

# REHAB IN REVIEW

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## URINARY INCONTINENCE IN ELITE ATHLETES

Urinary incontinence (UI) in women ages 15 to 44 years of age has been estimated to range from 6.2% to 12.4% in the general population. This cross-sectional study was designed to determine the prevalence of UI among elite female athletes.

Subjects were female athletes, ages 15 to 48 years, who had been members of their respective national teams for at least one year, and had reached an international level of competition. Age-matched controls were recruited from the general population. All subjects completed questionnaires regarding background variables, medical history and sports practice characteristics. The women were asked whether UI, if reported, was related to sports practice. The athletes were compared with controls, with athletes grouped by sports categories, including gravity sports, power sports, ballgame sports, weight sports, aesthetic sports, technical, and endurance sports.

Data were collected from 372 elite athletes and 372 controls. Urinary incontinence was reported by 29.6% of the athletes and 13.4% of the controls. Those involved in gravity sports (high jump, long jump, trampoline) reported the highest prevalence, at 84.4%, with the second highest group being weight sports at 44% (Karate, Judo and weightlifting). Most of the athletes with urinary incontinence reported leakage during sports practice. Fewer athletes than controls had told a physician about the condition.

**Conclusion:** This study found a high prevalence of urinary incontinence among elite, female, Portuguese athletes, which was significantly higher than that of matched controls.

Carvalho, A., et al. Performing High-Level Sport Is Strongly Associated with Urinary Incontinence in Elite

Athletes: A Comparative Study of 372 Elite Female Athletes and 372 Controls. *Br J Sports Med.* 2017; 0: 1-6. DOI: 10.1136/2017-097587.

## COFFEE AND ALL CAUSE MORTALITY

Previous studies have demonstrated health benefits of coffee intake. This study was designed to better understand the relationship between coffee consumption and mortality.

This population-based cohort followed patients prospectively, with the baseline analysis completed between 1993 and 1996. During that time, multiple medical and socioeconomic data were obtained, including lifestyle data. A dietary screen was completed using a validated food frequency questionnaire. The relationship between coffee intake and mortality over time was calculated.

Participants were 185,855 African Americans, Native Hawaiians, Japanese Americans, Latinos and whites, aged 45 to 75 years at recruitment, with an average follow-up of 16.2 years. Of these, 58,397 participants died.

Compared with those who drank no coffee, the adjusted mortality risk for those who drank coffee was 0.88 for one cup per day, 0.91 for two to three cups per day and 0.82 for four or more cups per day ( $p < 0.01$ ). The association was positive for both caffeinated and decaffeinated coffee. Inverse associations between coffee intake and mortality were observed for deaths due to heart disease, cancer, respiratory disease, stroke, diabetes and kidney disease.

**Conclusion:** This prospective study found that coffee intake was inversely associated with mortality.

Park, S. Association of Coffee Consumption with Total and Cause-Specific Mortality among Nonwhite

Populations. *Ann Intern Med.* 2017, July; 11. DOI:10.7326/M16-2472.

## BACTERIA IN ACHILLES TENDON RUPTURES

Spontaneous Achilles tendon (AT) ruptures are often associated with pre-existing, chronic, pathological changes. The causes of these pathologic changes are not fully understood. As bacterial involvement has been observed in a number of case reports of tendinopathy, this study assessed whether there is a relationship between AT ruptures and bacteria.

Subjects were recruited from among patients who had consented for surgical repair of a spontaneous AT rupture, as well as from a control group from patients undergoing elective ACL reconstruction (a healthy hamstring control group). Tissue samples were harvested from the stump ends of ruptured Achilles tendons, with control samples obtained from hamstring tendon grafts that were harvested for ACL reconstruction. DNA was extracted from the samples, and histology preparations were made for comparison.

Subjects included 20 patients with Achilles tendon rupture and 23 undergoing ACL reconstruction. Bacterial 16S rDNA was found in five of the 20 ruptured ATs, and in none of the controls ( $p = 0.016$ ). The species of bacteria identified were predominantly of the genus staphylococcus. No significant differences were noted in the histologic appearance between the bacterial DNA positive and DNA negative samples from the ruptured ATs.

**Conclusion:** This study of patients with spontaneous Achilles tendon ruptures found the presence of bacterial DNA in 25% of the tendons, with none present in unruptured control tendons.

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Rolf, C., et al. Presence of Bacteria in Spontaneous Achilles Tendon Ruptures. *Am J Sports Med.* 2017, July; 45(9): 2061-2067.

## **ALCOHOL AND HEALTHY COGNITION**

Several studies have reported the benefits of moderate alcohol intake on the maintenance of cognitive health in late life, although the association is often not consistent. This study examined the association between the amount and frequency of alcohol intake and cognitively healthy survival to age 85.

The Rancho Bernardo study was established in 1972 to 1974 when 82% (n=6,339) of residents aged 30 and older, from the San Diego, CA suburb of Rancho Bernardo, were recruited for a study of heart disease risk factors. Subjects were predominantly white, upper class adults, ages 30 to 79. In 1984 through 1987, participants were given a detailed questionnaire regarding alcohol intake. Changes in tests of cognitive function were compared with alcohol consumption responses.

Alcohol consumption was classified as moderate (≤one drink/day for men age 65 or older and all women, two drinks/day for men under 65), heavy (one to three drinks/day for men age 65 and older and all women, two to four for men under 65), or excessive (three drinks/day for men age 65 and older and all women, four drinks/day for men under 65). Those surviving to at least 85 years of age without cognitive impairment were classified as having cognitively healthy longevity (CHL), while those with cognitive impairment were classified as having cognitively impaired longevity (CIL).

Data were collected for 1,344 survivors. Over an average of 14.2 years' follow-up, 26% were classified as having CHL, 33% were classified as having CIL and 41% died before reaching the age of 85. The multivariate adjusted odds of CHL compared to CIL was approximately twice as high in moderate and heavy drinkers than in nondrinkers (OR 1.90 and OR 2.05, respectively). Compared to nondrinkers, those with near daily intake of alcohol had the highest odds of having CHL compared with CIL (OR 2.06).

**Conclusion:** This study found a positive association between moderate alcohol intake and

cognitively healthy longevity, with the association greatest in those with regular, moderate drinking patterns.

Richard, E. Alcohol Intake and Cognitively Healthy Longevity in Community-Dwelling Adults: The Rancho Bernardo Study. *J Alz Dis.* 2017; 59: 803-814.

## **BIPHOSPHONATES FOR COMPLEX REGIONAL PAIN SYNDROME**

Complex regional pain syndrome, type I, (CPRS-1) is characterized by pain, swelling and vasomotor disorders, often leading to severe disability. Several studies have reported that bisphosphonates may have significant analgesic efficacy for a number of bone related pathologies. This review summarized the findings concerning bisphosphonate use for the treatment of pain in CPRS-1.

After a literature search, 258 articles were identified, from which four trials, thought to be of moderate to good quality, were chosen for analysis.

From the data, it was determined that bisphosphonate use resulted in significant short-term pain relief, (within 30 to 40 days), as well as pain relief at two to three months (p<0.001 for both comparisons). Significantly better improvement in motion scores, as well as in physical functioning, as measured by the SF-36 was found in the bisphosphonate group than in the placebo group. No serious side effects were reported.

**Conclusion:** This literature review and meta-analysis of randomized, controlled trials of bisphosphonate for the treatment of complex regional pain syndrome, type I, found that this medication can reduce pain and improve function.

Chevreau, M., et al. Bisphosphonates for Treatment of Complex Regional Pain Syndrome, Type I: A Systematic Literature Review and Meta-Analysis of Randomized, Controlled Trials versus Placebo. *Joint Bone Spine.* 2017, Jul; 84(4): 393-399.

## **MINOCYCLINE AND ALLODYNIA**

Minocycline is a second-generation, semi-synthetic tetracycline used as a broad-spectrum antibiotic. In addition to its

antimicrobial effects, it has been shown to suppress pain sensation by a number of mechanisms. This study was designed to determine whether minocycline can be used to inhibit muscular hypersensitivity.

An experimental model of hypersensitivity was created using repetitive, acute noxious/painful stimuli, through intramuscular injections of one mL of five percent hypertonic saline, administered into the right tibialis anterior at 48-hour intervals. These injections began after the subjects had been randomized to pretreatment with either a placebo or minocycline, 100 mg, twice per day for seven days. After each noxious injection, the subjects were asked to provide an account of pain intensity on a visual analog scale. These ratings were compared between groups.

By session five, muscle soreness was significantly greater in the placebo group than in the minocycline group, both in the ipsilateral ( $p < 0.0001$ ) and contralateral limbs ( $p < 0.0001$ ). The contralateral cold pain threshold in placebo-treated participants was lower than that of the minocycline-treated participants ( $p = 0.0006$ ).

**Conclusion:** This study of experimental allodynia found that pretreatment with minocycline can reduce the onset of hypersensitivity.

Samour, M., et al. Minocycline Prevents Muscular Pain Hypersensitivity and Cutaneous Allodynia Produced by Repeated Intramuscular Injections of Hypertonic Saline in Healthy Human Participants. *J Pain*. 2017, August; 18(8): 994-1005.

### ARTHROSCOPIC KNEE SURGERY IN MIDDLE-AGED PATIENTS WITH MENISCAL SYMPTOMS

Recent data have brought into question whether surgical intervention is appropriate for patients with meniscal lesions. This study evaluated whether knee arthroscopic surgery, combined with exercise, provides additional, long-term benefit at three-year follow-up.

Subjects were 150 adults, 45 to 64 years of age, with symptomatic knee pain, all with a suspected meniscal injury. The groups were randomized to undergo physical therapy only or to receive surgical intervention in addition to the therapy.

All patients were allowed full weight bearing activities immediately after surgery. Outcome measures included the EuroQol 5 Dimensions (EQ-5D) and the Knee Injury and Osteoarthritis Outcome Score (KOOS), with evaluations completed at three, 12 and 36 months after baseline.

Significant improvement was noted in both treatment groups on the KOOS pain subscore at three-year follow-up ( $p < 0.001$ ). However, the between group difference at three years did not differ significantly between the groups ( $p = 0.216$ ). At one year, pain improvement was significantly greater in the surgical group than in the nonsurgical group ( $p = 0.005$ ). However, at three years differences between groups on the EQ-5D Quality of Life Index were not significant ( $p = 0.31$ ).

**Conclusion:** This study of middle-aged adults with meniscal injury found that arthroscopic surgery may provide better pain relief at one year than exercise alone, with this difference no longer significant at three years.

Gauffin, H., et al. Knee Arthroscopic Surgery in Middle-Aged Patients with Meniscal Symptoms. A Three-Year Follow-Up of a Prospective, Randomized Study. *Am J Sports Med*. 2017, July; 45(9): 2077-2084.

### HIP ARTHROPLASTY FOR FEMORACETABULAR IMPINGEMENT

Femoral acetabular impingement (FAI) has been implicated as a cause of hip pain, decreased function and osteoarthritis (OA). This study evaluated 10-year outcomes and hip survival following hip arthroscopy for FAI, comparing the results of labral debridement with those of labral repair.

Subjects were 169 patients undergoing arthroscopic hip surgery for FAI, all treated by single surgeon. Following surgery, the subjects were limited to 20 pounds of toe-touch weight bearing, and underwent four hours of continuous passive motion daily for the first two weeks. Those who underwent microfracture had weight bearing restrictions and passive motion extended to eight weeks. Patient-reported outcome measures were collected for up to 10 years postoperatively. The primary outcome measure was the Hip

Outcome Score (HOS) Activities of Daily Living (ADL) subscale.

Subjects included 79 patients undergoing labral repair and 75 undergoing debridement, with 94% available at 10-year follow-up. The Kaplan-Meier estimated survivorship of the entire population with total hip arthroplasty (THA) as the end point was 91% at 1 year, 75% at 5 years, and 63% at 10 years. A multivariate analysis showed an increased risk of THA for those with joint space of less than two mm ( $p < 0.001$ ), acetabular microfracture ( $p = 0.036$ ) and an increased age at surgery ( $p < 0.001$ ). There was no difference between the debridement and repair group in the primary outcome.

**Conclusion:** This long-term follow-up of patients undergoing hip arthroscopy for femoral acetabular impingement found that labral debridement or repair results in significant improvements in patient-reported outcomes and satisfaction. However, of the patients followed, 34% required conversion to total hip arthroplasty.

Travis, M., et al. Survivorship and Outcomes 10 Years Following Hip Arthroscopically for Femoral Acetabular Impingement: Labral Debridement Compared with Labral Repair. *JBJS*. 2017, June; 99(12): 997-1004.

### BODY MASS INDEX AND GAINS AFTER JOINT REPLACEMENT

Some data have indicated a higher risk of osteoarthritis (OA) among individuals with an elevated body mass index (BMI). This study was designed to better understand the relationship between a patient's BMI and functional outcome after a total joint replacement (TJR).

This prospective, national cohort enrolled patients from high-volume centers in more than 100, community, orthopedic practices in 22 states in United States. Data included physical function, joint pain, BMI, and a number of covariates. Function was measured with the Short Form-36 Physical Component Summary (PCS) summary score at baseline and six months, with mental health measured with the SF-36 mental component summary score. Pain severity was measured using the Hip Disability and Osteoarthritis Outcome Score (KOOS).

Subjects were 2,040 patients undergoing total hip replacement (THR) and 2,964 undergoing total knee replacement (TKR). A greater obesity level was associated with more pain at baseline but greater postoperative pain relief in all TJRs, so the average postoperative KOOS pain scores did not differ significantly according to BMI status. In addition, PCS function levels improved similarly at all BMI levels, though the 6-month function levels were worse at six months for both the TKR and THR patients ( $p < 0.001$  for both).

**Conclusion:** This large, prospective study of patients undergoing total joint replacement found that pain relief at six months is similar in all BMI categories. Among those undergoing total hip replacement, only those with severe and morbid obesity had less functional gains.

Li, W., et al. Functional Gain and Pain Relief after Total Joint Replacement According to Obesity Status. **JBJS**. 2017, July 19; 99(14): 1183-1189.

#### INHIBITION OF PARKINSONIAN TREMOR WITH TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION

Approximately 70% of patients with Parkinson's disease (PD) exhibit a resting tremor. Research has demonstrated that a cutaneous reflex evoked by stimulating finger skin may result in an inhibitory effect via pre-motor neuron interneurons. This study was designed to determine whether tremor in patients with PD can be reduced through stimulation with a transcutaneous cutaneous nerve stimulation (TENS) unit.

Eight patients with idiopathic PD with tremor dominant symptoms were recruited. Surface electromyography activity was recorded from multiple muscles in the upper extremity. Electrodes of a TENS unit were placed within the innervation zone of the superficial radial nerve. Electrical stimulation was then delivered in incremental steps until the subject felt a noticeable sensation at the dorsal skin (cutaneous perceptual amplitude (CPA)). The stimulus amplitude was then increased until the subject perceived a radiating sensation from the dorsal skin to the fingers (radiating threshold (RT)). The resting tremor of the hand was then

recorded during cutaneous stimulation at 1.5 to 1.7 times the RT.

During stimulation, the mean suppression of tremor across all joints was 61.56%. The suppression appeared to occur mainly in distal joints and muscles. The tremor recurred after stimulation was discontinued.

**Conclusion:** This study of patients with Parkinsonian tremor found that sensory stimulation of the radial nerve using a TENS unit can reduce resting tremor.

Hao, M., et al. Inhibition of Parkinsonian Tremor with Cutaneous Afferent Evoked by Transcutaneous Electrical Nerve Stimulation. **J Neuroeng Rehab**. 2017; 14:75. DOI 10.1186/s12984-017-0286-2.

#### DUAL-TASK GAIT AND INCIDENT DEMENTIA

Mild cognitive impairment (MCI) is considered a pre-dementia state, although one third of individuals with this diagnosis remained clinically stable. This study examined the longitudinal association of dual-task gait performance with the incidence of dementia in patients with MCI.

Subjects were community dwelling adults, 65 years of age or older, with MCI, as measured by the Global Rating of the Clinical Dementia Rating Scale. The participants underwent a comprehensive baseline evaluation, with biannual assessments during six years of follow-up. A gait analysis was completed, with the subjects first asked to walk at their usual pace without mobility aids. During the dual-task procedure, all were asked to walk at their usual pace while performing cognitive tasks aloud. The magnitude of the difference in gait velocity during baseline and dual tasks conditions was compared to incident dementia at follow-up.

Subjects were 112 adults with a mean age of 76.6 years. Gait studies revealed that a slow, single-task gait velocity ( $< 0.8$  meters/second) was not associated with a progression to dementia, while slowing of gait while counting backward ( $p = 0.05$ ) and naming animals ( $p = 0.003$ ) was associated with the progression to dementia.

**Conclusion:** This study of patients with mild cognitive impairment found that dual-task gait

is associated with progression to dementia.

Montero-Odasso, M., et al. Association of Dual-Task Gait with Incident Dementia and Mild Cognitive Impairment. Results from the Gait and Brain Study. **JAMA Neurol**. 2017, July; 74(7): 857-865.

#### EMPLOYMENT OF VETERANS AFTER TRAUMATIC BRAIN INJURY

Return to work after severe traumatic brain injury (TBI) varies by severity of injury and ranges from 38% to 54% at one year. This study was designed to identify predictors of employment outcome for armed service members and veterans with TBI.

The Department of Veterans Affairs established a Department of Veteran's Affairs Polytrauma Rehabilitation Centers Traumatic Brain Injury Model Systems (VA PRC TBIMS) national database. Subjects included adults with a diagnosis of TBI admitted to a VA PRC between January of 2009 and December of 2014. Data collected included mechanism of injury, medical history, demographic information and preinjury history. At one, two and five years post-injury, and then every five years thereafter, employment status was recorded.

Of the original cohort, 293 were available for the final analysis. Of these, 20.5% had obtained employment during year one, with an average time after discharge to employment of 156.6 days. Those employed reported a higher level of educational achievement, and had experienced less severe TBI, than those without employment. An adjusted analysis revealed that younger age at injury, minority status and injury severity were significantly associated with employment.

**Conclusion:** This prospective study of veterans hospitalized with traumatic brain injury found that, at one year, only 20.5% were employed, with employment beginning over six months after discharge from rehabilitation.

Dillahun-Aspillaga, C., et al. Predictors of Employment Outcomes in Veterans with Traumatic Brain Injury: a VA Traumatic Brain Injury Model Systems Study. **J Head**

### OUTCOME AFTER GRADES IV AND V ANEURYSMAL SUBARACHNOID HEMORRHAGE

The mortality of patients treated for grade IV and V subarachnoid hemorrhage (SAH) has improved recently, decreasing from 57% in 1981 to 27% in 2011. This study assessed the long-term functional and neurologic outcomes of patients who survive these hemorrhages.

This retrospective review included all patients with grades IV and V SAHs treated between 2005 and 2010. Functional outcome was assessed with the modified Rankin scale (mRS), and quality of life with the 36-Items Short Form Health Survey.

Subjects were 107 patients, of whom 23.4% died during the acute hospital phase. Of the 62 surviving patients available for long-term follow-up, 41.2% reached functional independence, 12.4% were moderately handicapped, and 10.3% were severely disabled. A multivariate regression analysis revealed that younger age (<50 years) and the absence of brain infarction on MRI during the acute phase of treatment were significant predictors of a favorable outcome.

**Conclusion:** This study of patients with grade IV and V subarachnoid hemorrhages found that two thirds survived the early aneurysm repair, and, among long-term survivors, two thirds were functionally independent at a mean of 3.2 years.

Schwartz, C., et al. Long-Term Neurological Outcome and Quality of Life after World Federation of Neurosurgical Societies Grades IV and V Aneurysmal Subarachnoid Hemorrhage in an Interdisciplinary Treatment Concept. *Neurosurg.* 2017, June; 80 (6): 967-974.

### EFFORT-REWARD IMBALANCE AND CORONARY HEART DISEASE

Cohort studies from different countries have found an association between stressful working conditions and an increased risk of subsequent coronary heart disease (CHD). This study used data from 11 European countries' prospective, cohort studies

to prospectively test the association between effort-reward imbalance at work and later CHD.

Data were reviewed from 11 cohort studies that were initiated between 1985 and 2005. From these 90,164 employed adults were followed for a mean of 9.8 years. All were assessed with an effort-reward imbalance questionnaire, with responses to effort items compared with responses to reward items. The subjects were followed for incident CHD. Covariates included age, gender, socioeconomic position, lifestyle related factors and job strain.

At entry, the mean age of the workers was 45.1 years, with 60.8% women. Of the subjects followed, 1,078 incident CHD events were recorded. After adjusting for confounding variables, a hazard ratio of 1.16 was observed for those reporting an effort-reward imbalance. Compared to those with no effort-reward imbalance and no job strain, those with effort-reward imbalance and job strain had a hazard ratio for CHD of 1.34.

**Conclusion:** This meta-analysis of data from 11 European countries found that perceived effort-reward imbalance at work is associated with an increased risk of coronary heart disease.

Dragano, N., et al. Effort-Reward Imbalance at Work and Incident Coronary Heart Disease. Multi-Cohorts Study of 90,164 Individuals. *Epidemiology.* 2017, July; 28(4): 619-626.

### RETURN TO WORK AFTER SEVERE TRAUMATIC BRAIN INJURY

After a severe traumatic brain injury (TBI), data regarding return to work (RTW) are often based on self-reported labor market attachment (LMA) data, which are susceptible to recall and lost to follow-up bias. This study was designed to better understand employment data up to five years after a severe TBI.

Both RTW and LMA data were retrieved from the DREAM register, a national register of public assistance benefits. Subjects included all patients 15 years of age or older living in Denmark, who were admitted to a neurorehabilitation unit with a severe TBI between 2004 and 2012. These patients were matched with up to four controls from the general

population. A national registry and the register of public assistance benefits were used to assess return to work and obtain LMA data.

At one and five years post-injury, personal income involved primarily health-related benefits in 80.7% and 69.7%, respectively. In the general population controls, these percentages were 22.1% and 19.5%. The attempt to return to work within two years post-injury was 30% among all persons with severe TBI. At one and two years post-injury, the LMA prevalences were 11% and 16%, respectively. From 2-1/2 years to five years post-injury the LMA prevalence declined to 11%. The LMA among the general population was stable, at 70%.

**Conclusion:** This study of adults in Denmark found that, among patients with severe traumatic brain injury, 30% attempted to return to work, and 16% achieved stable employment.

Odgaard, L., et al. Return to Work after Severe Traumatic Brain Injury: A Nationwide Follow-Up Study. *J Head Trauma Rehabil.* 2017, May/June; 32(3):E57-E 64.

### STATIN ADHERENCE AND RECURRENT STROKE

The role of statins in secondary stroke prevention has emerged from a single, randomized, controlled trial, the Stroke Prevention by Aggressive Reduction and Cholesterol Levels (SPARCL), which tested high dose atorvastatin in patients with ischemic strokes. Studies have suggested that statins may reduce the stroke risk by non-lipid-lowering mechanisms, including a reduced burden of atrial fibrillation (a-fib). This trial examined the relationship between outpatient statin adherence and the risk of recurrent stroke.

This study employed data from the inpatient/outpatient electronic medical records of Kaiser Permanente Northern California, a 21 Hospital integrated health care delivery system. Data were captured during 2008 through 2012 from 6,116 patients admitted with ischemic stroke and discharged with an active prescription for statins. Extracted from the medical records were data including the presence of a-fib and other stroke risk factors. The subjects were followed for the occurrence of recurrent ischemic

stroke beginning 30 days after the index event for up to three years.

An adjusted analysis revealed that stroke-free survival over three years was greater at higher levels of statin adherence. This was true of patients without a-fib ( $p=0.023$ ) and of patients with a-fib ( $p=0.001$ ). The use of warfarin was strongly associated with a reduced risk of recurrent stroke, although this effect was independent of the relationship between statin use and stroke risk.

**Conclusion:** This study of 6,116 patients with ischemic stroke found that statin use is associated with a significantly reduced risk of stroke among those with and without a-fib.

Flint, A., et al. Statin Adherence Is Associated with Reduced Recurrent Stroke Risk in Patients with or without Atrial Fibrillation. *Stroke* 2017, July; 48(7): 1788-1794.

### FESOTERODINE FOR OVERACTIVE BLADDER IN THE ELDERLY

Overactive bladder (OAB) is defined as urinary urgency, with or without urgency urinary incontinence. The prevalence of OAB increases with advancing age. The current, first-line therapy for OAB is antimuscarinic agents. Fesoterodine, one such agent, has a low propensity for central nervous system penetration. This literature review pooled available data to examine the efficacy and safety of this drug for patients over 65 years of age.

A literature review was completed, with the majority of analyses including age groups ranging from 65 to over 85 years of age. The data were pooled to examine the baseline to week 12 efficacy endpoints, including episodes of urgency and incontinence. Also included were treatment related, adverse events.

The pooled analysis included data from 4,040 patients, including 1,311 assigned to placebo, 999 to Fesoterodine four mg and 1,730 to Fesoterodine eight mg. Of those in the 65- to 75-year age range, 40.1% of the Fesoterodine patients experienced a major improvement on the Patient Perception of Bladder Condition Scores, as did 34.4% of those in the 75 year and older age group.

Subjects experiencing a central nervous system adverse event were 0.5% in the Fesoterodine four mg

group and 0.7% in the Fesoterodine eight mg group.

**Conclusion:** This study of elderly individuals with overactive bladder found that treatment with Fesoterodine can produce clinically significant improvement in bladder function, with a very small risk of central nervous system effects.

Wagg, A., et al. The Pooled Analysis of the Efficacy of Fesoterodine for the Treatment of Overactive Bladder and the Relationship between Safety, Comorbidity and Polypharmacy in Patients Aged 65 Years or Older. *Age Aging*. 2017, July; 46(2): 620-626.

### LARGE PERIVASCULAR SPACES AND RISK OF DEMENTIA

Neuroimaging hallmarks of small vessel disease include subcortical infarcts, white matter intensities (WMI) and micro-bleeds. Recently, magnetic resonance imaging studies have identified visible large perivascular spaces (L-PVSSs) as a potential SVD marker. This study explored the association between prevalent L-PVSSs and progression of markers of small vessel disease and new onset dementia.

This investigation was part of a prospective, population based, age, gene/environment susceptibility Reykjavik (AGES-Reykjavik) study, involving 5,764 adults born from 1907 to 1935. These individuals underwent extensive physical, cognitive and brain MRI examination at follow-up in 2002 through 2006. A subsequent examination was performed from 2007 through 2011, including a neuropsychological examination at a mean of 5.2 years from the previous one, as well as repeat MRI examinations. Based upon review of the MRIs, L-PVSSs were categorized as none, one, and greater than two.

Of the 2,612 subjects, 83.8% did not have L-PVSSs. Of those with L-PVSSs, 17.7% were in the white matter exclusively, and 82.3% were basal ganglion L-PVSSs. The presence of L-PVSSs at baseline was associated with an increased risk of incident subcortical infarcts and micro-bleeds and greater white matter intensity progression. The fully adjusted model indicated that the presence of L-PVSSs was associated with an increased risk of developing vascular dementia

( $p<0.01$ ), but not all-cause dementia or Alzheimer's disease.

**Conclusion:** This prospective, population based study of older individuals, all free of prevalent dementia, found that the presence of large perivascular spaces at baseline was associated with an increased risk of vascular dementia.

Ding, J., et al. Large Perivascular Spaces Visible on Magnetic Resonance Imaging, Cerebral Small Vessel Disease Progression, and Risk of Dementia. The Age, Gene/Environment Susceptibility-Reykjavik Study. *JAMA Neurol*. 2017, July. doi: 10.1001/jamaneurol.2017.1397

### MIGRAINE PREVENTION THROUGH TRANSCUTANEOUS OCCIPITAL NERVE STIMULATION

Migraine is a recurrent, disabling disorder which, according to the Global Burden of Disease Study, is the sixth leading cause of disability worldwide. This study was designed to determine the efficacy and tolerability of transcutaneous occipital nerve stimulation (TONS) for the prevention of migraine headache.

Subjects were adults, 18 to 65 years of age, all diagnosed with migraine without aura, and reporting at least a one-year history of migraine, with a minimum of four attacks per month. The subjects were randomized to receive TONS at a frequency of two Hz, 100 Hz, two/100 Hz or a sham intervention. A final group received oral topiramate. All patients were asked to keep a headache diary. The primary outcome measures were at least a 50% reduction in monthly migraine days compared with baseline, a change in headache intensity, as assessed with a visual analog scale (VAS) and headache duration.

The treatment groups all had responses superior to that of the sham control group, with a 50% responder rate occurring in 36.36%, 40.91%, 36.6% and 63.64%, compared with 4.55%. The stimulation groups did not differ from the topiramate group. A significant improvement in the number of headache days was realized only in the 100 Hz and topiramate groups, as compared to the sham group. The stimulation groups exhibited a significant reduction in VAS score as compared to the sham treatment group, although this finding was not

significantly better than that of the topiramate group.

**Conclusion:** This study of patients with chronic migraine headaches found that transcranial occipital nerve stimulation can be effective in preventing migraines, with an efficacy similar to that of topiramate.

Liu, Y., et al Migraine Prevention Using Different Frequencies of Transcutaneous Occipital Nerve Stimulation: A Randomized, Controlled Trial. **J Pain.** 2017, August; 18(8): 1006-1015.

### **DIFFUSION TENSOR IMAGING AND LEVELS OF CONSCIOUSNESS AFTER TRAUMATIC BRAIN INJURY**

Traumatic brain injury (TBI) is a common, severe injury responsible for approximately one third of injury related deaths. This data review was designed to determine whether diffusion tensor imaging (DTI) can be used to assess levels of consciousness.

A database review was conducted to identify studies involving DTI and TBI. The search identified 16 such studies, published between 2004 and 2016, which were included in this systematic review.

The meta-analysis using DTI demonstrated that impaired whole brain white matter is associated with levels of consciousness. The pooled relationships between DTI indices and consciousness revealed the relationships with fractional anisotropy (FA) to be marginally strong, with excellent significance in the corpus callosum, and moderate significance in the internal capsule ( $p=0.000$  for both comparisons). In addition, a significant relationship was found between consciousness and whole brain white matter. The correlation between FA and consciousness was significant for whole brain white matter, and the corpus callosum, as well as internal capsule.

**Conclusion:** This systematic review and meta-analysis demonstrated that diffusion tensor imaging can be used to assess levels of consciousness in patients with traumatic brain injury.

Zhang, J et al. Correlations between Diffusion Tensor Imaging and Levels of Consciousness in Patients with

Traumatic Brain Injury: A Systematic Review and Meta-Analysis. **Scientific Reports.** DOI: 10. 1038/ S4-1-5 9 8-0 1 7-0 295 0-3.

### **COMPOUNDS THAT MIMIC BENEFICIAL EFFECTS OF CALORIE RESTRICTION**

Previous studies have demonstrated that limiting the amount of food while maintaining necessary nutrients suppresses the progression of diseases and the aging process. As self-restraint/calorie restriction is difficult, some have looked to develop drugs that mimic the effects of calorie restriction without limiting food intake. These have included antidiabetic drugs, sirtuin activators, hyperlipidemic drugs, immunosuppressive drugs, antihypertensive drugs and hormone receptive activators. This literature review assessed the data concerning the life extending effects of these medications, adding taurine, as a recently suggested candidate.

Among those drugs found to have life extending properties were metformin, with a target of LKBI, simvastatin, with a target of HMG-COA reductase, metoprolol, with a target of ACE, rapamycin, with a target of mTOR, Rikkunshito, with a target of GHS-R and Taurine, with various targets.

**Conclusion:** This study demonstrates that metformin, simvastatin, metoprolol, rapamycin, rikkunshito and taurine all have evidence of lifespan extension by acting as calorie restriction mimetics.

Nishizono, S., et al. Mechanisms of Action of Compounds that Mimic Beneficial Effects of Calorie Restriction Such as Lifespan Extension: Is Taurine a Promising Candidate? **J Phys Fit Sports Med.** 2017; 6-4: 201-207.

### **LUMBAR SPINE STENOSIS SURGERY FOR OCTOGENARIANS**

Degenerative lumbar spine stenosis causes functional disability, with back and lower extremity pain, particularly in older individuals. This study investigated the effect of decompressive surgery without fusion in patients over the age of 80 years.

This retrospective study included all patients 80 years of age and older who underwent decompressive

surgery for symptomatic lumbar spinal canal stenosis between January of 2006 and August of 2013. Of the 121 patients identified, 82% were alive at the time of follow-up (November through December of 2013), with questionnaires completed by 72 patients. The participants were queried for the severity of pain symptoms, using a visual analog scale, and for walking distance, compared prior to and after surgery. Patient satisfaction scores were also obtained.

The VAS scores improved from an average of 7.2 at baseline to 4.5 at follow-up ( $p<0.001$ ), while walking distance improved from a mean of 147 m to 340 m at follow-up ( $p<0.001$ ).

**Conclusion:** This retrospect of study of patients, 80 years of age or older, all undergoing lumbar spine stenosis decompression, found significant improvement in pain and function after surgery.

Antoniadis, N., et al. Decompression Surgery for Lumbar Spinal Canal Stenosis in Octogenarians: A Single Center Experience of 121 Consecutive Patients. **Br J Neurosurg.** 2017, February; 31(1); 67-71.

### **SUBREGIONS OF THE PREFRONTAL CORTEX AND RECOVERY OF LANGUAGE AFTER STROKE**

Previous studies of language recovery after stroke have focused on regions that are classically considered to have language-specialized functions. Others have noted that the integrity of language also depends on domain-general brain systems which have a much broader function. This study investigated the relationship between cingular-opercular network activity and the longitudinal recovery of speech production after stroke.

Subjects were 27 patients with left hemisphere stroke and matched controls. All participants underwent event related, functional magnetic resonance imaging (fMRI) tasks within two weeks of stroke and then at four months post-stroke. The task-evoked, regional brain activations were compared with the longitudinal measure of recovery of language production.

The MRI data revealed that total lesion volume, percentage damage to



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a large, left lateralized, frontal-temporal-parietal language network and the domain general cingular-operacular network all correlated negatively with language outcome at four months. The task-evoked, regional brain activations within the pre-supplementary motor area/dorsal anterior cingulate during speech production correlated positively with recovery of speech, both in the early and in the late phase. In addition, pre-supplementary motor area/dorsal anterior cingulate activity predicted language recovery over time above that predicted by lesion volume, age or initial language impairment.

**Conclusion:** This study of patients with ischemic stroke found that the function of the pre-supplementary motor area/dorsal anterior cingulate contributes to language recovery after stroke.

Geranmayeh, F., et al. Domain-General Subregions of the Medial Prefrontal Cortex Contribute to Recovery of Language after Stroke. *Brain*. 2017, July; 140(7): 1947-1958.

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