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PSILOCYBIN VERSUS ESCITALOPRAM FOR DEPRESSION

For patients with major depressive disorder, selective serotonin reuptake inhibitors are first-line treatments. These medications take several weeks to take effect and are ineffective in many. The psychedelic compound psilocybin exerts its main effects through serotonin 5-hydroxytryptamine type 2A (5-HT_{2A}) receptor agonism, which is part of a pathway implicated in depression. This study compared the efficacy of psilocybin to escitalopram for the treatment of depression.

This open-label trial recruited men and women between 18 and 80 years of age. Those to score at least 17 on a Hamilton depression scale, indicating moderate to severe major depressive disorder, were eligible to participate. Those randomized to the psilocybin group received two separate doses of 25 mg of psilocybin three weeks apart plus six weeks of daily placebo. The escitalopram group received two separate doses of 1 mg of psilocybin three weeks apart plus six weeks of daily oral escitalopram 10 mg. The primary outcome measure was the change from baseline on the 16-item quick inventory of depressive symptomatology-self-report (QIDS-SR-16).

Data were completed for 59 patients. From baseline to follow-up QIDS-SR-16 depression scores improved by a mean of six points in the psilocybin group and eight points in the escitalopram group ($p=0.17$). A QIDS-SR-16 improvement of 50% or greater occurred in 70% of the patients in the psilocybin group and 48% of those in the escitalopram group.

Conclusion: This study of patients with a diagnosis of depression found no significant difference in treatment efficacy between psilocybin and escitalopram.

Carhart-Harris, R. Trial of Psilocybin versus Escitalopram for Depression.

N Eng J Med. 2021, April 15; 384 (9):1402-1411.

INTRA-ARTICULAR SPIRIFERMIN FOR KNEE ARTHRITIS

Current therapies for osteoarthritis (OA) focus on improving physical function and reducing pain. However, there is an urgent need for disease modifying osteoarthritis drugs (DMARDs) that inhibit disease progression. Spirifermin is a recombinant human fibroblast growth factor 18 that has cartilage regenerative properties. This study assessed the efficacy and safety of this medication for the treatment of patients with symptomatic OA of the knee.

The FGF-18 Osteoarthritis Randomized Trial with Administration of Repeated Doses (FORWARD) study included 549 patients 40-85 years of age with symptomatic radiographic knee OA. The patients were randomized to groups to receive; intra-articular placebo, Spirifermin 30 µg every 12 months, Spirifermin 30 µg every six months, Spirifermin 100µg every six months or Spirifermin 100 µg every 12 months. The primary endpoint was change in the total femorotibial joint (TFTJ) cartilage thickness at year two. The patients were followed for five years. Cartilage thickness was measured by quantitative MRI (qMRI).

A significant dose-response in TFTJ cartilage thickness was found at year two and maintained at year five ($p<0.001$). In addition, compared to the placebo group, the spirifermin 100 µg every six months group had a greater increase in TFTJ cartilage thickness at year five ($p=0.015$). The WOMAC pain scores improved by 50% from baseline in all groups. No patient in the 100 µg group required a total knee replacement of the treated knee.

Conclusion: This study of patients with osteoarthritis of the knee found that intraarticular Spirifermin (a recombinant human fibroblast growth

factor 18) could improve cartilage thickness.

Eckstein, F., et al. Long-Term Structural and Symptomatic Effects of Intra-Articular Spirifermin in Patients with Knee Osteoarthritis: 5 Year Results from The Forward Study. *Ann Rheum Dis.* 2021, May 7; 80 (8):1062-1069.

HIGH-FREQUENCY SPINAL CORD STIMULATION FOR DIABETIC NEUROPATHY

Approximately 20% of patients with diabetes will develop painful diabetic neuropathy (PND). The Comparison of 10 kHz SCS Combined with CMM to CMM Alone in the Treatment of Neuropathic Limb Pain (SENZA-PDN) trial compared the pain reduction effect of spinal cord stimulation (SCS) combined with conventional medical management (CMM) with CMM alone for patients with refractory PDN.

Subjects were adults with PND, refractory to gabapentin or pregabalin, and at least one other class of analgesic. All underwent a neurologic exam, including lower limb motor function, light touch sensation, and reflexes. Those in the SCS group had two percutaneous leads placed epidurally and received SCS with 10 kHz frequency, 30 µs pulse width, and an amplitude range of 0.5 to 3.5 mA. The primary endpoint was the percentage of participants with 50% pain relief or more on VAS at three months without worsening of baseline neurological deficits.

At three months follow-up, 5% of the CMM group and 79% of the SCS group met the primary endpoint ($p<0.01$). At six months follow-up, the mean VAS score in the CMM group was unchanged while that in the SCS group improved by 76.3%. Compared to the CMM group, the SCS group had significantly better improvement in EQ5D-5L VAS quality of life scores ($p<0.001$). At six months, sleep disturbance due to pain increased by 5.3% in the CMM

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group and decreased by 61.9% in the SCS group.

Conclusion: This study of patients with painful diabetic neuropathy of the lower extremities found that adding spinal cord stimulation to conventional medical management could significantly decrease pain when compared to conventional medical management alone.

Peterson, E., et al. Effect of High-Frequency (10 kHz) Spinal Cord Stimulation in Patients with Painful Diabetic Neuropathy: A Randomized Clinical Trial. *JAMA Neurol.* 2021, June; 78 (6): 688–698.

COMORBIDITIES ASSOCIATED WITH CERVICAL DEGENERATIVE DISCS

Studies have found that more than 80% of patients over the age of 60 years had evidence of cervical spine degenerative disc disease (DDD). This study was designed to determine whether age and/or medical comorbidities influence the severity of cervical disc disease.

The electronic medical records (EMRs) were searched to identify patients who underwent cervical spine MRI at the University of Missouri during the years 2011–2019. Each intervertebral disc was assigned a numerical grade using the Suzuki classification with a grade of zero indicating no desiccation or height loss and grade three indicating complete desiccation and near-complete height loss. Medical records were reviewed to determine comorbidities. The patients were then subdivided based on a documented diagnosis of diabetes mellitus.

Data were complete for a final cohort of 799 patients. Both grade and severity of disc degeneration were significantly worse in diabetics compared to those without diabetes. Comorbidities associated with an increased cumulative grade of disc degeneration included older age, diabetes, higher scores on the American Society of Anesthesiologists (ASA) Physical Status Classification system, peripheral vascular disease, number of previous cervical spine surgeries, smoking, and decreased median household income. In an adjusted multivariate analysis, factors associated with an increased cumulative grade of disc degeneration were self-pay, Medicare insurance, older age, and increased ASA. No association was found for

increased body mass index or diabetes status.

Conclusion: This study found that the severity of cervical spine degenerative disc disease is associated with multiple medical comorbidities, increasing age, and Medicare insurance, but not with increased body mass index or status of diabetes.

Lambrechts, M., et al. Comorbidities Associated with Cervical Spine Degenerative Disc Disease. *J Orthop.* 2021, July 16; 26: 98–102.

STEM CELLS FOR CHRONIC DEGENERATIVE DISC DISEASE PAIN

Many studies suggest that discogenic low back pain (LBP) is the most common cause of chronic back pain. For patients with chronic LBP who failed conservative therapy, few options other than surgical intervention are available. This study examined the safety and efficacy of a single intervertebral disc injection of mesenchymal precursor cells (MPCs) for the treatment of chronic LBP.

Subjects were adults with moderate degenerative disc disease (DDD) with LBP for at least six months and failed conservative treatment. The subjects were randomly assigned to receive six million MPCs with hyaluronic acid (HA), 18 million MPCs with HA, HA vehicle control, or saline. All were delivered directly into the nucleus pulposus. Subjects were clinically and radiographically evaluated at baseline, and up to 36 months after treatment. Assessments included LBP as measured with a Visual Analog Scale (VAS), Oswestry Disability Index (ODI), SF-36, and the Work Productivity and Activity Index.

Of the 100 subjects, the VAS for pain was more improved at 36 months in the treatment group than in the normal saline group ($p < 0.05$). For the ODI scores, improvement in the 18 million MPC group was significantly greater at 36 months as compared with the normal saline group ($p = 0.017$). Three adverse events resulted in discontinuation but were unrelated to the study agent or injection procedure.

Conclusion: This study of patients with chronic low back pain resulting from degenerative disc disease found that allogeneic mesenchymal stem cells may be useful for reducing pain and disability.

Amirdelfan, K., et al. Allogeneic Mesenchymal Precursor Cells

Treatment for Chronic Low Back Pain Associated with Degenerative Disc Disease: A Prospective Randomized, Placebo-Controlled 36 Month Study of Safety and Efficacy. *Spine J.* 2021, February; 21(2):212-230.

DEPRESSION OUTCOME AFTER STROKE

Depression affects one in every three people during the first year after a stroke. Previous studies have demonstrated that adults with a recent stroke who receive 20 mg of fluoxetine per day will experience enhanced motor recovery. This study assessed the effect of this treatment on the symptom of depression.

Subjects were adults with a diagnosis of stroke 2-15 days before study entry. Patients were randomized to receive fluoxetine 20 mg or a similar-appearing placebo once per day. The primary outcome was depression as measured by the PHQ-9, a self-administered scale, with depression defined as a score of ≥ 9 .

Data were collected for 1,220 individuals with an average age of 63.4 years. After four weeks, the PHQ-9 score of ≥ 9 was found in 14.6% of those in the placebo group and 12.8% of those in the fluoxetine group. At 26 weeks, 8.2% of those in the placebo and 7.0% of those in the fluoxetine group had a PHQ-9 score of ≥ 9 . The proportion of participants with a score of ≥ 9 decreased with time ($p < 0.001$), though the effect of treatment with fluoxetine was not statistically significant compared with placebo.

Conclusion: This randomized controlled trial of patients seen for acute stroke found that fluoxetine at 20 mg per day did not significantly decrease the proportion of patients affected by clinically significant depression.

Almeida, O., et al. Depression Outcomes Among Patients Treated with Fluoxetine for Stroke Recovery. The AFFINITY Randomized Clinical Trial. *JAMA Neurol* 2021. doi:10.1001/jamaneurol.2021.2418.

HIGH INTENSITY RESISTANCE EXERCISE AND COGNITION

Previous studies have demonstrated that acute bouts of moderate intensity aerobic exercise may elicit significant improvements on measurements of cognitive function. This study further examined

the influence of high intensity exercise and cognitive function.

Subjects were 10 men, who had experience in training with barbell squats exercise. All were assessed for their one repetition maximum for a back squat using a free weight barbell. The exercise involved 5-10 repetitions at 40-60% of the perceived maximum, followed by a second set of 3-5 repetitions at 60-80% of their one repetition maximum, with this set followed by one set with progressively heavier loads until failure. All were tested with the Automated Neuropsychological Assessment Metrics (ANAM), which measures various cognitive domains, including response speed, attention and concentration, immediate and delayed memory, spatial processing, and decision processing speed and efficiency. On the exercise days, the subjects underwent a baseline ANAM administration and then performed six sets of 10 repetitions of back squats, allowing a 2-minute rest period between sets.

Scores on the Mathematical Processing task were improved after exercise ($p < 0.003$). The Go/No-Go task scores after exercise were significantly lower than the pre-fatigue scores ($p = 0.006$). However, scores on the Coded Substitution-Delay (CDD) worsened after exercise ($p = 0.11$). The data suggest that the exercises facilitate cognitive domains associated with basic computational skills and response inhibition, while worsening skills requiring memory and recall.

Conclusion: This study demonstrated that high-intensity exercise may result in improvement in reaction time and processing speed while worsening tasks requiring memory and recall.

Anders, J., et al. Acute Effects of High-Intensity Resistance Exercise on Cognitive Function. *J Sports Sci Med.* 2021, September; 20(3):391-397.

FACTORS ASSOCIATED WITH LIGHT THERAPY RESPONSE FOR FATIGUE FOLLOWING BRAIN INJURY

Fatigue and sleep disturbance are common sequelae of traumatic brain injury (TBI) and stroke. Several studies have demonstrated the efficacy of light therapy as a treatment for fatigue. This study investigated the factors which moderate the response to in-home light therapy for individuals with fatigue following stroke and TBI.

The subjects were 30 individuals with mild-severe TBI or stroke sustained at least three months earlier. All reported significant fatigue, defined as Fatigue Severity Scale scores of ≥ 4 . The subjects were also evaluated with the Horne & Östberg Morningness-Eveningness Questionnaire (HOME), which determines the time of day of greatest productivity, termed chronotype. Serving as their own controls, a randomized crossover design was used to expose each subject to a blue light condition or to a control light condition. In the blue light condition blue-enriched high-intensity white light with a correlated color temperature (CCT) of approximately $> 5,000$ K was used during the day. In the evening, three hours prior to sleep, the light intensity was reduced, and blue-depleted white light was used ($\leq 3,000$ K). The settings on light-emitting devices (phone, iPad, computer) were modified to reduce exposure to short-wavelength light during evenings. In the sham control condition, researchers changed the lamps as per the treatment condition, but the lamps did not change in color from the participants' normal lighting (typically 3,000-4,000 K).

There was no significant difference in fatigue scores between the blue light and the control condition ($p = 0.036$). However, in a subgroup analysis, those whose HOME scores identified them as in the evening chronotype group, showed better improvement in fatigue and sleep quality with light therapy than for those in the morning chronotype group. Also, those with light eye color experienced a greater reduction in fatigue with treatment.

Conclusion: This study of patients with mild to severe traumatic brain injury or stroke found that light therapy could improve the complaint of fatigue among those with eye color of blue-gray or green, or a diagnosis of evening chronotype.

Connolly, L., et al. Factors Associated with Response to Pilot Home-Based Light Therapy for Fatigue Following Traumatic Brain Injury and Stroke. *Front Neurol.* 2021, July 15: <https://doi.org/10.3389/fneur.2021.651392>.

NEUROFILAMENT LIGHT AND FRONTOTEMPORAL DEMENTIA

Frontotemporal dementia (FTD) is the second most common early-onset neurodegenerative disorder. This study assessed the utility of neurofilament light chain (NFL) as a surrogate of cognitive decline in FTD.

Subjects were recruited from the memory clinic at the Neurology Department of Centro Hospitalar e Universitário de Coimbra. All were evaluated using a detailed history from the patient and another reliable source, neurological examination, psychiatric evaluation, and cognitive screening tests. A subgroup of FTD patients (n=28) also had cognitive data collected during their follow-up appointment. Blood and CSF samples were collected as part of their diagnostic investigation between 2012-2019.

The FTD patients had significantly higher NfL levels in the CSF ($p<0.001$) and serum than did those with Alzheimer's disease (AD) ($p<0.05$), and healthy controls (HC) ($p<0.001$). The AD patients had significantly higher serum NfL than HC ($p<0.001$). Significant correlations were found between NfL levels and overall cognitive function, abstract reasoning, executive functions, memory, and language.

Conclusion: This study found that serum neurofilament light chain may be useful as a surrogate for disease severity in patients with frontotemporal dementia.

Silva-Spinola, A., et al. Serum Neurofilament Light Chain as a Surrogate of Cognitive Decline in Sporadic and Familial Frontotemporal Dementia. *Europ J Neurol*. 2021, August 10. doi.org/10.1111/ene.15058.

SMALL VESSEL DISEASE AND INTRACEREBRAL HEMORRHAGE

While previous studies have shown that oral anticoagulants (OAC) are a risk factor for intracerebral hemorrhage (ICH), the direct contribution of these medications to ICH is unknown. This study assessed the association of small vessel disease (SVD) at baseline with future risk of hemorrhage or ischemic stroke in patients with atrial fibrillation (AF) who were exposed to anticoagulants.

This prospective observational trial, the Clinical Relevance of Microbleeds in Stroke (CROMIS-2) study enrolled adult patients with AF who were started on an OAC for secondary stroke prevention (AF cohort). All patients underwent a baseline brain MRI. A second study enrolled patients who had image confirmed nontraumatic intracerebral hemorrhage with or without treatment with an OAC (ICH cohort). In the ICH cohort, the main variable of interest was prevalence and severity of small

vessel disease markers at ICH. In the AF cohort, the primary outcome was symptomatic ICH.

Data were obtained for 1,030 patients in the ICH cohort and 1,447 patients in the AF cohort. In the ICH cohort, medium to high severity small vessel disease was more prevalent in patients with OAC-associated ICH than in those without prior anticoagulant therapy ($p<0.001$). In the ICH cohort, the rate of ICH was 0.56%/year in patients with SVD, and 0.06%/year in those without ($p=0.001$); ICH was independently associated with severity of SVD ($p=0.001$).

Conclusions: This study found that small vessel disease is associated with intracerebral hemorrhage among those receiving anticoagulants at the time of their stroke, and independently predicts ICH in patients with atrial fibrillation who receive oral anticoagulants.

Seiffge, D., et al. Small Vessel Disease Burden and Intracerebral Hemorrhage in Patients Taking Oral Anticoagulants. *J Neurol Neurosurg Psych*. 2021, August; 92(8): 805–814.

ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION REVISION AND GRAFT CHOICE

Early data from the Multicenter ACL Revision Study (MARS) Group demonstrated that revisions using an autograft could improve surgical outcomes as compared with an allograft. This study further explored the influence of graft choice on the outcomes of anterior cruciate ligament (ACL) revisions.

This prospective study included patients 12 to 65 years of age who were scheduled to undergo an ACL reconstruction. The study enrolled 1,234 patients with a median age of 26 years. Of these, 48% were autograft reconstructions, 49% were allograft reconstructions, and 3% used a combination. At baseline and follow up, the patients completed knee-specific outcome measures including the Knee Injury and Osteoarthritis Outcome Score (KOOS), the International Knee Documentation Committee (IKDC) Subjective form, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and the Marx Activity Rating Scale (MARS). The outcome of the surgeries was compared between the type of graft received.

Scores on all measurements, in both groups, improved between

baseline and six-year follow-up ($p<0.001$). At six years, activity levels were better in the bone-tendon-bone (BTB) autograft group as compared with the BTB allograft group ($p=0.009$). At six years re-rupture had occurred in 3.1% of the soft tissue autografts, 3.8% of the BTB autografts, 6.2% of the soft tissue allografts, and 10.6% of the BTB allografts ($p=0.007$).

Conclusion: This prospective study of patients undergoing revision anterior cruciate ligament reconstruction found that the rate of re-rupture was 3.9 times higher among those receiving an allograft than for those receiving an autograft.

Wright, R., et al. Association between Graft Choice and 6-Year Outcomes of Revision Anterior Cruciate Ligament Reconstruction in the MARS Cohort. *Am J Sport Med*. 2021, August; 49(10):2589-2598.

LOSARTAN TO ENHANCE MICROFRACTURE

Microfracture is a widely used surgical technique for the management of cartilage injuries. However, this technique is known to produce fibrocartilage rather than actual cartilage growth. As angiotensin receptors are expressed in hypertrophic cartilage, and/or implicated in osteoarthritis development, this study investigated the effect of an intra-articular injection of losartan on microfracture-mediated cartilage repair.

This animal study involved 30 rabbits for which an osteochondral defect was created in the distal femur of one hind limb. A microfracture was performed immediately after the defect was created. Both knees were injected with 0.1, 1, 10, or 100 mg of losartan immediately after surgery and at two and four weeks. At six weeks the animals were harvested for assessment.

At six weeks the microfracture group, as well as the group with losartan at the doses of 0.1, 1, and 10 mg, showed near complete healing. The 100 mg group demonstrated neither bone nor cartilage healing.

Conclusion: This animal study of chondral defects of the knee, repaired by microfracture, found that an intra-articular injection of losartan was effective for enhancing the effects of the surgery without damaging the native tissue.

Logan, C., et al. The Beneficial Effect of An Intra-Articular Injection of Losartan on Microfracture-Mediated

Cartilage Repair Is Dose Dependent.
Am J Sports Med. 2021, July; 49
(9): 2509-2521.

ENDOVASCULAR TREATMENT FOR CEREBRAL VENOUS SINUS THROMBOSIS

Cerebral venous sinus thrombosis (CVST) is a rare cerebrovascular disorder, which account for less than 1% of all strokes. A recent randomized controlled trial, TO-ACT (Thrombolysis or Anticoagulation for Cerebral Venous Thrombosis), was stopped for futility after the first interim analysis. This single center study reviews the outcomes of endovascular intervention for patients with CVST.

This retrospective study included 28 consecutive patients presenting with CVST who were treated with endovascular therapy. Endovascular therapy was initiated while the patient was receiving unfractionated heparin with APTT target of 50-75 seconds. Clinical outcome was assessed using the modified Rankin scale (mRS) score at baseline and up to six months. A favorable outcome was defined as an mRS of 0-2 or a return to baseline.

Of the 28 patients, 75% were females with a median age of 37.5 years. The median time from diagnosis to first endovascular procedure was 10 hours, with 93% receiving local thrombolysis. The median mRS was two at three-month follow-up improving to one at six-month follow-up. A favorable outcome was achieved by 63% of patients at three months improving to 79% at six months. Periprocedural complications were found in 39%, including 32% who experienced a postprocedural intracerebral hemorrhage or volume expansion of ICH.

Conclusion: This study of patients with cerebral venous sinus thrombosis found that endovascular therapy with systemic anticoagulation may be effective in achieving recanalization.

Andersen, T., et al. Endovascular Treatment for Cerebral Venous Sinus Thrombosis – A Single Center Study. **Br J Neurosurg**, 2021, 35:3, 259-265.

RECOVERY OF VISUOSPATIAL NEGLECT AFTER STROKE

Visuospatial neglect is a common consequence of stroke. This study investigated specific attributes of

acute neglect impairment and their relationship to the recovery of functional outcome.

A secondary analysis of data collected within the Oxford cognition screen (OCS) and OCS-Tablet studies was completed. Subjects were 400 stroke survivors who underwent acute cognitive screening and six-month follow-up. Data were reviewed to assess the factors associated with chronic neglect, and the interaction between acute neglect subtype and outcome.

Of the 400 patients involved in the study, 35.5% exhibited significant neglect at baseline. Of these 50% involved only egocentric neglect, 28.9% only allocentric neglect, and 21.1% involved both. At follow-up, 69% of the neglect cases had fully recovered. The regression analysis found that the initial severity of acute allocentric neglect was a significant predictor of poor long-term functional outcome ($p < 0.001$). This was not true of egocentric neglect.

Conclusion: This study of stroke survivors found that the severity of allocentric neglect is a significant predictor of functional outcomes.

Moore, M., et al. Recovery of Visuospatial Neglect Subtypes and Relationship to Functional Outcome Six Months after Stroke. **Neurorehabil Neural Repair**. 2021. <https://doi.org/10.1177/15459683211032977>

COGNITIVE PERFORMANCE AND LOWER EXTREMITY BIOMECHANICS

Studies have demonstrated that previously concussed athletes have a significantly greater chance of lower extremity injury, as compared to non-concussed athletes. This study explored the correlation between cognitive assessments of reaction time and working memory to the biomechanical patterns of athletic performance.

Subjects were 20 college athletes with a prior sports-related concussion, and 20 matched controls. All performed land and cut drills while monitored in a motion analysis lab. During the trials, functional visuomotor reaction time (FVMRT) was measured. Kinetic and kinematic data were collected using a motion capture system. Each variable was assessed during the first 100 milliseconds of ground contact with the force platform, as lower extremity injuries including anterior cruciate ligament ruptures occur within that time. Cognitive performance was

assessed with the immediate post-concussion assessment and cognitive test (ImPACT) and the Senaptec Sensory Station (Senaptec LLC).

Most of the cognitive measures did not correlate with visual-motor reaction time. In the concussed cohort, slower FVMRT was moderately correlated with decreased knee flexion. An increased abduction moment in the dominant knee was correlated with decreased ImPACT visual memory scores and slower impact reaction time.

Conclusion: In this study of athletes with a history of a sports-related concussion, several moderate correlations were found between decreased cognitive performance and lower extremity biomechanics.

Avedesian J., et al. Relationship between Cognitive Performance and Lower Extremity Biomechanics: Implications for Sports-Related Concussion. **Orthop J Sports Med**. August 2021. [doi:10.1177/23259671211032246](https://doi.org/10.1177/23259671211032246).

COMMON EXTENSOR TENDON PATHOLOGY IN CARPAL TUNNEL SYNDROME

Lateral epicondylitis (LE) is an overuse injury due to eccentric overload of the common extensor tendon (CET). Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy, also considered an overuse syndrome. This study assessed whether patients with CTS without clinical LE would have an increased rate of abnormalities within the CET.

Subjects were recruited from patients referred to a neurophysiology laboratory for possible CTS. Control subjects were recruited from asymptomatic relatives and caregivers of these patients. All underwent electrodiagnostic studies, followed by B-mode and power Doppler ultrasound examination of the CET. The total number of abnormalities in both B-mode ultrasound and power Doppler were summed to obtain the sonographic abnormality score, which ranged from zero to six, with each abnormality given one point.

Data were collected for 39 limbs of 27 patients with CTS and 20 limbs of 20 volunteers. The mean CET abnormalities score was higher in the CTS patients than in the controls ($p = 0.006$). The CTS patients with sonographically abnormal CET had a lower median sensory amplitude than did those with sonographically normal CET ($p < 0.05$). The mean CET

stiffness was lower in CTS patients than controls ($p=0.033$), though there were no significant differences in CET stiffness associated with increasing severity of CTS.

Conclusion: This study of patients with carpal tunnel syndrome found that common extensor tendon abnormalities occur frequently and may relate to common pathologic mechanisms.

Wee, T., et al. Asymptomatic Common Extensor Tendon Pathology in Patients with Carpal Tunnel Syndrome. **Muscle Nerve**. 2021, July; 64(1): 64–69.

PHYSICAL REHABILITATION FOR HOSPITALIZED ELDERLY WITH HEART FAILURE

Among older patients with acute heart failure, physical function is markedly impaired. When patients with chronic heart failure transition to acute decompensated heart failure requiring hospitalization, physical function worsens further during hospitalization and bed rest. Many patients never recover their baseline function. This study, the Rehabilitation Therapy in Older Acute Heart Failure Patients (REHAB-HF) trial, assessed the effect of an early progressive rehabilitation intervention on the physical function and rehospitalization of these patients.

Subjects were 349 adults, 60 years of age or older, admitted for acute decompensated heart failure. Eligible patients were unable to walk at least four meters at enrollment but were independent before admission and expected to be discharged to home. Those randomized to the treatment group underwent an early, transitional, tailored, progressive physical rehabilitation program that focused on strength, balance, mobility, and endurance. The intervention was initiated in the hospital and transitioned to outpatient facilities after discharge. Sessions were 60 minutes, occurring three days per week for 12 weeks. These were complemented by home exercise on non-program days. Outcome measures of physical and cognitive function were made by blinded evaluations. The primary outcome was the Short Physical Performance Battery (SPPB) at three months.

At three months, improvement in the SPPB was 8.3 in the intervention group and 6.9 in the control group ($p<0.001$). The rates of rehospitalization for any cause within six months were 1.18 in the

intervention group and 1.28 in the control group.

Conclusion: This study of older patients hospitalized for acute decompensated heart failure found that an early progressive rehabilitation intervention could result in greater improvement in physical function and reduced readmissions compared to usual care.

Kitzman, D., et al. Physical Rehabilitation for Older Patients Hospitalized for Heart Failure. **N Engl J Med**. 2021, June 15; 385 (3): 203-216.

FOOT DROP IN CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

Distal lower extremity weakness, including foot drop, is common in patients with chronic inflammatory demyelinating polyneuropathy (CIDP). As foot drop is an important cause of gait difficulties and falls, this study assessed the recovery of foot drop in patients with CIDP, and to determine predictive factors of this recovery.

Subjects were consecutive patients with CIDP, presenting with moderate to severe foot drop. All patients received standard immunomodulatory treatment and were followed for at least one year. At baseline and follow-up, patients underwent electrodiagnostic studies to determine the distal compound muscle action potential (CMAP) amplitude, gross measure of residual fibular motor axon number. Ambulatory status at baseline and at one year was characterized as independent, dependent on cane for balance, use of ankle-foot orthoses (AFO), use of walker or rollator with or without AFO, wheelchair dependent or bedbound.

Subjects were 27 patients with a mean age of 51 years, with 21 patients presenting with bilateral foot drop. At one year, ankle dorsiflexion had recovered to antigravity strength in 60%, and to full strength in 27% of the patients. Wheelchair use declined from 48% at baseline to 7% at one year, with independent ambulation found occurring in 44% at one year. A multivariate analysis found that Medical Research Council manual muscle testing (ADF MRC power) at presentation was not dependent on CIDP type, gender, age, symptom duration, or the presence of diabetes. The predictors of recovery of ankle dorsiflexion power were tibialis anterior CMAP

amplitude at presentation, shorter disease duration, and female gender.

Conclusion: This study of patients with chronic inflammatory demyelinating polyneuropathy found that foot drop returns to antigravity power in most patients, depending on the severity of fibular motor axon loss at the onset of treatment.

Weerasinghe, D., et al. Recovery of Foot Drop in Chronic Inflammatory Demyelinating Polyneuropathy (CIDP). **Muscle Nerve**. 2021, July;64:59–63.

POSTURE GARMENT FOR NONSPECIFIC NECK PAIN

The prevalence of cervical symptoms in the general population ranges between 10% and 15% with a higher prevalence among females. This study was designed to assess the effect of a postural garment, designed to enhance abdominal contraction and shoulder proprioception, for patients with a complaint of chronic cervical pain.

This randomized crossover clinical trial included women 21-55 years of age with nonspecific cervical pain with a rating of three or greater on a visual analog scale (VAS). The subjects were randomized to an exercise group (Ex), or Ex plus garment group (Ex+) to wear a T-shirt garment, the PosturePlusForce. Both groups attended five exercise sessions of 20 minutes, once per week. After a three-month washout, the participants swapped intervention groups for another three months. The primary outcomes were pain intensity measured with a VAS, and posture, measured with a computerized measurement of the surface curvature (Spinal Mouse).

A total of 29 participants completed the study. Between baseline and the first three-month follow-up, the Ex+ group improved by 58% and the Ex group by 38% ($p=0.26$). Among subjects with dorsal hyperkyphosis ($>45^\circ$), the Ex+ group demonstrated a greater reduction in pain than the Ex group ($p=0.019$). Those in the Ex+ group needed fewer pain relievers than did the Ex group ($p=0.007$).

Conclusion: This study of adults with neck pain demonstrated that the garment designed to improve posture could result in a decrease in pain, particularly among those with dorsal hyperkyphosis.

Avellanet, M., et al. A Comparative Study of a Novel Posture Garment Versus Exercise for Women with

Nonspecific Cervical Pain: A Randomized Cross-Over Trial. **Spine**. 2021. <https://doi.org/10.1097/BRS.0000000000004123>.

NITROGEN DIOXIDE AND PARKINSON DISEASE

The Braak staging scheme of Parkinson disease (PD) proposed that the pathologic aggregation of α -synuclein begins in the olfactory bulb and gut before spreading through the central nervous system. This suggests that exposure to environmental pollutants may be a risk factor. This study evaluated the associations between the incidence of PD and six types of air pollutants.

This study used data from the National Health Insurance Service (NHIS), including 97% of residents of South Korea. Subjects were chosen from this database who were 40 years of age or older without PD who lived in Seoul between January 2002 and December 2006. Harvested data included body mass index, physical activity, tobacco abuse, drinking habits, and physical activity. During that time the Seoul Research Institute of Public Health and Environment provided hourly monitored data on PM_{2.5}, PM₁₀, NO₂, O₃, SO₂, and CO from 25 monitoring sites. The primary outcome was a comparison between the exposure and newly diagnosed PD.

During nine years of follow-up, 330 participants developed PD, resulting in an incidence rate of 44.6 cases per 100,000 person-years. Exposure to NO₂ was associated with an increase in the risk of PD at one year ($p=0.045$). There was no increased risk of developing PD and exposure to the other pollutants. This association was robust even after controlling for covariates.

Conclusion: This large cohort study found a significant association between nitrogen dioxide exposure and the risk of Parkinson disease.

Jo, S., et al. Association of Nitrogen Dioxide and Other Air Pollution Exposures with the Risk of Parkinson Disease. **JAMA Neurol**. 2021, July; 78(7):800-808.

PATIENT ATTITUDES TOWARDS PHYSICIAN ATTIRE

In recent years, casual physician attire has gained popularity as an alternative to white coats. This study was designed to characterize public perceptions of casual physician attire, including fleece and softshell jackets,

compared with the traditional professional physician attire of business suits and a white coat.

A web-based survey was distributed to adult United States residents. Survey questions including demographic information, prior exposure to healthcare and the healthcare employment status of respondents or their family members. Photographs of models wearing permutations of various health care attire were presented. The respondents were asked to rate professionalism, experience, and friendliness of the male and female models in various attire and perceptions of the models most likely health care profession.

Of 487 completed surveys, experience was perceived as the most important trait of healthcare professionals. For models shown in either business or scrub inner wear, a white coat was associated with a perception of the practitioner being experienced ($p<0.01$) professional ($p<0.003$) as well as friendly ($p<0.01$). Comparing males with female wearing the same attire, subjects perceived males to be significantly more professional, and more likely to be a physician.

Conclusion: This study found that respondents rated physicians wearing casual attire as less professional and less experienced than those wearing a white coat.

Xun, H., et al. Public Perceptions of Physician Attire and Professionalism in the US. **JAMA Open**. 2021;4(7):e2117779. doi:10.1001/jamanetworkopen.2021.17779.

MARTIAL ARTS TRAINING AND RESILIENCE IN SECONDARY STUDENTS

The World Health Organization estimated that the annual global cost of mental health problems in 2010 was \$2.5 trillion. Resilience is defined as capacity to cope with adversity, risk, or stress and achieve positive outcomes. This study evaluated the effects of martial arts training on resilience in secondary school students.

Subjects were 283 students with an average age of 12.76 years, recruited from five secondary schools in Australia. Those randomized to the treatment group received 60-minute training sessions once per week for 10 weeks. Each session began with a 10-minute discussion of respect, goal setting, self-concept, self-esteem, courage, resilience, bullying, and peer pressure. The

remainder of the sessions included training in stance, blocks, punching, and kicking. The primary outcome was the Child and Youth Resilience Measure (CYRM), at baseline, post-intervention and 12 weeks post-intervention.

Compared to baseline scores, those in the intervention group demonstrated improved levels of overall resilience ($p=0.000$). The training effect on the scores was stronger immediately following the intervention compared with 12-week follow-up.

Conclusion: This study of seventh and eighth grade students with an average age of 12.8 years found that martial arts training for 10 weeks could improve resilience scores.

Moore, B., et al. Well-Being Warriors: A Randomized Controlled Trial Examining the Effects of Martial Arts Training on Secondary Students Resilience. **Br J Educ Psychol**. 2021. <https://doi.org/10.1111/bjep.12422>.

TICAGRELOR AND ASPIRIN FOR MODERATE ISCHEMIC STROKE

Dual antiplatelet therapy (DAPT) is a pivotal strategy for the early management of minor non-cardioembolic ischemic stroke as well as transient ischemic attack (TIA). In the Acute Stroke or Transient Ischaemic Attack Treated With Ticagrelor and ASA for Prevention of Stroke and Death (THALES) trial, DAPT with ticagrelor and aspirin was evaluated in patients with TIA or acute ischemic stroke presenting with an NIHSS score of five or less. This study characterized the efficacy of this therapy for patients with NIHSS scores of four or five.

This multicenter, double-blind, placebo-controlled, parallel-group randomized clinical trial was conducted at 414 sites in 28 countries. The subjects were 40 years or older, had an acute noncardioembolic ischemic stroke with an NIHSS score of five or less, or a high-risk TIA (ABCD₂ score of six or greater, or symptomatic intracranial or extracranial arterial stenosis). All patients took aspirin (300 to 325 mg on day one followed by 75 to 100 mg daily on days two to 30) in the first 30 days. The subjects were randomized to receive a placebo or ticagrelor (180-mg loading dose on day one followed by 90 mg twice daily on days two to 30). The primary efficacy outcome was time from randomization to the first

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occurrence of new stroke (ischemic
or hemorrhagic) or death within 30
days.

The subjects were 3,312 patients
(30.1%) with moderate stroke and
6,671 patients (60.6%) with less
severe stroke. Among the 3,312
patients with moderate stroke, 1,671
patients were assigned to the
ticagrelor group, and 1,641 to the
placebo group. In patients with
moderate stroke, the primary
endpoint occurred in 7.6% of those
taking ticagrelor + aspirin and 9.1% of
those receiving a placebo + aspirin
(HR 0.84). This effect size was similar
to that in patients with less severe
stroke, with an HR of 0.82.

Conclusion: This study of
patients with acute ischemic stroke
with a baseline NIHSS score of 4 to 5
found that adding Ticagrelor to aspirin
reduced the risk of stroke or death
within 30 days.

Wang, Y et al., Efficacy and Safety of
Ticagrelor and Aspirin in Patients
With Moderate Ischemic Stroke: An
Exploratory Analysis of the THALES
Randomized Clinical Trial. **JAMA
Neurol.** 2021, July 9; doi:10.1001/
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