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VAGUS NERVE STIMULATION FOR MIGRAINE

As the Prospective Study of nVNS for the Acute Treatment of Migraine (PRESTO) study demonstrated that noninvasive vagal nerve stimulation (nVNS) can safely and significantly decrease the pain of migraine, this study reports on data from that trial which addressed the consistency and durability of this treatment.

This multicenter, double-blind, controlled study included patients 18 to 75 years of age previously diagnosed with migraine. Within 20 minutes of migraine onset, those in the treatment group received self-administered, 120-second sham or actual nVNS stimulation to both sides of the neck. The participants recorded pain levels for up to 48 hours after completion. The endpoints were percentages of all treated attacks achieving freedom from pain, pain relief, the difference between groups in mean change in pain scores, the number of rescue medications used per migraine attack and the sustained treatment response.

Data were available for 237 participants. The percent of all attacks that were pain-free were greater in the treatment group than in the sham group at 60 minutes (16.3% versus 8.6%) and at 120 minutes (22.9% versus 14.8%). The percentages of attacks with pain relief at 60 minutes and 120 minutes were significantly greater in the treatment group than in the sham group ($p=0.025$ and $p=0.018$, respectively). For the first attack, the treatment group had significantly greater decreases than the sham group in mean pain scores from baseline at 60 minutes and 120 minutes ($p=0.029$ and $p=0.011$, respectively).

Conclusion: This study of patients with episodic migraine found that vagus nerve stimulation is effective for pain reduction for up to two hours after the event.

Martelletti, P., et al. Consistent Effects of Non-Invasive Vagus Nerve

Stimulation (nVNS) for the Acute Treatment of Migraine: Additional Findings from the Randomized, Sham-Controlled, Double-Blind PRESTO Trial. *J Headache Pain*. 2018. 19: 101. doi: 10.1186/s10194-018-0929-0.

RESISTANCE EXERCISE AND CARDIOVASCULAR DISEASE

While the cardiovascular benefits of aerobic exercise have been well documented, most studies of resistance exercise have focused on bone health, physical function and quality of life. This study investigated the effect of resistance exercise on the risk of cardiovascular disease (CVD).

The Aerobics Center Longitudinal Study included 12,591 participants, 18 to 89 years of age. All underwent baseline, comprehensive medical examinations, with sociodemographic and lifestyle data also gathered. The subjects answered questions about their aerobic and resistance exercise during the previous three months. Four categories of resistance exercise exposure were established by total time, including zero, one to 59 minutes, 60 to 119 minutes and more than 120 minutes per week. The primary endpoint was CVD mortality.

At 10.5-year follow-up, among the 12,591 participants, there were 276 all-cause deaths. Compared with no resistance exercise, up to 60 minutes was associated with a 40 to 70% decreased risk of total CVD events, independent of aerobic exercise. No further reductions were found with resistance exercise of greater than 60 minutes per week.

Conclusion: This prospective study of adults up to 90 years of age found that up to one hour per week of resistance exercise is associated with a significantly reduced risk of cardiovascular events.

Liu, Y., et al. Associations of Resistance Exercise with Cardiovascular Disease Morbidity

and Mortality. *Med Sci Sports Exerc*. 2019, March; 51(3): 499-508.

EFFECT OF BOTULINUM MIGRAINE PROTOCOL ON AFFECT

Depression and anxiety are often comorbid with migraine. Studies have suggested a shared etiology or underlying pathway for depression and migraine. This study, the Chronic Migraine OnabotulinumtoxinA Prolonged Efficacy Open Label Study, explored the affective outcomes of patients undergoing long-term onabotulinumtoxinA management of chronic migraine.

This international, multicenter, open label, prospective study included adult patients with chronic migraines. All subjects underwent injections of onabotulinumtoxinA, 155 units, every 12 weeks for nine treatment cycles. The primary outcome variable was the change from baseline in headache days. Additional outcome measures included the Patient Health Questionnaire (PHQ-9), the Generalized Anxiety Disorder (GAD) measure, the Pittsburgh Sleep Quality Index (PSQI), and the Fatigue Severity Scale (FSS).

A significant reduction in headache days was noted at week 24 relative to baseline. For the 529 patients with depressive symptoms at baseline, PHQ-9 scores were significantly improved beginning at 12 weeks, continuing through final follow-up at 108 weeks ($p<0.001$ for all comparisons). This finding also held true for GAD anxiety scores ($p<0.001$), PSQI scores ($p<0.001$) and FSS ($p<0.001$) scores.

Conclusion: This study found that patients treated with onabotulinumtoxinA for chronic migraine headaches experienced significant reductions in symptoms of depression and anxiety.

Blumenfeld, A., et al. Effects of OnabotulinumtoxinA Treatment for Chronic Migraine on Common

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Comorbidities Including Depression and Anxiety. **J Neurol Neurosurg Psychiatry.** 2019; 90: 353-360.

CHRONIC MIGRAINE TREATMENT

Chronic migraine (CM) occurs in 1.4% to 2.2% of adults globally. The efficacy and safety of onabotulinumtoxin A for the prevention of migraine was first established in the PREEMPT trial. The COMPEL study was designed to extend the understanding of the long-term management of CM by evaluating the efficacy and safety of onabotulinumtoxin A after nine treatments (108 weeks).

This open label, prospective study included adults with CM, randomly assigned to 155 units of onabotulinumtoxinA or placebo every 12 weeks for nine treatment cycles. The primary outcome measure was the change from baseline headache days per 28 days, with secondary outcomes including changes from baseline headache days at week 60 and the six-item Headache Impact Test score.

Of the 716 people enrolled, 641 completed a headache diary for the 28 days of screening. Of these, 21.5% met study criteria for daily headache. The number of headache days was reduced from baseline to the second treatment, and continued throughout the 108-week study. Of those with daily headache, 17% had a 50% or greater reduction in frequency at week 24, falling to 39% at week 108.

Conclusion: This study of patients with daily migraine headaches found that onabotulinumtoxinA is associated with reduced headache day frequency and improvements in disability and quality of life for up to 108 days.

Young, W., et al. Effects of OnabotulinumtoxinA Treatment in Chronic Migraine Patients with and without Daily Headache at Baseline: Results from the COMPEL Study. **J Headache Pain.** 2019; 20: 12.

DULOXETINE AND PAIN AFTER TOTAL KNEE ARTHROPLASTY

Central sensitization due to chronic knee pain can occur in the 20 to 40% of those with advanced osteoarthritis of the knee. This is a known risk factor for persistent pain after total knee arthroplasty (TKA). This study investigated the effect of

duloxetine for pain reduction among patients with centralized pain undergoing TKA.

This prospective, randomized, clinical trial enrolled patients scheduled for TKA. All were screened preoperatively with the Central Sensitization Inventory (CSI). Those with scores of 40 or greater were invited to participate. Eighty patients were randomized to either a duloxetine group or a control group. The treatment group took 30 mg of oral duloxetine the night before surgery, and then 30 mg per day for six weeks. All received 200 mg of celecoxib and 150 mg of pregabalin two hours preoperatively for preemptive pain control. The primary outcome measure was a visual analogue scale (VAS) for pain severity, as assessed by the sensory dimension of the Brief Pain Inventory.

Those in the treatment group had better average and worst VAS pain scores during postoperative weeks two through six, ($p<0.01$) and week 12 ($p=0.014$). Pain while walking, resting and at nighttime was superior in the duloxetine group beginning at two weeks and continuing through 12 weeks ($p=0.012$ for resting pain at 12 weeks and $p<0.01$ for all other comparisons). There was no significant difference in adverse medical reactions between the groups.

Conclusion: This study of patients with centralized pain, each undergoing total knee arthroplasty, found that treatment with duloxetine beginning the day before surgery and continuing for 12 weeks resulted in significantly less pain beginning at two weeks post-surgery.

Koh, J., et al. Duloxetine Reduces Pain and Improves Quality of Recovery following Total Knee Arthroplasty in Centrally Sensitized Patients. **J Bone Joint Surg.** 2019, January 2; 101 (1): 64-73.

HEART RATE VARIABILITY AFTER CONCUSSION

Modulations between sympathetic and parasympathetic branches of the autonomic nervous system during physiologic stimuli are determinates of spontaneous heart rate variability (HRV). In the traumatic brain injury (TBI) population, reductions in HRV have been found to be proportional to the severity of TBI and also associated with worse outcome. This study assessed whether HRV at rest and while performing cognitive tests is affected after concussion.

Participants were 23, high-level athletes with a sports-related concussion and 23, matched athletes without. A continuous R-R interval was acquired using a three-lead electrocardiogram for three minutes at rest and during a cognitive test (2-Back task). This task was designed to measure sustained attention and executive function. The HRV was quantified as percent of high frequency power (HFP).

At rest, no difference was observed between groups in heart rate, blood pressure or respiratory rate. The concussed group reported higher symptom number and severity than the controls. At rest, lower HFP was found in the concussed athletes as compared to the controls ($p=0.0027$). During the cognitive task, higher HFP was observed in the concussed group ($p=0.0008$) as compared with rest, with no such difference in the controls. Enhanced HRV reactivity during the cognitive task was observed in the concussed group, as measured by increases in high HFP.

Conclusion: This study found that athletes with concussions demonstrate lower resting heart rate variability as early as four days after concussion, with a mild cognitive task eliminating the differences in heart rate variability between concussed and control groups.

Huang, M., et al. Reduced Resting and Increased Elevation of Heart Rate Variability with Cognitive Task Performance in Concussed Athletes. *J Head Trauma Rehabil.* 2019, Jan/ Feb; 34(1): 45-51.

METAL CHAPERONES FOR BRAIN INJURY

Traumatic brain injury (TBI) literature suggests that zinc homeostasis may be an important factor in the pathobiology of brain injury. Fluctuations in zinc are hypothesized to be neurotoxic, potentially through excitotoxicity, and are thought to contribute to neurodegeneration. This animal study assessed the effect of a zinc chelator, PBT2, for the treatment of acute brain injury.

The subjects were male mice, all of whom underwent controlled cortical impact, designed to produce a TBI. The animals were then randomized to be gavaged with vehicle or PBT2 30mg/kg once per day for the duration of the study. All underwent behavioral assessment, followed by postmortem histological assessment.

At 24 hours, no significant difference in lesion volume was seen between the treatment and control groups. At seven days, however, the PBT2 group had a significantly smaller lesion area ($p=0.01$). Histological assessment demonstrated a greater decrease in lesion area and a greater increase in the numbers of neurons in the treatment group, as compared to the control group. In addition, cognitive assessment, using the Y-maze test, and motor assessment, using a rotarod test, were normalized in the treatment group and maintained throughout the 26 days of the study.

Conclusion: This animal study provides evidence that a metal chaperone may be effective in reducing the effects of a traumatic brain injury.

Portbury, S., et al. Metal Chaperones: A Novel Therapeutic Strategy for Brain Injury? *Brain Inj.* 2019; 33 (3): 305-312.

CARPAL TUNNEL SYNDROME PRESENTING WITH ULNAR DISTRIBUTION SYMPTOMS

Symptoms of carpal tunnel syndrome are traditionally seen in the distribution of the median nerve. This prospective study was designed to determine the prevalence of subjects with median nerve neuropathy who present with symptoms of pain and/or paresthesias in the ulnar nerve distribution.

The study included patients between 20 and 75 years of age, with each contacted to complete a computer-based survey evaluating general health and well-being. Within the questionnaire were evaluations of hand symptoms, including localization and severity. The degree of impairment resulting from the symptoms was measured by the Boston Carpal Tunnel Questionnaire Symptoms Severity Scale. Ulnar neuropathy was defined as a score of greater than two and localization of symptoms in the small and ring fingers. Subjects then underwent a physical examination, which included electrodiagnostic testing and ultrasound evaluation.

From the questionnaires, 30 subjects were diagnosed with ulnar neuropathy. Of those, 37% had exclusive median nerve neuropathy at the wrist, based on electrodiagnostic criteria. In addition, 30% had ulnar nerve pathology, based on electrodiagnostic and/or ultrasound test results. Of these,

nine subjects, six had ulnar nerve neuropathy based on ultrasound criteria only, and three based upon both electrodiagnostic and ultrasound criteria.

Conclusion: This study found that, of patients presenting with ulnar nerve distribution symptoms, 37% were diagnosed with median nerve neuropathy, as determined by electrodiagnostics.

Colorado, B., et al. Prevalence of Carpal Tunnel Syndrome Presenting with Symptoms in an Ulnar Nerve Distribution: A Prospective Study. *Musc Nerve.* 2019, January; 59(1): 60-63.

HYDRODISSECTION FOR CARPAL TUNNEL SYNDROME

Carpal tunnel syndrome (CTS) is a common nerve entrapment that can be treated by conservative or surgical intervention. Hydrodissection is a procedure involving the injection of fluid into anatomic space to facilitate dissection and adhesiolysis. This study was designed to determine the clinical efficacy of nerve hydrodissection for mild to moderate CTS.

This prospective study included 40 patients with mild to moderate CTS of at least three months' duration. All underwent electrodiagnostic testing, with the evaluations performed at baseline and at one, two, three and six months after intervention. The treatment group received an injection of three mL of normal saline (NS) to detach the median nerve from the transverse carpal ligament. An additional two mL of NS was injected to separate the median nerve from the flexor tendons. In the control group, five mL of normal saline was delivered into the subcutaneous region beyond the carpal tunnel. The primary outcome measures were scores on the Boston Carpal Tunnel Syndrome questionnaire and its two subtests, the Symptom Severity Scale (SSS) and the Functional Status Scale (FSS). The secondary outcome was the cross-sectional area (CSA) of the median nerve.

The treatment group demonstrated better improvement than the control group on the SSS, beginning at one month ($p=0.029$) and continuing through six months ($p=0.006$). The treatment group also had superior results on the FSS, beginning at month three ($p=0.016$) and continuing through months six ($p=0.041$). The treatment group had

better recovery at one- and three-months' follow-up in sensory nerve velocities ($p=0.049$ and $p=0.018$, respectively), with the results falling at month six to marginally significant ($p=0.079$).

Conclusion: This study of patients with mild to moderate carpal tunnel syndrome found that hydrodissection with normal saline may improve functional outcome and results on electrodiagnostic measures.

Wu, Y., et al. Nerve Hydrodissection for Carpal Tunnel Syndrome: A Prospective, Randomized, Double-Blind, Controlled Trial. **Muscle Nerve**. 2019, February; 59(2): 174-180.

OUTCOMES THREE YEARS AFTER MINOR LACUNAR OR CORTICAL ISCHEMIC STROKE

While a number of studies have documented stroke risk factors and outcomes, most have used short follow-up periods and have not focused on minor stroke. This study assessed physical and cognitive impairments at three years following minor ischemic stroke.

This prospective study included consecutive patients assessed at the Lothian Stroke Services, Scotland, all diagnosed with a lacunar or minor cortical stroke. Stroke was defined as focal onset of neurologic symptoms lasting more than 24 hours, with a NIHSS score of less than eight, and not expected to result in dependency, as defined by a modified Rankin Scale score of less than three.

The participants were invited for follow-up at one and three years. Data collected included sociodemographic and medical information as well as scores on the modified Rankin Scale, the Clinical Dementia Rating Scale, the Stroke Impact Scale and the European Quality of Life Scale. Those seen in person were assessed for current cognition with the Montréal Cognitive Assessment, Addenbrooke's Cognitive Examination, and the Mini-Mental State Examination.

At three years, of the 264 initial patients, 202 were available to participate. Of those not participating, three percent were deceased. Among the 202, cognitive impairment was found in 44%, depression in 39%, mild dementia in 53% and moderate to severe disability in 12%.

Conclusion: This study of patients with minor ischemic stroke

reveals that long-term cognitive and physical dysfunction is common.

McHutchison, C., et al. Functional, Cognitive and Physical Outcomes Three Years after Minor Lacunar or Cortical Ischaemic Stroke. **J Neurol Neurosurg Psychiatry**. doi: 10.1136/jnnp-2018-31913.

INFARCT LOCATION AND FUNCTIONAL OUTCOME AFTER ENDOVASCULAR THERAPY

This study was designed to determine whether patients who have been treated by endovascular therapy for large vessel occlusion in the anterior circulation demonstrate critical regions of the brain, which when preserved, are associated with a good outcome at three months.

Subjects were patients treated by endovascular therapy for an anterior circulation ischemic stroke within six hours of symptom onset. Using the DWI-ASPECTS scoring system, DWI-visible damage to specific regions were cataloged. The participants were assessed at baseline with the National Institute of Health Stroke Scale and for function at three-months with the modified Rankin scale (mRS). The mRS was compared to DWI-ASPECTS data.

Data were analyzed for 405 patients, including 190 with left-sided and 215 with right-sided strokes. For left-sided strokes, stepwise logistic regression revealed that the preservation of the caudate (OR: 2.07), the internal capsule (OR: 4.55) and the M5 frontoparietal region (OR: 3.39) were correlated with good outcome. For right-sided strokes, the preservation of M3 (OR: 2.89) and M6 (OR: 2.76) were correlated with good outcome.

Conclusion: This study found specific areas of the brain, when preserved after a stroke, are correlated with good functional outcome.

Rosso, C., et al. Impact of Infarct Location on Functional Outcome Following Endovascular Therapy for Stroke. **J Neurol Neurosurg Psychiatry**. 2019; 90(3): 313-319.

EXTERNAL COUNTERPULSATION FOR STROKE RECOVERY

External counterpulsation (ECP) is a noninvasive method to improve perfusion in vital organs. Using an ECG to trigger pressure to lower extremities during diastole, the

technique has been found to reduce systolic afterload and increase blood flow to the heart, brain and kidneys. This study of patients with stroke was designed to determine whether ECP can enhance ipsilateral cortical motor excitability and improve upper limb performance.

Subjects were first ever ischemic stroke patients with upper limb impairment between 14 and 21 days. Exclusion criteria included sustained hypertension and cardioembolic stroke. The patients were randomized to undergo either real or sham ECP, performed one hour per day, with 10 sessions delivered over two weeks. The ECP was delivered at 150 mmHg for the treatment group and at 75 mmHg for the sham group. Both groups received routine rehabilitation treatments. Motor impairment was measured bilaterally with a handgrip dynamometer and a pinch grip, with motor function measured using the Purdue Pegboard Test. Cortical motor excitability was assessed with transcranial magnetic stimulation of the primary motor cortex.

Data were assessed for 30 patients with a mean age of 62 years and a mean interval from stroke onset to baseline assessment of six days. At 30 days, greater improvements were noted in the treatment group than in the control group in handgrip strength, normalized resting motor threshold and normalized evoked potential amplitude ($p<0.001$ for all comparisons).

Conclusion: This study of patients with recent ischemic stroke found that external counterpulsation can improve motor function and cortical motor excitability.

Liu, J., et al. External Counterpulsation Enhances Neuroplasticity to Promote Stroke Recovery. **J Neurol Neurosurg Psychiatry**. 2019, March; 90(3): 362-363.

ENDOVASCULAR TREATMENT FOR MINOR ISCHEMIC STROKE

Endovascular treatment (EVT) for acute ischemic stroke resulting from an intracranial proximal arterial occlusion has been found to be safe and effective. This study was designed to better understand the effect of EVT for patients with minor ischemic stroke caused by an intracranial proximal arterial occlusion of the anterior circulation.

Data were pulled from the MR CLEAN registry, a multicenter, prospective, observational study

involving all stroke intervention centers in the Netherlands. All patients undergoing EVT for acute ischemic stroke were enrolled in the MR CLEAN registry. Of the 1,628 patients registered, 5.5% presented with minor ischemic stroke and 1,221 with moderate to severe ischemic stroke.

Of those with baseline NIHSS scores of five or less, the modified Rankin scale (mRS), administered at 90 days, revealed excellent functional outcomes in 47% and good functional outcomes in 75% of the patients. For those with baseline NIHSS scores of six or more, these figures were 20% and 40%, respectively.

Conclusion: This study, using data from the MR CLEAN registry, found that, of patients presenting with NIHSS scores of five or less, with ischemic stroke due to an intracranial proximal arterial occlusion, undergoing endovascular treatment, almost half achieved an excellent functional outcome.

Goldhoorn, R., et al. Safety and Outcome of Endovascular Treatment for Minor Ischemic Stroke: Results from the Multicenter Clinical Registry of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands. *J Stroke Cerebrovasc Dis.* 2019, March; 28(3): 542-549.

GLUCAGON-LIKE PEPTIDE 1 RECEPTOR AGONISTS

Diabetic stroke patients are prone to a poor clinical outcome. Preclinical animal studies have found that glucose lowering drugs, especially dipeptidyl peptidase 4 inhibitors and glucagon-like peptide -1 receptor agonists (GLP-1R) are associated with neuroprotective properties. However, evidence from human trials is sparse. This meta-analysis was performed to evaluate the effect of GLP-1R on the risk of stroke.

The authors reviewed medical literature through October of 2018. Research terms included GLP-1R cardiovascular, stroke and type II diabetes. Studies were chosen including patients with type II diabetes. All were double-blind, randomized, placebo-controlled trials assessing the effect of treatment with a GLP-1R agonist on the risk of stroke.

Five trials were included in the analysis, with the intervention range from 2.1 to 3.8 years. A pooled analysis demonstrated that, as compared to placebo, treatment with a GLP-1R agonist resulted in a

reduction in the risk of stroke by 13% ($p=0.0006$). In addition, the GLP-1R agonist decreased the risk of nonfatal stroke by 12% and that of fatal stroke by 16%.

Conclusion: This meta-analysis of randomized, controlled trials of patients with type II diabetes found that treatment with GLP-1R significantly reduces the risk of stroke.

Barkas, F., et al. Protection against Stroke with Glucagon like Peptide 1 Receptor Agonists: A Systematic Review and Meta-Analysis. *Eur J Neurol.* 2019. doi: 10.1111/ene.13905.

THERAPEUTIC ELECTRICAL STIMULATION OF INJURED PERIPHERAL NERVE TISSUE

Previous studies have found that thin-film wireless receivers are able to reliably deliver electrical impulses to recruit peripheral nerve tissue and activate distal musculature for the purpose of tracking postoperative functional recovery. This study examined the effect of electrostimulation by an implanted stimulator on the recovery of an injured sciatic nerve.

Subjects were 25 male rats, all undergoing surgical implantation of a wireless nerve stimulator adjacent to the sciatic nerve. Group one served as a control and underwent surgical exposure with no injury. Groups two and three received a crush injury, while groups four and five underwent a transection and repair. Groups three and five received one hour of therapeutic stimulation immediately after surgery. All animals underwent weekly assessment of functional recovery, measured at the gluteus maximus (GM), tibialis anterior (TA), gastrocnemius (GS) and plantaris (PL) muscles.

At four weeks, EMG recordings in TA, GS and PL muscles revealed recovery of, respectively, 35.4%, 38.3% and 43.8% of native function with electrical stimulation, in contrast to 25.1%, 25.8% and 20.4% in its absence. At week 13 post-surgery, the TA, GS, and PL muscles demonstrated recovery of, respectively, 79.0%, 79.2% and 90.0% of native function in the presence of therapeutic electrical stimulation, and 65.4%, 64.2% and 66.8% in its absence.

Conclusion: This study found that a wireless implant successfully delivering therapeutic electrostimulation to injured

peripheral nerve tissue can accelerate functional recovery.

MacEwan, M., et al. Therapeutic Electrical Stimulation of Injured Peripheral Nerve Tissue Using Implantable Thin Film Wireless Nerve Stimulators. *J Neurosurg.* 2019, February; 2:130:486-495.

NON-FAILURE BLOOD FLOW RESTRICTED EXERCISE

Using partial blood flow restriction, low resistance exercise has been shown to stimulate increases in muscle size and function with training loads as low as 20% of the one repetition maximum. However, some studies have found that blood flow restriction exercise (BFRE) may be limited by discomfort and/or pain. This study compared BFRE, performed to volitional failure, with a protocol to non-failure.

Subjects were healthy men, with BFR set at 40% of their resting systolic blood pressure. All participants were initially tested for their one repetition maximum, and then by performing four sets of unilateral knee extensions at 25% of that weight, with each set performed to volitional failure (VF). The contralateral leg served as a non-failure group (NF), for which number of repetitions was set at 75% of the number reached in the failure trial. On alternate days, the subjects exercised the VF and the NF legs. Training involved 22 bouts, over eight weeks, of knee extension exercises. Strength and muscle volume gains were assessed using cumulative and peak perceived exertion, while discomfort and muscle soreness were evaluated.

Both groups had increases in muscle cross sectional area (CSA), with ranges of 2.5% to 3.8% for the quadriceps, 8.1% to 8.5% for the vastus lateralis and 7.9% to 25.0% for the rectus femoris, with no significant differences noted between the groups. In addition, significant increases were noted in maximal isometric strength (18% for both) and maximal dynamic strength (10.7% for the VF group and 13.8% for the NF group), with no significant difference between the groups. The accumulated rates of discomfort and peak discomfort were all greater in the VF group, as were accumulated and peak ratings for exertion.

Conclusion: This study, using partial blood flow restriction (40% of SBP) found that training at 25% of the one-repetition maximum, with repetition set at 75% of the number to

individual failure, resulted in similar strength and mass gains, as does exercise to failure, with significantly less discomfort.

Sieljacks, P., et al. Non-Failure Blood Flow Restrictive Exercise Induces Similar Muscle Adaptations and Less Discomfort than Failure Protocols. *Scan J Med Sci Sports*. 2019, March; 29(3): 336-347.

BRAIN STATE-DEPENDENT STIMULATION FOLLOWING STROKE

Recently, several therapies based on noninvasive brain stimulation have been devised for enhancing the spontaneous biological recovery processes following stroke. This study assessed whether brain state-dependent peripheral stimulation could improve function in patients with stroke.

Subjects were 24 adults with middle cerebral artery stroke within four months of that event. All underwent neuropsychological assessment, had no seizure history and no contraindications to transcranial magnetic stimulation. The participants were divided into an intervention group and a sham group, all with three sessions per week for four weeks. The subjects were asked to watch a screen on which a cue provided information regarding when to attempt dorsiflexion of the affected leg. They were cued to attempt the movement while brain activity was assessed. At the time of the peak negative phase of the movement—the related cortical potential was determined during the first 30 trials, with subsequent trials using this time to provide an output command for an electrical stimulator. The stimulator applied a single, one ms pulse to the deep branch of the common peroneal nerve. The induced sensory signal provided by the stimulation was timed to arrive at the motor cortex during the time of maximum activation of the motor cortex as seen in the EEG.

During intervention sessions, corticospinal output properties were assessed using TMS. Baseline follow-up assessments were made using clinical and behavioral measures, including the Modified Rankin Scale, the LAD-FIM Motor Performance Assessment and the Ashworth Scale for Spasticity and Functional Ambulation Classification.

The treatment group demonstrated significantly better recovery than the control group as measured by lower extremity Fugl-Meyer scores ($p=0.029$). In addition, a significant increase in motor evoked potential amplitude was observed in

all sessions in the associated group, but in none in the control group.

Conclusion: This study of patients with a recent stroke found that by timing peripheral nerve stimulation with TMS-determined cortical activity, the motor recovery could be accelerated.

Mrachacz-Kersting, N., et al. Brain State-Dependent Stimulation Produced Functional Recovery following Stroke. *Ann Neurol*. 2019, January; 85(1): 84-95.

CONTEMPORARY DANCE INJURIES

Contemporary dance requires long hours of training with repetitive movements. This study was designed to establish the extent and characteristics of injuries in contemporary dance students.

Subjects were 134 contemporary dance students enrolled in a four-year educational program of dance. During the first month of the academic year, baseline characteristics were recorded, with the students then asked to complete monthly questionnaires using the Performance Artists' and Athletes' Health Monitor. An injury was defined as any physical complaint sustained by a dancer resulting in a severity score of greater than zero and leading to a reduction in participation in training, a reduced volume of training or decreased performance. Exposure was defined as one dancer participating in one class, rehearsal or performance.

During the academic year, 96.9% of the students reported at least one injury, mental complaint or other health problem, with 64.3% reporting a substantial health problem. The percentage of subjects who reported an injury in one academic year was 81%, of whom 58.1% reported a substantial injury. For any one month, the percentage of students reporting an injury ranged from 23.1% to 42.6%. For the year, the incidence of injury was 1.9 per 1,000 hours of exposure. The anatomical regions with most injuries were ankle/foot (30%), lower back (17.3%) and knee (14.6%).

Conclusion: This prospective study of dance students found the one-year incidence of injury to be 81%, of which 58% were substantial.

van Winden, D., et al. Detailed Injury Epidemiology in Contemporary Dance: A One-Year, Prospective Study of 134 Students. *BMJ Open Sport Exer Med*. 2019; doi:10.1136/bmjsem-2018-000453.

IMMOBILIZATION FOR STABLE ANKLE FRACTURES

Data have shown that 70% of ankle fractures are Weber type B fibula fractures. Traditional non-operative treatment of stable Weber B fractures involves below the knee casting for six weeks. However, after cast removal, common sequelae include ankle stiffness and deep vein thrombosis. This study compared the outcomes of patients immobilized by casting for three versus six weeks.

Subjects with stable Weber B fractures were randomized in a 1:1:1 ratio to receive six-week casting, three-week casting or three-week immobilization with an orthosis. The primary outcome measure was the Olerud-Molander Ankle Score (OMAS), as measured at 52 weeks. Secondary outcome measures included the Foot and Ankle Outcome Score, the RAND 36-Item Health Survey and range of motion of the ankle.

Subjects included 247 patients, with 86% available at 52-week follow-up. At 52 weeks, the mean OMAS scores were 87.6 for the six-week cast group, 91.7 for the three-week cast group and 89.8 for the three-week orthosis group. Asymptomatic deep vein thrombosis was diagnosed in eight patients, five in the six-week cast group, three in the three-week cast group and none in the orthosis group. Two cases of nonunion were found, both in the three-week cast group.

Conclusion: This study of patients with stable Weber B type fibular fractures found that three-week immobilization, either in a traditional cast or a simple orthosis, results in ankle function and healing that is noninferior to conventional cast immobilization of six weeks.

Kortekangas, T., et al. Three-Week versus Six-Week Immobilization for Stable Weber B Type Ankle Fractures: Randomized, Multicenter, Noninferiority Clinical Trial. *BMJ*. 2019; 36: K5432.

DURATION OF SURGERY AND POSTOPERATIVE DELIRIUM AFTER HIP FRACTURE REPAIR

Research has shown that elderly patients with fractures are vulnerable to post-operative delirium, with the incidence ranging from five percent to 61%. This prospective study addressed the association between the duration of hip fracture surgery and the risk for postoperative delirium in elderly adults.

This population-based cohort study used administrative data from Ontario Canada. Subjects were patients who received acute surgical management for hip fracture between April 1, 2009, and March 31, 2017. Procedures shorter than 30 minutes or longer than 240 minutes were excluded. Diagnoses, comorbidities and sociodemographic data were recorded. The primary outcome variable was the occurrence of postoperative delirium during hospitalization.

Of the 68,131 patients identified, 7,150 were diagnosed with postoperative delirium. Compared with those who received a regional anesthetic, those receiving a general anesthetic had a slightly higher rate of postoperative delirium (11% versus 10.2%; $p=0.001$). After controlling for comorbidities, increased surgical duration was associated with an increased risk of delirium, with an adjusted odds ratio of 1.06 per 30 minutes of surgery ($p<0.001$). This association was stronger among those receiving general anesthesia than among those receiving a regional anesthetic.

Conclusion: This cohort study of elderly patients undergoing hip fracture surgery found a significant association between length of surgery and risk of postoperative delirium.

Ravi, B., et al. Association of Duration of Surgery with Postoperative Delirium among Patients Receiving Hip Fracture Repair. **JAMA Open**. 2019, Feb; 22: 4-11.

FISH CONSUMPTION AND STROKE RISK

Studies concerning the health benefits of fish and cardiovascular disease have produced inconsistent results. This meta-analysis was designed to better understand the association between fish consumption and cerebrovascular health.

Data were reviewed from prospective, cohort studies evaluating the association between fish intake and stroke risk in adults. Of the 33 studies chosen, 31 were published between 1994 and 2018.

The pooled, adjusted hazard ratio (HR) of stroke risk for the highest fish consumption as compared to the lowest was 0.90. Additional analysis revealed that there was a borderline significant relationship between fish consumption and stroke mortality (HR 0.92). When separating by gender, the HRs for stroke were 0.97 for men and 0.83 for women. By stroke subtype, the association was more pronounced for hemorrhagic stroke

(HR 0.88), with an insignificant trend for ischemic stroke (HR 0.96). There was no significant association between stroke risk and any specific types of fish.

Conclusion: This meta-analysis found that fish consumption is associated with a decreased risk of stroke.

Zhao, W., et al. Fish Consumption and Stroke Risk: A Meta-Analysis of Prospective Cohort Studies. **J Stroke Cerebrovasc Dis**. 2019, March; 28 (3): 604-611.

ELECTRONIC CIGARETTES VERSUS NICOTINE REPLACEMENT FOR SMOKING CESSATION

Previous studies have suggested that electronic cigarettes (EC) with nicotine are more effective for smoking cessation than nicotine-free ECs. This study evaluated the one-year efficacy of refillable ECs as compared with nicotine replacement for patients seeking help in cessation of tobacco abuse.

This multicenter trial was completed from May of 2015 to February of 2018. Smokers were recruited and randomized to an EC group or to receive a nicotine replacement product, choosing from several delivery options (patch, gum, lozenge, nasal spray, inhalator, mouth spray, mouth strip or microtabs). Those in the EC group received refillable EC products with nicotine at a concentration of 18 mg/mL. Trial data were recorded, including smoking status, carbon monoxide levels, ratings of trial products, withdrawal symptoms and sleep disturbances. The primary outcome variable was sustained abstinence from tobacco use.

A total of 439 subjects were randomized to the EC group and 447 to the nicotine replacement group. The rates of sustained abstinence at one year were 18% in the EC group and 9.9% in the nicotine replacement group ($p<0.001$). The ECs were rated by the participants as more satisfying than were nicotine replacement products.

Conclusion: This prospective study found that, among adults requesting assistance with cigarette cessation, those using e-cigarettes were more successful than were those using nicotine replacement products.

Hajek, P., et al. A Randomized Trial of E-Cigarettes versus Nicotine Replacement Therapy. **N Engl J Med**. 2019, February 14: 380(7): 629-637.

DYNAMIC BALANCE AND RISK OF CONCUSSION

Evidence suggests that, after a concussion, athletes are at a higher risk of sustaining a repeat concussion. This study investigated the association between dynamic balance performance and the risk of future concussion.

Subjects were 109, elite, male rugby union players from four senior Irish teams. All subjects underwent baseline testing sessions, and were fitted with a single inertial sensor, mounted at the level of the fourth lumbar vertebrae to match the body's center of mass. While wearing the sensor, the participants completed four practice trials and three recorded trials of the pre-defined directions of the Star Excursion Balance Test (YBT).

Reach distances were normalized to each individual according to leg length. The subjects were followed during the ensuing rugby season, with the incidence of training or match related concussion recorded. Independent variables included self-reported concussion history, playing position, age group, dynamic balance variables and gyroscope magnitude signal during each YBT excursion.

Of the 109 players, 44 had a history of concussion with 21 sustaining a concussion in the follow-up season. Those with suboptimal YBT performance at baseline were 2.81 times more likely to sustain a concussion during the following season, even after controlling for concussion history.

Conclusion: This study of professional rugby players found that those with suboptimal balance at baseline had a significantly increased risk of concussion during the following season.

Johnston, W., et al. Association of Dynamic Balance with Sports-Related Concussion: A Prospective Cohort Study. **Am J Sport Med**. 2019; 47 (1): 197-205.

EFFECTS OF BETA AMYLOID AND TAU ON COGNITIVE DECLINE

The two hallmark pathologies of Alzheimer's disease are amyloid-beta ($A\beta$) and tau. This study investigated the association of $A\beta$ and tau imaging markers in prospective cognitive trajectories of clinically normal participants.

A total of 137 participants from the Harvard Aging Brain Study were studied. All had a baseline global clinical dementia rating of zero and a Mini-Mental Status Examination of 27 or higher. All subjects underwent

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frequent cognitive assessments, as well as positron emission tomography to measure A β and tau. The PET studies were compared to cognitive change. In addition, all subjects underwent blood tests for APOE characteristics.

Older age was associated with higher continuous cortical A β (p=0.034). In addition, higher A β was associated with higher tau, independent of age (p<0.001). After controlling for age, continuous levels of A β were found to be associated with greater longitudinal decline in the memory composite, but not in executive function. By anatomical location, higher levels of A β in the medial orbital and lateral prefrontal, posterior cingulate, precuneus and lateral parietal regions were associated with worsening memory performance (p<0.001). Rapid, prospective memory decline was observed in participants who had high levels of both A β and tau.

Conclusion: This study found that both amyloid beta and tau are important for memory decline in the preclinical stages of Alzheimer's disease.

Sperling, R., et al. The Impact of Amyloid-Beta and Tau on Prospective Cognitive Decline in Older Individuals. *Ann Neurol.* 2019, February; 85(2): 181-193.

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