of pain, disability and loss of function. Obesity is a known risk factor for OA, with hyaluronic acid

(HA) plus glucosaminoglycan concentrations decreased in end-stage OA. This randomized, double-blind, placebo-controlled trial assessed the effect of an oral preparation for patients with OA and obesity.

Subjects were 51 patients, 50 to 75 years of age with knee pain of at least 50 mm as assessed with a 100 mm visual analogue scale. All had an effusion requiring joint aspiration or injection. The participants were randomized to receive either 80 mg of Oralvisc or a similar appearing placebo. Outcome measures included pain, function, and inflammatory markers in the serum synovial fluid.  $^2\text{H}_2\text{O}$  analysis was completed to evaluate hyaluronic acid turnover and metabolic scores.

At three months, the HA group demonstrated greater improvements in pain and function ( $p < 0.005$ ), with decreased concentrations of inflammatory cytokines ( $p < 0.05$ ), bradykinin ( $p < 0.05$ ), leptin ( $p < 0.05$ ) and mean rate of HA decline in synovial fluid ( $p = 0.046$ ).

**Conclusion:** This study suggests that oral preparations containing hyaluronic acid and glycosaminoglycan can effectively treat pain and dysfunction in obese patients with osteoarthritis and active knee effusion.

Nelson, F., et al. Effects Of An Oral Preparation Containing Hyaluronic Acid on Obese Knee Osteoarthritis Patients Determined by Pain, Function, Bradykinin, Leptin, Inflammatory Cytokines and Heavy Water Analysis. *Rheum Intern*. 2015, January; 35(1): 43-50.

### ACE INHIBITORS AND ALS RISK

Amyotrophic lateral sclerosis (ALS) is the most common form of motor neuron disease, causing degeneration of both lower and upper neurons. As some studies have shown that angiotensin converting enzyme inhibitors (ACEI) have neuroprotective qualities, this study assessed the association between the use of ACEIs and the development of ALS.

This case controlled study surveyed the entire Taiwanese population to identify 729 patients with newly diagnosed ALS, and compared these to 14,580 matched controls. The use of ACEIs in the

years prior to diagnosis was identified through prescription records, and compared between the two groups. The cumulative total of doses of ACEIs was compared against the risk of ALS.

Approximately 15% of patients with ALS reported ACEI use two to five years prior to diagnosis, with 18% of patients without ALS reporting such use in the same time frame. When compared with the no-ACEIs group, the adjusted odds ratio was 0.74 for the group that was prescribed ACEIs ( $p < 0.001$ ). When compared with the no-ACEIs group, the adjusted odds ratios were 0.83 for the group who were prescribed a cumulative defined daily dose (cDDD) of less than 449.5 and 0.43 for the group who were prescribed ACEIs at a cDDD of greater than 449.5 ( $p = 0.15$  and  $p = 0.001$ , respectively).

**Conclusion:** This large population study suggests that a high dose of ACEIs may have a protective effect against the development of amyotrophic lateral sclerosis.

Lin, F., et al. Angiotensin-Converting Enzyme Inhibitors and Amyotrophic Lateral Sclerosis Risk. A Total Population Based, Case-Control Study. *JAMA Neurol*. 2015, January; 72(1): 40-48

### ADVERSE EFFECTS OF CAROTID ENDARTERECTOMY IN OCTOGENARIANS

Among patients in need of a carotid endarterectomy (CEA), advanced age is considered a contraindication. This study investigated perioperative adverse events and outcomes in patients undergoing CEA, comparing octogenarians to younger patients.

This prospective Japanese study included 145 patients who underwent CEA between 2008 and 2013, including 19 octogenarians and 123 who were younger. All had symptomatic carotid stenosis, with risk factors recorded. The perioperative major adverse events included major stroke, myocardial infarction and death from any cause. Results were compared between those who were octogenarians at the time of the surgery and those who were younger.

During the 30 days after surgery, stroke occurred in two patients, with no cases of myocardial infarction or

death. Thirteen patients died of causes unrelated to stroke. No significant difference was seen in baseline clinical characteristics between the octogenarians and the younger group. No major, adverse events occurred during the perioperative period. In the octogenarians, the estimated one-, three- and five-year survival rates in the octogenarians were 92.9%, 92.9% and 61.9%, respectively. In non-octogenarians the survival rates were 98.3%, 94.3% 93.1%, respectively. Survival did not differ significantly between the two groups ( $p = 0.371$ ).

**Conclusion:** This study of patients undergoing carotid endarterectomy found that the surgery is relatively safe for octogenarians.

Okawa, M., et al. Do Octogenarians Still Have a High Risk of Adverse Outcomes after Carotid Endarterectomy in the Era of a Super Aged Society? A Single Center Study in Japan. *J Stroke Cerebrovasc Diseases*. 2015, February; 24(2): 370-373.

### AEROBIC EXERCISE, THE HIPPOCAMPUS AND MILD COGNITIVE IMPAIRMENT

Mild cognitive impairment (MCI) is a recognized risk factor for dementia and may represent the prodromal stage of Alzheimer's disease (AD). This study explored the effects of resistance training (RT) and aerobic exercise on hippocampal volume among older women with probable MCI.

This 26-week, single blinded, randomized trial included women between the ages of 70 and 80 years, living independently with probable MCI. The women were randomized to twice-weekly RT, aerobic training (AT) or balance and tone training (BAT). The classes were 60 minutes in duration. To calculate hippocampal volume at baseline and at trial completion, the subjects underwent T1 weighted MRI. The patients were also assessed with the Rey Auditory Verbal Learning Test, wherein they were read a list of 15 words and asked to recall as many words as possible. The primary outcome measure was the change in hippocampal volume.

At trial completion, the AT group had significantly increased total hippocampal volume compared with the BAT group ( $p=0.01$ ). Both the left and right hippocampal volumes improved in the AT group as compared with the BAT group ( $p=0.03$ ). Compared with the BAT group, the RT group did not demonstrate a significant increase in total hippocampal volume at trial completion.

**Conclusion:** This study of patients with MCI suggests that twice-weekly aerobic training may be effective in maintaining hippocampal volume.

Brinke, L., et al. Aerobic Exercise Increases Hippocampal Volume in Older Women with Probable Mild Cognitive Impairment: A Six-Month, Randomized, Controlled Trial. **Br J Sports Med.** 2015, February; 49(4): 248-254.

#### EFFECTIVENESS OF SURGERY FOR SPONDYLOLISTHESIS AND LUMBAR STENOSIS IN OCTOGENARIANS

While the surgical treatment of lumbar stenosis and degenerative spondylolisthesis has been found to have substantial and lasting benefits, data are sparse concerning the effect of age on this outcome. This study assessed the clinical outcomes of this surgical intervention for patients at least 80 years of age.

The Spine Patient Outcomes Research Trial (SPORT) included patients with neurogenic claudication or radicular leg pain with associated neurological signs, spinal stenosis on cross-sectional imaging and symptoms persisting for at least 12 weeks. The subjects were randomized to receive either surgical or nonsurgical treatment. The primary outcome measure was the American Academy of Orthopedic Surgeons Musculoskeletal Outcomes Data Evaluation And Management System Version of the Oswestry Disability Index (ODI), as well as the Physical Function and Bodily Pain domains of the SF-36. Secondary outcomes included the Stenosis Bothersome Index, the Low Back Pain Bothersome Scale, patient satisfaction and patient self-reported improvement.

Of the patients with lumbar stenosis, 105 were at least 80 years

of age and 1,130 were younger. For patients at least 80 years of age, improvement in all primary outcome measures from baseline was significantly greater in the surgical group, including the SF-36 Bodily Pain score, the SF-36 Physical Function score and the ODI ( $p<0.05$ ). The surgical treatment effect as measured by the SF-36 Bodily Pain score was significantly better in the younger patients ( $p<0.01$ ). In the older group improvement in all secondary outcome measures from baseline was significantly greater in the surgically treated group ( $p<0.05$ ).

**Conclusion:** This prospective study of octogenarian patients with spondylolisthesis and lumbar stenosis found that surgery offers a significant benefit as compared to nonsurgical intervention.

Rihn, J., et al. Effectiveness of Surgery for Lumbar Stenosis and Degenerative Spondylolisthesis in the Octogenarian Population. Analysis of the Spine Patient Outcomes Research Trial SPORT Data. **J Bone Joint Surg.** 2015, February 4; 97(3): 177-185.

#### CALCITONIN AND NERVE REGENERATION

Calcium ions play an important role in normal neuronal function. Previous studies have shown that after nerve crush injury, functional recovery is correlated with calcium absorption and that accelerated calcium absorption can greatly improve nerve regeneration. This study tested the effect of an implantable mini-osmotic pump on the delivery of calcitonin to a damaged nerve.

This animal study included sixteen, healthy Sprague-Dawley rats, undergoing sciatic nerve transection followed by direct repair. The treatment group received an implantable mini osmotic pump with an attached catheter routed along the injured nerve. The pump delivered calcitonin at a constant, gradual rate to the injury site. A control group underwent the nerve transection repair without pump placement. The animals were evaluated at 12 weeks by electrophysiological and histologic studies, comparing the results between the two groups.

At follow-up, the relative fluorescent units (the calculated

calcium intensity of the entire nerve segment) was significantly better in the treatment than in the control group ( $p<0.001$ ). The treatment group had significantly more improved compound muscle action potentials ( $p<0.001$ ), tetanic muscle force ( $p<0.001$ ) and nerve fiber counts ( $p<0.001$ ) compared to the control group.

**Conclusion:** This animal study of surgically resected nerves found that calcitonin, applied by a pump directly to the healing nerve, improves nerve regeneration and functional recovery.

Yan, J., Calcitonin Pump Improves Nerve Regeneration after Transaction Injury and Repair. **Muscle Nerve.** 2015, February; 51(2): 229-234.

#### COMBINED HYPERCAPNIA AND HYPOXIA FOR ISCHEMIC BRAIN INJURY

Previous studies have suggested a possible neuroprotective effect of permissive hypercapnia and hypoxia. This study compared the neuroprotective effect of isolated and combined hypoxia and hypercapnia preceding focal cerebral ischemic injury.

This animal study involved adult rats, divided into four experimental groups. Group 1 received normobaric hypoxia (NbH),  $PO_2$  90 mmHg,  $PCO_2$  1mmHg for 20 minutes per day. Group 2, permissive hypocapnea (PH) received  $PO_2$  150 mmHg,  $PCO_2$  50mmHg, for 20 minutes per day. Group 3, hypercapnic hypoxia (HH) received  $PO_2$  90 mmHg,  $PCO_2$  50mmHg for 20 minutes per day. The reference group(R) received  $PO_2$  150mmHg,  $PCO_2$  1mmHg for 20 minutes per day. The rats underwent 15 sessions, followed by focal cerebral ischemic injury. At 72 hours post-injury, the rats underwent estimation of neurologic disorders by means of the Rotarod test and the testing with the scale of Neurologic Deficit Neurological Severity (NSS). The brains were then removed for histologic study and morphometric analysis.

Scores on the NSS scale found the HH group to have the least neurologic deficit, as compared with the reference and NbH groups ( $p<0.01$ ). In all experimental groups, a greater decrease in motor coordination disturbances and an increase in retention time on the

Rotarod were observed, as compared to the control group. The smallest infarction volumes were found in rats from the HH group, with reduced infarction by 45.7% compared with the R group ( $p < .01$ ), by 31.5% compared with the NbH group ( $p < .01$ ), and by 27% compared with the PH group ( $p < .05$ ).

**Conclusion:** This animal study found that hypercapnia has a greater neuroprotective effect than does hypoxia, and that hypercapnia potentiates the protective effects of hypoxia.

Tregub, P., et al. Combined Exposure to Hypercapnia and Hypoxia Provides Its Maximum Neuroprotective Effect during Focal Ischemic Injury in the Brain. *J Stroke Cerebrovasc Diseases*. 2015, February; 24(2): 381-387.

#### NON-ADHERENCE TO ORAL ANTICOAGULANTS IN STROKE PATIENTS WITH A-FIB

Despite scientific evidence of its efficacy, over 40% of patients with atrial fibrillation (a-fib) who have indications for long-term oral anticoagulation (OA) remain untreated. This study assessed the reasons for non-adherence in this patient population.

This prospective, observational trial included patients with ischemic stroke or transient ischemic attack presenting to an emergency room. After a period of 15 months, a semi-structured interview was offered to patients who had received a recommendation for OA related to a diagnosis of a-fib. The interview queried about adherence to, and any interruptions in, OA therapy. Data were collected concerning the reasons for nonuse.

One hundred thirty-nine patients with a-fib as an indication for OA completed the interview. Of those, 61% were adherent to therapy. Multivariate analysis revealed that independent risk factors for nonadherence were dementia and residing in a nursing home. In approximately two thirds of the nonadherent cases, OA was not prescribed or was discontinued by the primary care provider. Interviews of the primary care physicians revealed that the main reasons for not prescribing OA were dementia, functional status and the risk of falls.

**Conclusion:** This study of patients treated for ischemic stroke or transient ischemic attack found that, at follow-up, nonadherence to recommendations for oral anticoagulation was associated with living in a nursing home, dementia and not beginning the oral anticoagulation during the initial hospital visit.

Gumbinger, C et al. Reasons Underlying Nonadherence to and Discontinuation of Anti-Coagulation Secondary Stroke Prevention among Patients with Atrial Fibrillation. *Euro Neurol*. 2015; 73(3-4): 184-191.

#### THROMBOLYSIS FOR STROKE WITHIN THE FIRST HOUR

Among patients with acute ischemic stroke, intravenous thrombolysis with tissue plasminogen activator (tPA) has been found to be most beneficial if given within 60 minutes of symptom onset (the golden hour). This study was designed to determine whether the use of a specialized stroke ambulance could increase the rates of patients receiving therapy within the one hour window.

This prospective, controlled trial included 2,111 patients with ischemic stroke. The stroke emergency mobile unit (STEMO), equipped with a CT scanner, laboratory capability, a trained neurologist and tPA administration capabilities, was dispatched when patients with typical stroke symptoms were identified. Lysis was started in the ambulance if a stroke was confirmed and no contraindication was determined. During control weeks, patients received standard ambulance transportation. The primary outcome measures were the use of thrombolysis within the first hour, as well as 70- and 90-day mortality, intracerebral hemorrhage and discharge to home.

Thrombolysis occurred within one hour of symptom onset in 10.1% of the STEMO cases, as compared to 1.1% when a conventional ambulance was dispatched. The mean time from symptom onset to treatment was 24.5 minutes shorter in the STEMO group. Those who received treatment within one hour had median NIHSS scores higher than those among patients who received treatment more than 60

minutes after symptom onset ( $p=0.006$ ). There was no significant difference in 70- and 90-day mortality between those receiving treatment within the golden hour and those receiving treatment later. Those receiving golden hour lysis were more likely to be discharged to home ( $p=0.02$ ).

**Conclusion:** This study of patients with acute ischemic stroke found that those receiving thrombolysis within the first hour of symptom onset, within a specialized ambulance, had better stroke outcomes and were more likely to be discharged to home.

Ebinger, M., et al. Effects of Golden Hours from the Lysis: A Prehospital, Acute, Neurological Treatment of Optimization of Medical Care in Stroke (PHANTOM-S) Substudy. *JAMA Neurol*. 2015, January; 72(1): 25-30.

#### PELVIC FLOOR MUSCLE TRAINING IN OLDER WOMEN WITH MILD PELVIC ORGAN PROLAPSE

Pelvic organ prolapse is a relatively common condition. Women with milder forms of prolapse experience symptoms such as pelvic pressure, heaviness, pelvic pain and urinary or bowel symptoms. This study compared the effects of pelvic floor muscle training with those of watchful waiting on pelvic floor symptoms in women with symptomatic mild prolapse.

Participants were recruited from 15 Dutch general medical practices. All subjects were at least 55 years of age, and all had symptomatic, mild prolapse. The women were randomized to a muscle training group, to receive monitored pelvic floor physiotherapy, or to a watchful waiting group. The primary outcomes were changes in bladder, bowel and pelvic floor symptoms three months after the start of treatment, as measured by the Pelvic Floor Distress Inventory.

At three months, 57% of the women in the pelvic floor muscle training group reported improvement in symptoms, as compared to 13% in the watchful waiting group. The largest improvement was noted on the urinary symptom subscale. Quality of life measurements were

improved in both groups, though the difference was not significant.

**Conclusion:** This study found that pelvic floor muscle training can significantly improve symptoms in patients with mild pelvic organ prolapse, although the improvement was below the presumed level of clinical relevance.

Wieggersma, M., et al. Effect of Pelvic Floor Muscle Training Compared with Watchful Waiting in Older Women with Symptomatic Mild Pelvic Organ Prolapse: Randomized Controlled Trial in Primary Care. *Br Med J*. 2014; 10.1136/bmj.g7378

### COGNITIVE BEHAVIORAL THERAPY FOR TREATMENT OF DEPRESSION FOLLOWING TRAUMATIC BRAIN INJURY

Depression is a commonly reported symptom after traumatic brain injury (TBI), with its prevalence as high as 60%. Pharmacologic and behavioral treatments have proven effective for depression in the general population, although few studies have focused on the treatment of depression among those with a TBI. This study compared the effects of supportive psychotherapy (SBT) with those of cognitive behavioral therapy (CBT) for adults with TBI-related depression.

This study included 54 patients between the ages of 18 and 55 years of age with a history of TBI and a diagnosis of depression. The subjects were randomized to undergo 16 sessions of CBT or SPT, administered by postdoctoral fellows in clinical neuropsychology. Outcome measures included changes in depression scores, as measured by the Beck Depression Inventory (BDI), quality of life, as measured by the Anxiety and Quality-Of-Life Scale and anxiety, measured with the State-Trait Anxiety Inventory (STAI).

At the end of treatment, 35% of the CBT group and 17% of the SPT group no longer met the criteria for depression ( $p=0.16$ ). Analysis of variance revealed significant time effects for the BDI, STAI and QOL measures, although no group effects.

**Conclusion:** This study of patients with depression due to traumatic brain injury did not find cognitive behavioral therapy to be superior to supportive psychotherapy for the treatment of symptoms of depression.

Ashman, T., et al. Comparison of Cognitive Behavioral Therapy and Supportive Psychotherapy for the Treatment of Depression following Traumatic Brain Injury: A Randomized, Controlled Trial. *J Head Trauma Rehab*. 2014, December; 29 (6): 467-478.

### PREVALENCE OF CHRONIC HEADACHE AND MEDICATION OVERUSE

The Global Burden of Disease studies show that tension headache and migraine are the second and third most prevalent disabling conditions. Medication overuse can, at times, aggravate pain, leading to medication overuse headaches (MOHs), a subset of chronic headaches. This study examined the prevalence of chronic headaches, with and without medication overuse, and the factors associated with these conditions.

The sample comprised 129,150 individuals, 16 years of age or older, invited to participate in the Danish National Health Survey. From these data, information concerning chronic headache and its subtypes was obtained. Medication use data were obtained using the Danish National Prescription Registry, and then cross referenced against the data from the health survey. Chronic headache was defined as the presence of a headache at least 15 days per month for three or more months.

Individuals with concurrent over-the-counter analgesic use of at least 15 days per month or prescription medication use of at least 20 or 30 defined daily doses per month (depending upon the drug) were classified as having medication overuse headaches. Data were compared with socioeconomic data, obtained using the Denmark National Health Survey, while health data were obtained using the SF-12 Health Survey.

Chronic headache was identified in 3.3% of the respondents, and was more common among women ( $p<0.001$ ). Among those with chronic headache, 53% were identified as having medication overuse headaches, with 85.8% of those using over-the-counter medications. Chronic headache prevalence, with or without medication overuse, was highest in groups with low socioeconomic status.

**Conclusion:** This cross-sectional Danish study found that chronic

headache is prevalent in 3.3% of the population, with 53% engaging in concurrent medication overuse.

Westergaard, M., et al. Prevalence of Chronic Headache with and without Medication Overuse: Associations with Socioeconomic Position and Physical and Mental Health Status. *Pain*. 2014, October; 155(10): 2015-2013.

### HOSPITALIZATION AND FUNCTIONAL DECLINE

Hospitalizations for non-disabling conditions frequently result in new disability. This study, the Hospitalization Process Effects on Functional Outcomes on Recovery (HoPE-FOR), assessed the relationship between hospital processes and functional decline in adults with nondisabling conditions at admission.

This prospective cohort study enrolled 684 participants, 70 years of age or older, urgently admitted for nondisabling conditions. The baseline interview asked about information concerning function upon admission and function as estimated at 2 weeks before hospitalization. Participants were then interviewed four to six times during hospitalization, with information obtained concerning mobility level, continence care, sleep medication and nutritional intake during hospitalization. Hospital environment was assessed using the Perceived Hospital Environment Quality Index, which gauges participants' perceptions of the hospital physical and human environment. At one month post-discharge, a telephone interview was used to collect data concerning current functional status and rehospitalization during that month. The study's outcomes included function, as measured by the Barthel index, reviewing premorbid function to discharge and one month follow-up.

The mean hospital stay was 6.2 days, with the mean caloric intake 60% of recommended. The rates of functional decline were 41.2% at discharge and 46.3% at one month post-discharge. At discharge, functional decline was directly related to continence care ( $p<0.001$ ), length of stay ( $p<0.001$ ), and in-hospital mobility ( $p<0.001$ ). Nutritional consumption was related to functional decline at one month post-discharge ( $p<0.001$ ).

**Conclusion:** This study of older adults, hospitalized for nondisabling conditions, found that post-hospital functional decline is related to in-hospital factors, including low mobility, suboptimal continence care and low nutritional support.

Zisberg, A., et al. Hospital-Associated Functional Decline: The Role of Hospitalization Processes beyond Individual Risk Factors. **J Amer Ger Soc.** 2015, January; 63(1): 55-62.

#### TRAMADOL AND RISK OF HOSPITALIZATION FOR HYPOGLYCEMIA

Tramadol is a weak opioid analgesic whose use has increased steadily worldwide. Several reports have raised concerns that this use may be associated with a risk of hypoglycemia. This study was designed to better understand whether the use of tramadol is associated with increased hospitalization for hypoglycemia.

This study was conducted using the United Kingdom Clinical Practice Research Datalink, linked to the Hospital Episode Statistics Database. From these data were assembled a population-based cohort of patients newly treated with oral formulations of tramadol or codeine between 1998 and 2012. Excluded were patients who had been prescribed other opioids, had received a cancer diagnosis before cohort entry or had been previously hospitalized for hypoglycemia. The subjects were classified as using codeine or tramadol or with concurrent use of both in the year before the index date. The incidence of hospitalization for hypoglycemia was calculated, comparing medication groups.

The subjects included 28,110 new users of tramadol and 305,924 new users of codeine. During a mean follow-up of five years, compared with codeine use, tramadol use was associated with a 52% increased risk of hospitalization for hypoglycemia. A secondary analysis revealed that the risk was highest in patients who initiated treatment within 30 days of the index date (odds ratio, 2.61).

**Conclusion:** This study found that the initiation of tramadol therapy is associated with an increased risk of hypoglycemia requiring hospitalization.

Fournier, J., et al. Tramadol Use and the Risk of Hospitalization for

Hypoglycemia in Patients with Noncancer Pain. **JAMA Intern Med.** 2015, February; 175(2): 186-193.

#### HOSPITALIZATION FOR CARDIOVASCULAR DISEASE IN PATIENTS WITH INFLAMMATORY ARTHRITIS

Previous studies have demonstrated that patients with inflammatory arthritis (IA) are at significantly elevated risk for cardiovascular disease (CVD). As such, CVD related hospitalizations for patients with inflammatory arthritis are expected to be higher than those in the general population. However, data concerning this relationship are sparse. This study was designed to explore the relative risk of hospitalization for CVD among patients with IA.

This Dutch study employed data from the Netherlands Institute for Health Services Research Primary Care Database (NIVEL PCD) between 2001 and 2010. From those data were identified patients with IA, with each patient age and gender matched to two control patients. In addition, the Dutch Hospital Database (DHD) was accessed over the same time frame for inpatient admissions and treatment.

The search identified 3,356 newly diagnosed patients with IA and 6,708 controls. At an average of 4.2 years' follow-up, patients with IA were at a higher risk for inpatient hospital admission ( $p < 0.001$ ) and for hospitalization attributable to ischemic heart disease ( $p < 0.001$ ) and other types of heart disease ( $p = 0.042$ ).

**Conclusion:** This Dutch study found that, between 2001 and 2010, patients diagnosed with inflammatory arthritis had a significantly higher hospital admission rate, as well as rates of hospitalization for ischemic and other types of heart disease, as compared with controls.

Ursum, J., et al. Cardiovascular Disease-Related Hospital Admissions of Patients with Inflammatory Arthritis. **J Rheum.** 2015, February; 42(2): 188-192.

#### SATELLITE CELL DIFFERENTIATION AND ELECTRICAL STIMULATION

Muscle satellite cells act as reserve cells, able to proliferate in

response to injury and give rise to regenerated muscles. As electrical stimulation has positive effects on maintaining muscle contractile function and preventing muscle atrophy, this study reviewed the effects of electrical stimulation on satellite cell population after a nerve crush injury.

Subjects were 72 adult male Sprague-Dawley rats, randomly divided into three groups: Sham, sciatic nerve crush injury and sciatic nerve crush injury plus daily electrical stimulation. The animals in the electrical stimulation group received 30 minutes daily of electrical stimulation over the gastrocnemius muscle. Animals from each group were chosen randomly at two, four and six weeks post-injury for muscle harvest and analysis of muscle force production, Pax7 (measure of satellite cell nuclei), MyoD (measure of total nuclei) and embryonic myosin heavy chain assessment.

At follow-up, muscle mass was greatest in the sham group and least in the injury without stimulation group. In the injury group, the percentage of Pax7/MyoD was higher than in the sham group. Embryonic myosin heavy chain expression was elevated in stimulated muscles with this found to correlate with enhanced force production.

**Conclusion:** This animal study of crush injury to the sciatic nerve found that satellite cell differentiation is improved by electrical stimulation resulting in increased fiber regeneration and restoration of muscle function.

Xing, H., et al. Electrical Stimulation Influences Satellite Cell Differentiation after Sciatic Nerve Crush Injury in Rats. **Muscle Nerve.** 2015; 51(3), March: 400-411.

#### OCCUPATIONS ASSOCIATED WITH NECK PAIN

Research concerning the occupational patterns of neck pain has found that certain occupational groups have a higher prevalence of neck pain. This study further analyzed the associations among occupation, work hours and neck pain, as well as demographic factors which impact this pain.

Data were obtained from the National Health Interview Survey, a series of cross-sectional surveys of the health of the United States civilian, noninstitutionalized adults.



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This study reviewed 63,629 subjects ages 18 to 64, all of whom were employed at the time of the survey. Neck pain was defined as nonspecific neck pain within the past three months. Data collected included occupation classification, hours of work, demographic characteristics, socioeconomic status, leisure time physical activity and psychological distress. The odds ratios for neck pain were calculated using univariate and multivariate logistic regression.

The top five occupations for increased risk of neck pain were: 1) military specific; 2) health care support; 3) arts, design, entertainment, sports, and media; 4) community and social services; and 5) personal care and services. Compared to those who worked 40 hours per week, those working higher and lower amounts had increased rates of neck pain.

**Conclusion:** This study suggests that certain demographics, occupations and work hours are related to a higher incidence of neck pain.

Yang, H., et al. Work Related Risk Factors for Neck Pain in the U.S. Working Population. *Spine*. 2015, February 1; 40(3): 184-192.

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