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VESTIBULAR NERVE STIMULATION FOR INSOMNIA

Insomnia is a prevalent health condition, characterized by difficulty initiating or maintaining sleep as well as dissatisfaction with sleep quality or quantity. As the vestibular system is known to affect sleep, vestibular nerve stimulation has been trialed, demonstrating this procedure to be safe and effective. This study was designed to better understand the effect of repeated electrical vestibular nerve stimulation (VeNS), applied at home for adults experiencing insomnia symptoms.

This randomized, double-blinded, sham-controlled trial included patients complaining of moderate to severe insomnia. The participants were instructed to use their allocated VeNS device at home for 30 minutes a day, over four weeks. The treatment device was the Modius Sleep, a portable battery-operated vestibular nerve stimulation device with electrodes placed over the mastoid processes, set at 0.25Hz, with stimulation at 0.1 mA-1.0 mA (titrated until a subjective feeling of swaying). The placebo group used a visually similar sham device. The primary outcome measure was the Insomnia Severity Index (ISI), with secondary outcomes including the Pittsburgh Sleep Quality Index (PSQI), health related quality of life, assessed with the SF-36, and caffeine diaries.

Data were obtained from 126 participants who completed the intervention. Both groups demonstrated improvement in ISI scores. Compared to the control the VeNS group had a mean ISI score reduction 2.26 times greater than the control (p=0.002). Greater improvement was also noted in the SF-36 energy/fatigue component (p=0.004).

Conclusion: This study of patients with chronic insomnia found that a non-invasive stimulation of the vestibular nerve may be an effective treatment option.

Curry, G., et al. Repeated Electrical Vestibular Nerve Stimulation (VeNS) Reduces Severity in Moderate to Severe Insomnia; A Randomized, Sham-Controlled Trial; The Modius Sleep Study. **Brain Stim**. 2024, May 24 https://doi.org/10.1016/j.brs.2024.05.010.

LONELINESS AND MEMORY IN THE ELDERLY

Memory loss in the elderly is frequently exacerbated by preventable social factors. This study examined the association between combinations of social isolation and loneliness in a large study of middle age and older adults.

Data were obtained from the Tracking cohort of the Canadian Longitudinal Study on Aging (CLSA). Social isolation (SI) was quantified using a scale which awarded points for; living alone, retired and engaged in ≤ one social activity/month, <monthly visits with friends/neighbors, <monthly visits with children, <monthly visits with family. Loneliness was measured by asking, “In the last week, how often did you feel lonely?” Responses were scored on a four-point Likert scale. All responses were dichotomized to create four groups, only social isolation (I), only lonely (L), both isolated and lonely (I+L), neither isolated nor lonely (N). Memory was assessed using a modified version of the Rey Auditory Verbal Learning Test (RAVLT), with these results compared to the four categories.

Data were analyzed from 12,234 participants. Of these, 82.9% were neither socially isolated nor lonely, 7.88% were only socially isolated, 7.98% were only lonely, and 1.23% were both isolated and lonely. Both SI and L were significantly and inversely associated with memory (p<0.001 for both). A multivariable mixed effects regression analysis revealed that the worst memory occurred in the I+L group, followed by the L group, and then by the I group, with the least memory disruption seen in the N group. The prevalence of impaired memory was twice as high in the I+L group, compared to the N group.

Conclusion: This large study found that memory is adversely affected by social isolation and feelings of loneliness, with the worst memory impairment found among those who experience both.

Kang, J., et al. Exploring the Differential Impacts of Social Isolation, Loneliness, and Their Combination on the Memory of an Aging Population: A Six-Year Longitudinal Study of the CLSA. **Arch Gerontol Geriatr**. 2024; 125: 105483.

TIROFIBAN TO REDUCE NEUROLOGIC DETERIORATION AFTER ISCHEMIC STROKE

After an acute ischemic stroke (AIS), five to 40% of patients experience neurological deterioration (ND), leading to poorer outcomes and increased morbidity. Tirofiban is a selective inhibitor of the platelet glycoprotein IIb/IIIa receptor, which prevents thrombus formation by inhibiting the common pathway for platelet aggregation. This study assessed the efficacy of Tirofiban for the prevention of ND after an AIS.

The subjects were patients 18 to 80 years of age who presented with an AIS within 24 hours of symptom onset, with an NIHSS score of four to 20 points. Those participants were randomized to receive aspirin (150-300mg/day) or intravenous Tirofiban for up to 72 hours. The primary efficacy endpoint was early ND, defined as an increase in NIHSS score of four or more points at any time within 72 hours.

Of 682 patients screened at 10 comprehensive stroke centers, 425 were selected for participation. Early ND was diagnosed in 4.2% in the treatment group and 13.2% in the aspirin group (p<0.002). Tirofiban appeared to be more effective in those over 60 years of age, and in

those without pre-stroke antiplatelet therapy. No patients in the treatment group experienced an intracerebral hemorrhage.

Conclusion: This study of patients with acute ischemic stroke found that treatment with Tirofiban within 24 hours of stroke onset resulted in a significant decrease in the risk of neurologic deterioration.

Zhao, W., et al. Effects of Tirofiban on Neurological Deterioration in Patients with Acute Ischemic Stroke. A Randomized, Clinical Trial. **JAMA Neurol**. 2024. doi: 10.1001/ jamaneurol.2024.0868.

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LOWER EXTREMITY CONSTRAINT INDUCED MOVEMENT THERAPY IN CHRONIC STROKE

Between 1990 and 2019, the incidence of stroke has grown by 70%, and the related disability adjusted life years has increased by 32%. Constraint induced movement therapies (CIMT) have been found to be a successful intervention for upper limb recovery following stroke. This study explored the efficacy of lower extremity CIMT (LE-CIMT) for patients with chronic stroke with lower extremity disability.

Participating subjects had a diagnosis of stroke at least six months before study participation, with residual hemiparesis. The participants were randomized to a control group to receive physiotherapy for 2.5 hours per day for 15 days or a treatment group to receive LE-CIMT for three hours per day for 15 days. The primary outcome measures were the Six-Minute Walk Test (6mWT) and the Mini-BESTest (including the subscales of Anticipatory Postural Control, Reactive Postural Control, Sensory Orientation, and Gait Stability). Secondary outcomes included the Six-Minute Walk Test, the Timed Up and Go (TUG), 3-D Gait Analysis (3-DGA), and the Lower Extremity Motor Activity Log (LE-MAL), a subjective scale of effectiveness of use of LE outside of the clinic, with subscales of Assistance, Confidence, and Performance.

At six months follow up, compared to the control group, the LE-CIMT group demonstrated greater improvements on the Mini-BESTest ($p=0.01$), the Six-Minute Walk Test ($p=0.02$), and the LE-MAL subscales of Assistance ($p=0.04$) and Confidence ($p=0.01$).

Conclusion: This study of patients with a chronic stroke found that lower extremity constraint induced therapy, three hours per day for 15 days, could produce significant improvements on the Six-Minute Walk Test, as well as improved confidence in daily activities, balance, and gait capacity.

Menezes-Oliveira, E., et al. Improvement of Gait and Balance Function in Chronic, Post-Stroke Patients, Induced by Lower Extremity Constraint Induced Movement Therapy: A Randomized, Controlled, Clinical Trial. **Brain Inj**. 2024; 38(7): 559-568.

QUALITY OF PLANT BASED DIETS AND FRAILTY INCIDENCE

Frailty is a medical syndrome characterized by reduced physiological reserve and increased vulnerability to health stressors. One of the means by which frailty can be managed is dietary intervention. While research has demonstrated an association between high quality diets and a lower risk of frailty, the evidence regarding plant-based diets is less robust. This study assessed the association between frailty and the quality of plant-based diets.

Data were obtained from the United Kingdom Biobank Cohort, a multi-center, prospective, population-based study with over 500,000 participants, 40 to 70 years of age at enrollment. Up to five dietary assessments were completed, with the results graded using the Healthy Plant-Based Diet Index (PDI). This measure identifies plants that are healthy (hPDI) and those that are unhealthy (uPDI). Frailty was assessed using five criteria (weight loss, exhaustion, low physical activity, slow walking speed, and weak hand grip), then compared to the PDI.

The subjects were 24,996 individuals with a median follow-up of 6.72 years. An adjusted analysis found that those with higher hPDI scores had a lower risk of frailty ($p<0.001$), and that those with higher uPDI scores had an increased risk of frailty ($p<0.001$). In a subgroup analysis, these relationships were consistent for exhaustion, low physical activity, slow walking speed, and weak hand grip.

Conclusion: This large, population-based study of middle age and older adults found that a greater adherence to healthy plant-based diets reduces the risk of frailty, while

unhealthy plant-based diets increased this risk.

Maroto-Rodriguez, J., et al. Quality of Plant-Based Diets and Frailty Incidence: A Prospective Analysis of U.K. Biobank Participants. **Age Ageing**. 2024, May 1; 53(5): afae092. doi: 10.1093/ageing/afae092.

GHRELIN FOR NEUROPROTECTION AFTER CARDIAC ARREST COMA

Ghrelin is an endogenous appetite -stimulating peptide hormone. The activated form, acyl-ghrelin, has shown improved functional and histological brain recovery in experimental models of cardiac arrest and was safe in a wide variety of human study populations. This study, the Ghrelin Treatment of Comatose Patients After Cardiac Arrest: A Clinical Trial to Promote Cerebral Recovery (GRECO) evaluated the effect of acyl-ghrelin in humans, to improve neurological outcomes after a cardiac arrest.

The subjects were adult patients, in comas, after undergoing resuscitation for cardiac arrest. The subjects were randomized to receive either an infusion of acyl-ghrelin, 600 µg, or placebo, twice daily for one week, starting within 12 hours of the cardiac arrest. The primary outcome variable was the cerebral performance category (CPC) scale at six months. Secondary outcomes included mortality and the CPC at three and 12 months. Levels of neuron specific enolase (NSE) were tested on days one and three.

The subjects numbered 160 patients admitted to the ICU after resuscitation. At six months follow-up, the common odds ratio (OR) for any CPC improvement in the intervention group was 1.78 (p=0.06). Mortality occurred in 37% of the treatment group and 51% of the control group. Significantly reduced levels of NSE were found in the treatment group.

Conclusion: This phase two study of patients comatose after cardiac arrest found that intravenous treatment with Ghrelin may have the potential to improve neurological outcome.

Nutma, S., et al. Ghrelin for Neuroprotection in Post Cardiac Arrest Coma: A Randomized, Clinical Trial. **JAMA Neurol**. 2024, May 6:e241088. doi: 10.1001/ jamaneurol.2024.1088.

THROMBECTOMY FOR ISCHEMIC STROKE OF UNRESTRICTED SIZE

In early studies of thrombectomy, due to concerns about the deleterious effects associated with reperfusion of large infarctions, patients with the largest infarctions were excluded from enrollment. This study, the Large Stroke Therapy Evaluation (LASTE) trial, assessed the efficacy and safety of endovascular thrombectomy in patients with large infarctions.

Subjects were 333 patients with proximal cerebral vessel occlusion and a large infarction, defined as an Alberta Stroke Program Early Computed Tomographic Score (ASPECTS) of five or less. Eligible participants presented within 6.5 hours of their last known well (LKW). The patients were randomized to undergo endovascular thrombectomy and to receive medical care (a treatment group) or to medical care alone (a control group). The primary outcome measure was the modified Rankin Scale (mRS) score at 90 days.

The treatment group demonstrated better mRS scores at 90 days than the control group (Odds Ratio [OR] 1.63 [p<0.001]), with this benefit maintained at six months. Death from any cause at 90 days had occurred in 36.1% of the treatment group and 55.5% of the control group. (p<0.001). Symptomatic hemorrhage within 24 hours was observed in 9.6% in the thrombectomy group and 5.7% in the control group.

Conclusion: This study of patients with acute stroke with proximal large vessel occlusion and a large baseline infarction demonstrated that endovascular thrombectomy decreased mortality and improved functional outcome at 90 days.

Costalat, V., et al. Trial of Thrombectomy for Stroke with a Large Infarct of Unrestricted Size. **N Engl J Med**. 2024, May 9; 390(18): 1677-1689.

RISK FACTORS FOR RE-RUPTURE OF HAMSTRING INJURY

Proximal hamstring avulsion injury (PHAI) is a debilitating injury, associated with a forceful flexion of the hip, during full extension of the knee. The treatment of these injuries depends on the degree of retraction, type of tear, chronicity of the lesion, and associated symptoms. This study was designed to better understand the re-rupture rate after a PHAI repair.

This retrospective study used prospectively collected data from the French Proximal Hamstring Evolution Surgery Cohort between January of 2002 and July of 2022. The subjects all underwent primary surgical repair of a PHAI, with a minimum follow-up of 12 months. The primary outcome measure was the post-repair rupture rate.

The sample included 740 participants with a mean age of 45.9 years. The median time from injury to surgery was 26 days. The rate of recurrent rupture, confirmed clinically and by MRI, was 4.59% within the first six months post-surgery. Only three of the 34 re-ruptures occurred after the first year. Those who experienced a significantly longer delay between injury and repair were more likely to experience re-rupture (41 days versus 26 days [p=0.04]). The re-rupture-free survival rates at five years were 93% for the late-surgery group (>32 days) and 97.2% for the early surgery group.

Conclusion: This study of patients undergoing surgical repair of a proximal hamstring rupture found that most re-ruptures occurred within the first six months and are less likely among those who undergo surgery early.

Lefevre, N., et al. Risk Factors for Rerupture after Proximal Hamstring Avulsion Injury, Including the Optimal Timing for Surgery. **Am J Sports Med**. 2024, April; 52(5) 1173-1182.

CHRONIC ANKLE INSTABILIY AND STRENGTH OF KNEE FLEXORS AND EXTENSORS

A relatively high number of individuals experiencing a first ankle sprain injury will develop chronic ankle instability (CAI). Studies have shown that those with CAI have several neuromuscular impairments, including abnormal balance and proprioception. This study explores the effects of CAI on muscle strength at the knee.

The subjects were 15 patients with CAI, with an average age of 32 years. Peak forces were measured during a maximal isometric voluntary contraction of the knee extensor and flexor muscles at 30° and 90° of knee flexion. Muscle activity during testing was assessed by surface electromyography. At both angles, contractions at 20%, 50%, and 80% of the maximal voluntary isometric contraction were used to analyze

strength steadiness and strength accuracy.

Compared to the healthy control group, the CAI group demonstrated a lower knee flexor maximal strength in the injured limb at both 30° and 90° degrees ($p<0.05$ for both). No significant difference was found between groups for the knee extensors. Knee extensor and flexor steadiness was significantly lower in both the injured and non-injured limbs of individuals with CAI, as compared to controls, at both 90°and at 30° degrees. Knee extensor and flexor accuracy was worse in the CAI group than in controls in both the injured and non-injured limbs.

Conclusion: This study found that patients with chronic ankle instability have reduced knee strength, steadiness, and accuracy.

Labanca, L., et al. Individuals with Chronic Ankle Instability Show Abnormalities in Maximal and Submaximal Isometric Strength of the Knee Extensor and Flexor Muscles. **Am J Sport Med**. 2024, May; 52(5): 1328-1335.

ANTIVIRAL EFFECT OF INTRANASAL NEOMYCIN

Human respiratory viruses (HSV) typically begin in the upper respiratory tract, which can then spread into the lower respiratory tract. This paper reports on a multi-stage assessment of intranasal Neosporin (IN) for inhibiting lower respiratory infection by HSV. The authors focused on the effect of IN on interferon stimulated genes (ISGs) as a means to interfere with various stages of the viral life cycle.

In the first experiment, mice were treated with two mg of IN. On days one through seven, the levels of ISG were measured in the nasal turbinate. In a second study, mice were treated with IN, 2 mg or 0.2 mg. One day after IN treatment, the subjects were infected with SARS-CoV-2 or variants of SARS-CoV-2. Viral replication was measured and compared to that of controls. In the next experiment, the mice received a placebo or IN of up to 25 mL per nostril and then inoculated with highly virulent influenza A virus A/PR8. In the final experiment the IN was applied at doses of 2.0 or 0.2 after inoculation with SARS-CoV-2. IN was applied at doses of two or 0.2. The effects of additional doses were tested by the application of additional IN doses on days one and three. Finally, the effects of IN in humans were trialed in a small, pilot, randomized, double-blind, placebo- controlled study.

All studies involving IN demonstrated increased levels of ISG peaking at day three. In all experiments the IN provided antiviral protection against upper and lower respiratory infections, when applied before the exposure, with the effect dose dependent. Twice per day delivery raised ISG levels up to 20 times that of baseline.

Conclusion: This study found that intra-nasal delivery of neomycin (Neosporin cream), a generic aminoglycoside antibiotic, can protect against upper respiratory and lower respiratory infections in a mouse model through the induction of interferon stimulating genes (ISG). In a human model, intranasal neomycin induced ISG, peaking at day three and lasting for 11 days.

Mao, T., et al. Intranasal Neomycin Evokes Broad-Spectrum Antiviral Immunity in the Upper Respiratory Tract. **PNAS**. 2024, April 30: 121(18): e2319566121.

MULTIPLE SCLEROSIS DISEASE ACTIVITY AFTER TWO YEARS OF CLADRIBINE TREATMENT

Among the new disease-modifying therapies (DMTs) for the treatment of Multiple Sclerosis (MS) is cladribine, a purine analogue antimetabolite, which inhibits the action of the adenosine deaminase enzyme. This study investigated the effects of a two-year course of this medication.

This multicenter, retrospective study enrolled 204 patients with MS who had completed two years of treatment with cladribine. Data collection included MRIs, relapse occurrences, and changes in Expanded Disability Status Scale (EDSS) scores at six and 12 months after treatment cessation. Disability was deemed progressive in those whose EDSS scores increased by one point or more. The primary outcomes of the study were all medication choices and clinical disease activity measured as the annualized relapse rate (ARR) following two years of treatment.

Compared to the baseline year, the ARR improved significantly as early as 12 months (< 0.001), confirmed at 24 months ($p < 0.001$). The ARR further decreased after 12 months of follow-up after medication cessation ($p < 0.001$). At 12 months, the probability of starting a new treatment was 12.1%, increasing to 24.6% at 24 months. The most common treatments were ocrelizumab (n=15, 7.4%) and natalizumab (n=8, 3.9%). The probability of starting a new therapy decreased with the patient's age but was not affected by disease activity before treatment onset.

Conclusion: This study of patients with multiple sclerosis found that, after ending 24 months of treatment with cladribine, the relapse rate remained significantly reduced.

Schiavetti, I., et al. Therapeutic Choices and Disease Activity after Two Years of Treatment with Cladribine: An Italian, Multicenter Study (Cladstop). **Euro J Neurol**. 2024 Jun; 31(6): e16250. doi: 10.1111/ene.16250.

UTILITY OF THE MOCA IN ACUTE STROKE

Despite being recommended in stroke guidelines, early cognitive screening is not always implemented. This study examined whether the Montreal Cognitive Assessment (MoCA) adds diagnostic value as compared to clinical observation alone.

This prospective, observational study was conducted between 2021 and 2022 at Maastricht University Medical Center. The subjects were adults who had sustained any kind of stroke (hemorrhagic or ischemic; first or recurrent) confirmed by a neurologist. All had been admitted to the stroke unit. Forty-four stroke patients were screened with the MoCA during the stroke unit admission.

The charts were reviewed to determine whether any cognitive impairments were documented by the stroke care team, who were held blind to screening scores. Proportions of detected cognitive deficits were compared between screening (MoCA scores<26) and patients' charts. Discharge distribution of home versus rehabilitation was also explored.

Thirty-seven patients (84.1%) scored below 26 points on the MoCA. However, cognitive deficits were reported in the chart in only 11 of the patient charts (25%). No significant difference was noted in discharge destination between the two groups.

Conclusion: This study revealed that the MoCA detects more cognitive deficits than clinical assessment alone but may not have an impact on discharge destination. Further research is suggested, in order to determine whether identifying these

cognitive deficits plays a role in long-term outcomes.

Stiekema, A., et al. The Montreal Cognitive Assessment Detects Cognitive Deficits that Go Unnoticed during Clinical Observation in the Acute Phase after Stroke. **Brain Injury**. 2024. doi.org/10.1080/02699052.2024.2341039.

CAVEOLIN-1 LEVELS AND SYMPTOMATIC HEMORRHAGE AFTER ENDOVASCULAR THROMBECTOMY

Endovascular thrombectomy (EVT) is the most effective approach for large vessel occlusion in the anterior circulation (LVO-AC). Symptomatic intracranial hemorrhage (sICH) is the most serious complication after EVT. Caveolin-1 (Cav-1), a twenty-two kDa coat protein of caveolae, is highly expressed in brain vascular endothelium, with studies indicating its potential utility as a predictor of bleeding events. This study investigated whether circulating levels of Cav-1 can help predict the risk of sICH after EVT.

The subjects were 325 adult patients, presenting with an LVO-AC who were treated by EVT, with 42.8% also receiving thrombolysis. Levels of serum Cav-1 were tested post-EVT from each subject, typically within 24 hours of stroke onset. The diagnosis of sICH was made using the Heidelberg Bleeding Classification.

A sICH was found within 72 h of thrombectomy in 47 patients (14.5%), with these patients exhibiting a decreased level of Cav-1 compared to the non-sICH group (p=0.011). Compared to the quartile with the highest Cav-1 levels, the quartile with the lowest levels of Cav-1 were at increased risk of an sICH with an odds ratio of 3.077 (p=0.028)

Conclusion: This study of patients with a large vessel ischemic stroke, undergoing endovascular thrombectomy, found that decreased levels of Caveolin-1 were associated with an increased risk of intracerebral hemorrhage.

Xie, Y., et al. Low Caveolin-1 Levels and Symptomatic Intracranial Haemorrhage Risk in Large-Vessel Occlusive Stroke Patients after Endovascular Thrombectomy. **Eur J Neurol**. 2024, May 17: e16342. doi: 10.1111/ene.16342.

LIPID LOWERING THERAPY AFTER MYOCARDIAL INFARCTION

A number of studies have demonstrated the benefits of statins and lipid lowering therapy (LLT) after an acute myocardial infarction (AMI). Studies of patients 80 years of age or older are lacking, as many patients in this age group have been excluded from randomized trials. This study examined the association between lipid lowering therapy and the five-year survival of older patients with a recent AMI.

The subjects were participants in the French Registry of Acute ST-Elevation or Non-ST-Elevation Myocardial Infarction (FAST-MI) trial of adults admitted within 48 hours of symptom onset. Of the 13,130 patients, 2,264 were ≥80 years of age. Of these, 415 (18.4%) were discharged without a prescription of LLT, 866 (38.4%) with a conventional dose of LLT, and 977 (43.2%) with a high dose of LLT.

The five-year survival rates were 58% for patients discharged with high -intensity LLT, 47.5% for patients on the conventional dose of LLT, and 36% for those discharged without a prescription for an LLT. A multivariable regression analysis revealed that high-dose LLT was associated with lower five-year mortality (p=0.0008), while conventional doses were not (p=0.39).

Conclusion: This study of patients with an acute myocardial infarction, 80 years of age or older, found that high-dose lipid lowering therapy, but not standard dose, was associated with improved five-year mortality.

Fayol, A., et al. Association of Use and Dose of Lipid-Lowering Therapy Post-Acute Myocardial Infarction with 5-Year Survival in Older Adults. **Circ Cardiovasc Qual Outcomes**. 2024, May;17(5):e010685.

POST-CONCUSSIVE SYMPTOMS AND BLOOD BIOMARKERS OF INFLAMMATION

Following a mild traumatic brain injury (mTBI), some patients report persistent physical, cognitive, and emotional symptoms, referred to as persistent post concussive symptoms (PPCS). This study explored the relationship between PPCS and blood biomarkers of central nervous system damage and inflammation.

This prospective study included patients between 16 and 60 years of age, all diagnosed with mTBI. Clinical information was obtained from patient interviews and medical records, with the British Columbia Post-Concussion Symptom Inventory (BC-PSI) used to evaluate PPCS at three months. All subjects underwent a standardized brain MRI scan within 72 hours of injury. Blood samples were taken at admission, two weeks, 12 weeks, and 12 months to assess levels of central nervous system damage and inflammation (27 cytokines).

Data were available for 172 patients. Those with findings on the MRI were significantly more likely to develop PPCS as compared to those without such findings. No single biomarker differentiated between those with and those without PPCS. Those with PPCS had higher concentrations of inflammatory biomarkers including interleukin 8 and interleukin 9, and lower concentrations of TNF, interleukin 17A, and MCP1.

Conclusion: This study of patients with mild traumatic brain injury found that early inflammation was significantly related to prolonged symptoms of concussion.

Clarke, G., et al. Longitudinal Associations between Persistent Post -Concussion Symptoms and Blood Biomarkers of Inflammation and CNS Injury after Mild Traumatic Brain Injury. **J Neurotraum**. 2024, May (7-8):862-878.

NEBULIZED KETAMINE VERSUS IV MORPHINE FOR ELDERLY ADULTS WITH ACUTE PAIN

When treating pain in the elderly, it is important to consider age-related physiological changes such as declines in renal and hepatic function. Ketamine is a non-competitive N-methyl-D-aspartate (NMDA) glutamate receptor complex antagonist that provides analgesia by reducing central sensitization at the spinal cord and central nervous system levels. This study compared the efficacy of nebulized ketamine with that of IV morphine.

The subjects were ≥65 years of age, who presented to the emergency department with a chief complaint of musculoskeletal pain with a pain score of ≥5/11. The patients were randomized to receive nebulized ketamine at 0.75 mg/kg plus IV saline or 0.1 mg/kg IV morphine plus a placebo nebulizer. The primary outcome measure was the reduction

in pain scores, as measured by an 11 -point numeric rating system (NRS).

Data were analyzed for 92 patients. The mean pain scores were lower in the ketamine group at all times measured between 15 and 120 minutes after treatment ($p<0.001$ for all comparisons). At 30 minutes the difference in changes in pain scores did not differ between the groups ($p=0.2$). At 60 minutes, all patients in both groups reported an acceptable reduction in pain scores. The rates of rescue therapy required were 23.9% in the morphine group and 10.9% in the ketamine group.

Conclusion: This study of elderly men presenting to the emergency department with acute musculoskeletal pain found that nebulized ketamine was no less effective than IV morphine for reducing pain.

Sirasa K., et al., A Non-Inferiority, Randomized, Controlled Trial Comparing Nebulized Ketamine to Intravenous Morphine for Older Adults in the Emergency Department with Acute Musculoskeletal Pain. **Age Ageing**, 2024, Jan; 53(1): doi: 10.1093/ageing/afad255.

TRANSCRANIAL FOCUSED ULTRASOUND FOR THE TREATMENT OF TREMOR

Essential tremors (ETs) are characterized by tremors in the hands, trunk, head, and/or voice when performing voluntary movements. Several studies have demonstrated that ablation of thalamic subregions using high-intensity focused ultrasound (HIFU) can reduce ETs. As low intensity focused ultrasound (LIFU) has been shown to produce brain effects without the risk of damage to tissues, this study explored the effects of LIFU on ETs.

Subjects were patients diagnosed with ET, with a prominent action tremor and no bradykinesia or rigidity. The ventral intermediate nucleus (VIM) was located for targeting. Over one week, the intervention involved eight, ten-minute sessions of LIFU at the VIM. At baseline and at follow-up, all subjects underwent symptom evaluation using The Essential Tremor Rating Scale (TETRAS), which provided sub-scores in activities of daily living (ADL) and performance.

The TETRAS scores improved significantly for all participants ($p<0.001$). The ADL scores improved in eight of 10 subjects ($p=0.035$). In addition, a clinically significant improvement (defined as a change greater than 8.9 %) on the ADL Performance subscale was seen in all 10 patients ($p<0.001$).

Conclusion: This small study of patients with essential tremor demonstrates that low intensity, focused, transcranial ultrasound may improve the tremor and performance of activities of daily living.

Deveney, C., et al. Transcranial Focused Ultrasound for the Treatment of Tremor: A Preliminary Case Series. **Brain Stim**. 2024, Jan; 17(1): 35-38.

LEUKOCYTE- POOR PLATELET RICH PLASMA WITH ROTATOR CUFF SURGERY

Despite advances in rotator cuff repair techniques, the rate of unhealed or recurrent rotator cuff tears remains elevated. This study investigated the effects of leukocyte poor platelet rich plasma (LP-PRP) as an adjunct to reduce rotator cuff retears after a surgical repair.

The subjects were 96 patients with rotator cuff tears of less than three centimeters. The subjects were randomized to receive either surgical repair alone or surgical repair followed by LP-PRP. The primary outcome measure was change in lesion status as assessed with magnetic resonance imaging studies, at six months post-surgery. Secondary outcome measures included the Visual Analog Scale (VAS) for Pain, the American Shoulder and Elbow Surgeon Score (ASES), the Single Assessment Numeric Evaluation (SANE), and the Pittsburgh Sleep Quality Index (PSQI), with all scores collected at baseline and at six- and 12-months post-surgery.

At six months' follow-up, the average retear rate in the PRP group was 15.2%, while that of the control subjects was 34.1% ($p=0.037$). Significant improvements were noted in secondary outcomes in both groups, with no significant difference between the groups on scores on the VAS for pain, ASES, SANE, or PSQI.

Conclusion: This prospective, double-blind study of patients undergoing surgical repair for a rotator cuff tear found that leukocyte poor-platelet rich plasma delivered during surgery could reduce the rate of retears, but did not improve patient reported outcomes, including pain.

Rossi, L., et al. Leukocyte Poor Platelet Rich Plasma as an Adjuvant to Arthroscopic Rotator Cuff Repair Reduces the Retear Rate but Does Not Improve Functional Outcomes: A Double-Blind, Randomized, Controlled Trial. **Am J Sports Med**. 2024, May; 52(6): 1403-1410.

BOTULINUM TOXIN TYPE A FOR THE TREATMENT OF TRIGEMINAL NEURALGIA

Trigeminal neuralgia (TN) is a chronic facial pain syndrome which primarily affects the trigeminal or fifth cranial nerve. As Botulinum Toxin Type A (BTXa) has been found effective for neuropathic pain, this review investigated the effectiveness of this medication for the treatment of recalcitrant TN.

A literature review was conducted for randomized, controlled studies of patients diagnosed with TN, treated with BTX injections. Selected studies had outcomes including visual analog scale (VAS) pain scores and pain attack frequency. The authors identified 586 records, including four randomized, controlled trials (RTCs) and 19 open-label studies.

From the RTCs, treatment with BTXa resulted in significant improvement in mean VAS pain scores by week four compared to baseline ($p=0.002$). In 19 non-randomized studies, BTXa treatment resulted in a decrease in VAS pain scores ($p<0.001$), and pain attack frequency ($p<0.001$). Compared with the placebo groups, the BTX-A groups had a slightly higher incidence of side effects, which were generally mild and manageable.

Conclusion: This literature review of studies involving patients with trigeminal neuralgia found that botulinum toxin injections may be effective in providing significant pain relief.

Xinyu, H., et al. Efficacy and Safety of Botulinum Toxin Type A in the Treatment of Trigeminal Neuralgia: An Update on Systematic Review with Meta-Analyses. **Clin J Pain**. 2024, June; 40(6): 383-392.

PROPRIOCEPTION AFTER ANTERIOR CRUCIATE LIGAMENT REPAIR

The anterior cruciate ligament (ACL) has several types of neural mechanoreceptors with a proprioception function. This study compared the proprioception of

patients with primary ACL repair to those with ACL reconstruction (ACLR).

The subjects were patients with an ACL repair who underwent either ACLR or ACL primary repair, with clinical follow-up for at least two years. Of the 63 patients in the study, 29 underwent primary ACL repair and 34 underwent ACLR. A control group included 33 healthy participants who had knee MRI scans taken for any reason, with no meniscal, chondral, or ligamentous damage detected.

Proprioception was evaluated by the active joint position sensation method, using a digital inclinometer. During this testing, the participants were instructed to pause for 10 seconds at angles of 15°, 30°, and 60° of knee flexion. The patients were then asked to flex the knee and stop at these angles. The difference between the target angle shown to the participants and the angle at which they brought their knees was calculated as the deviation angle (DA).

The DA of operated knee was significantly larger in the ACLR than in the primary repair group at all target angles ($p<0.001$).

Conclusion: This study of patients with anterior cruciate ligament (ACL) tears found that those who underwent primary repair had a greater preservation of proprioception than those who underwent ACL replacement.

Ciceklidag, M., et al. Proprioception after Primary Repair of the Anterior Cruciate Ligament. **Am J Sport Med**. 2024, April; 52(5): 1199-1208.

LACTIC ACID, NEURON-SPECIFIC ENOLASE, AND THE BLOOD-BRAIN BARRIER AFTER A SEVERE BRAIN INJURY

Biomarkers in cerebral spinal fluid have become a useful index for monitoring pathophysiological changes after a severe traumatic brain injury (sTBI). This study assessed the utility of lactic acid (Lac) and neuron-specific enolase (NSE) and the blood-brain barrier index (BBBi), defined as the ratio of CSF albumin and serum albumin.

The subjects were 52 adults hospitalized for sTBI. The primary outcome variable at six months was the Glasgow Outcome Scale-Extended (GOSE-E) score. Patients were divided into two groups based upon the resulting GOS-E score, a poor prognosis group (GOS-E, score of one to four) and a good prognosis group (GOS-E, score of five to eight). These scores were compared to CSF and serum-derived concentrations of Lac, NSE, and the BBBi.

The median CSF Lac levels for the poor prognosis group was 6.94 mmol/L and that for the good prognosis group was 5.51 mmol/L. The median serum Lac for the poor prognosis patients was 7.57, while that for the good prognosis group was 6.34 ($p<0.05$). The median CSF NSE for the poor prognosis group was 73.99 ng/mL and that for the good prognosis group was 61.61 ng/mL ($p<0.05$). The median BBBi for the poor prognosis group was 25.70×10^{-3}, significantly higher than that of the median of the good prognosis group, which was 6.20×10^{-3} ($p< 0.05$).

Conclusion: This study of patients hospitalized with a severe traumatic brain injury found that serum and cerebral spinal fluid levels of lactic acid and neuron-specific enolase correlated with patient outcomes at six months post-injury. This was also true of the degree of disruption of the blood-brain barrier, as estimated by the BBBi.

Lu, W., et al. Lactic Acid, Neuron Specific Enolase, and Blood Brain Barrier Index after a Severe Traumatic Brain Injury: A Prospective Study. **Br J Neurosurg**. 2024; 38(2): 220-224.

EDARAVONE DEXBORNEOL FOR ACUTE, ISCHEMIC STROKE

Edaravone dexborneol is an intravenous brain cytoprotective agent composed of edaravone and dexborneol. The Treatment of Acute Ischemic Stroke (AIS) with Edaravone Dexborneol (TASTE) trial found that, compared with edaravone alone, intravenous edaravone dexborneol could improve 90-day functional outcomes in patients with AIS. To eliminate the delay and logistical issues involved with intravenous (IV) delivery, this study assessed the effect of sublingual delivery of edaravone combined with dexborneol (edaravone dexborneol).

The subjects were adult patients diagnosed with an AIS presenting within 24 hours of symptom onset. The subjects were randomized to receive sublingual placebo or edaravone 30 mg and dexborneol 6 mg twice per day for 14 days. The primary outcome measure was a favorable outcome, defined as a modified Rankin Scale (mRS) score of one or below at 90 days.

Data were collected from 793 patients with a median age of 64.1 years. A favorable outcome at 90 days was realized by 64.4% of the treatment group and 54.7% of the placebo group ($p=0.003$). Adverse events occurred in 89.8% of the treatment group and in 90.1% of the placebo group.

Conclusion: This study of patients with an acute ischemic stroke found that treatment with sublingual edaravone combined with dexborneol significantly increased the number of patients with a good outcome.

Fu, Y., et al. Sublingual Edaravone Dexborneol for the Treatment of Acute Ischemic Stroke. The TASTE-SL Randomized Clinical Trial. **JAMA Neurol**. 2024, April; 81(4): 319-326.

TIBIAL NERVE RADIOFREQUENCY AND INTRALESIONAL RADIOFREQUENCY THERMAL COAGULATION FOR CALCANEAL SPUR AND PLANTAR FASCIITIS

Painful calcaneal spurs (PCS) and plantar fasciitis (PF) affect approximately 10-15% of the population. The causes of PCS and PF are not fully understood, but are associated with several risk factors, including repetitive stress, overuse, obesity, and aging. Treatment of these conditions is sometimes resistant to conventional therapies, such as rest, ice, stretching, orthotics, and anti-inflammatory drugs. Two modalities that have been used to treat chronic pain conditions include pulse radiofrequency (PRF) and radiofrequency thermal coagulation (RTC). The PRF delivers short bursts of high-voltage electrical current to the target nerve, modulating the transmission of pain signals. The RFT delivers continuous current that heats the tissue causing coagulation and thinning of spurs and fascia. This study compared the effectiveness of these interventions for patients with PCF and PF.

This prospective blinded study included 46 adult patients with > 6 months PCF and PF. The patients were randomized to receive either US -guided tibial nerve PRF at 42°C for 240 seconds, or fluoro-guided intralesional RFT at 80°C for 90 seconds. Outcome assessments included the Numerical Rating Scale (NRS) for pain and the American Orthopedic Foot and Ankle Society (AOFAS) ankle hindfoot score, both

(Continued from page 2)

measured at baseline and three months follow up.

At one-month post-procedure, improvement in NRS pain scores of ≥50% with the first steps of the morning was reported by 72% of the PRF and 75% of the RFT group. At three months these rates fell to 60% and 58%. There was no significant difference between the two groups. The change in the AOFAS score over time was statistically significant in both groups ($p<0.001$).

Conclusion: This study of patients with painful plantar fasciitis and calcaneal heel spurs found that both ultrasound-guided tibial nerve pulsed radiofrequency and fluoroscopy-guided intralesional radiofrequency thermocoagulation may provide significant pain relief.

Yildiz, G., et al. Comparison of Tibial Nerve Pulsed Radiofrequency and Intralesional Radiofrequency Thermocoagulation in The Treatment of Painful Calcaneal Spur and Plantar Fasciitis: A Randomized Clinical Trial. **Pain Med**. 2024. pnae029, https://doi-org.proxy.library.emory.edu/10.1093/pm/pnae029.

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