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CHRONIC LOW BACK PAIN AND BRAIN ATROPHY

Chronic low back pain (CLBP) is the leading cause of years lived with disability. The concept of nociplastic pain syndromes was recently proposed, wherein augmented pain and sensory processing altered pain modulation in the central nervous system are thought to play prominent roles. This study investigated the association between CLBP and regional brain atrophy in an elderly Japanese population.

The Hisayama Study is an ongoing, population-based, cohort study of cerebrovascular disease in the town of Hisayama Japan. In addition to annual health examinations for those ≥ 65 years of age, comprehensive screening surveys of dementia and activities of daily living were conducted every five to seven years beginning in 1985. In 2017 and 2018, 2,202 residents were surveyed for dementia, among whom 71.6% underwent brain magnetic resonance imaging (MRI) scans to measure volumes of cortical and subcortical structures. The subjects were assessed for pain, with chronic pain defined as subjective pain for more than three months.

Individuals suffering mainly from chronic low back pain (CLBP) accounted for 17% of the total sample. In a multivariable analysis, adjusted for cerebrovascular risk factors, the CLBP group had lower volumes of the ventrolateral prefrontal cortex ($p=0.009$) dorsolateral prefrontal cortex ($p=0.02$), posterior cingulate cortex ($p=0.03$), and the amygdala ($p=0.02$) than did those with no chronic pain.

Conclusion: This study of elderly Japanese adults found an association between chronic low back pain and regional brain atrophy, with lower brain volumes found in the prefrontal cortex, posterior cingulate cortex, and amygdala.

Asada, M., et al. Association Between Chronic Low Back Pain and Regional Brain Atrophy in a Japanese Older

Population: The Hisayama Study.
Pain. 2022, November; 163(11): 2185-2193.

EVENINGNESS, MUSCULOSKELETAL PAIN AND QUALITY OF LIFE

Musculoskeletal pain can be a disabling condition with reduced health-related quality of life (HRQoL). Circadian rhythms reflect the 24-hour physiological and behavioral cycles within each individual. These can be categorized into three phenotypes, morning (M-alertness level at its highest in the morning), evening (E-most active in the evening), and intermediate (I-neither M nor E). This study investigated whether musculoskeletal pain and HRQoL differ by phenotype.

Data were obtained from the Northern Finland Birth Cohort 1966 ($N=4,257$), a large representative sample of individuals born in 1966. The subjects were assessed for QoL using the 15D, a standardized measurement of HRQoL. A questionnaire asked about musculoskeletal pain within the previous year, with responses grouped by frequency and intensity [numerical rating scale (NRS)-pain]. Chronotypes were established using the Morningness-Eveningness Questionnaire (sMEQ), with subjects characterized as Evening, Morning or Intermediate. Covariates included gender, sufficiency of sleep duration, mental distress, and coexisting diseases.

The chronotype distribution included 534 Evening, 1,878 Intermediate, and 1,845 Morning subjects. The Evening group had higher pain intensity, pain-related disability at work, NPS pain scores, and daily pain frequency than did the other chronotypes ($p<0.001$ for all comparisons). After adjusting for all covariates, the reduction in pain related HRQoL was more pronounced in the Evening group, demonstrating that eveningness

intensified the association between MSK pain and HRQoL.

Conclusion: This study of working-age individuals found that the reduction in health-related quality of life in relation to pain was more pronounced among those with an evening chronotype than in those with other chronotypes.

Heikkala, E., et al. Eveningness Intensifies the Association between Musculoskeletal Pain and Health-Related Quality of Life: A Northern Finland Birth Cohort Study 1966.
Pain. 2022, Nov 1; 163(11): 2154-2161.

PHYSICAL ACTIVITY PARADOX

Studies have shown that a high level of occupational physical activity is associated with an increase in the risk of coronary heart disease, compared with low occupational physical activity, even after adjusting for confounders. The opposite holds true for leisure time physical activity. This is referred to as the "physical activity paradox". To better understand this paradox, this study compared the inflammation associated with physical activity at work with that occurring during leisure activity.

This cross-sectional study used data from the Copenhagen Aging and Midlife Biobank (CAMB) cohort. The participants were 7,243 middle-aged men and women, of whom 5,576 participated in a physical examination, and 5,304 had serum drawn to determine levels of high-sensitivity CRP (hs-CRP) as a measure of systemic inflammation. Levels of occupational and leisure physical activity were determined, with each categorized as low or high. The association between the types and levels of physical activity were compared to the levels of hs-CRP.

An unadjusted analysis revealed that, compared to those with a low level of occupational activity, those with a high level of occupational activity had a mean hs-CRP that was

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23% higher ($p < 0.0001$). Conversely, compared to those with the highest level of recreational activity, those with the lowest level had a 27% higher level of hs-CRP ($p < 0.0001$). An adjusted analysis found that the increase in hs-CRP attributable to lower leisure-time physical activity was 12% ($p < 0.0001$), and that attributable to a higher level of occupational physical activity was six percent, which did not reach statistical significance ($p = 0.0657$).

Conclusion: This study found higher systemic inflammation (hs-CRP) to be associated with high occupational physical activity but with low recreational physical activity.

Feinberg, J., et al. Physical Activity Paradox: Could Inflammation Be a Key Factor? *Br J Sport Med.* 2022, November; 56 (21): 1224-1229.

ASSOCIATION BETWEEN SOCIAL CONNECTIONS AND COGNITION

In 2020, the Lancet Commission on Dementia Prevention estimated that tackling social isolation could prevent four percent of dementia cases worldwide. This meta-analysis aimed to better understand the associations between various markers of social connectivity and the annual change in cognition.

Data were collected from 13 longitudinal cohort studies of aging, with baseline data for social connection markers, and at least two follow-up periods that collected cognitive scores. A meta-analysis was used to examine the associations between baseline social connections and the change in cognition over time. In the fully adjusted models, data were controlled for age, gender, education, history of diabetes, hypertension, smoking, cardiovascular disease risk, and depression.

The analysis included 38,614 adults, with follow-up periods ranging from two to 15 years across cohorts. Being married or in a relationship was associated with a slower global cognitive decline than being single or never married ($p = 0.01$). Living with others was associated with a slower decline in global cognition, memory, and language than was living alone ($p = 0.007$). Weekly engagement in a community group was associated with a slower annual memory decline ($p = 0.012$) as were weekly interactions with family and friends ($p = 0.006$). Never feeling lonely was associated with a slower decline of

global cognition and executive function ($p = 0.047$).

Conclusion: This meta-analysis found that slower cognitive decline was associated with being married or in a relationship, living with one or more people, and never feeling lonely.

Samtani, S., et al. Associations between Social Connections and Cognition: A Global, Collaborative, Individual Participant Data Meta-Analysis. *Lancet Healthy Longev.* 2022, October; doi.org/10.1016/S2666-7568(22)00199-4.

SMALL HIGH DENSITY LIPOPROTEIN PARTICLES, PHYSICAL ACTIVITY, AND LONGEVITY

Prior cross-sectional cohort studies of the causal determinants of aging have been impeded by selection biases. To overcome these, the Duke Established Populations for Epidemiologic studies of the Elderly (D-EPESE) was established.

The D-EPESE is a longitudinal cohort of community dwelling older adults which includes 1,507 participants, 71 years of age or older, with biomarker data and 27 years of death data from the time of blood sample acquisition in 1992. Data included 186 clinically accessible measures, body mass index, medical morbidities, self-rated health, depression, health behaviors, cognitive and physical activity status, 48 traditional medical blood tests, six inflammation parameters, and 48 lipoprotein biomarkers. A Markov boundary (MV) analysis was completed to identify predictive variables for longevity.

The rates of all-cause mortality at two, five, and 10 years were 11.8%, 31.3%, and 71.7%, respectively. The mean time to death was 7.86 years. The variables with the strongest performance for predicting longevity were the numbers of small high density lipoprotein particles (sHDL), younger age, and fewer pack-years of cigarette smoking. Physical function was a prominent predictor at all time horizons.

Conclusion: This study of patients 71 years of age or older found that age, fewer cigarettes smoked, and greater numbers of small high density lipoprotein particles were the strongest predictors of longevity.

Kraus, V., et al. Causal Analysis Identifies Small HDL Particles and

COARSE GRAIN CONSUMPTION AND CARDIOMETABOLIC DISEASES

Low consumption of whole grains has been recognized as a major, modifiable risk factor for cardiometabolic diseases. In addition, several large-scale meta-analyses of prospective studies have reported inverse associations of whole-grain consumption with incident diabetes and coronary heart disease. This prospective study assessed the effects of coarse grains on the risk of cardiometabolic diseases and diabetes.

The China Kadoorie Biobank (CKB) is a prospective study, involving people in 10 geographic regions. All permanent residents 35 to 74 years of age were invited to participate. After excluding those with diabetes, heart disease, stroke, or cancer at baseline, 461,047 subjects, ages 30 to 79 years, were enrolled. Data gathered included sociodemographic factors and medical history. Dietary information was collected using a short, semi-quantitative food frequency questionnaire (FFQ), with participants asked to report their habitual consumption frequencies for each food group during the previous 12 months. The subjects were divided into four groups by levels of coarse grain consumption of four days per week or more, one to three days per month, monthly, or never/rarely.

Compared with those who reported never or rare consumption, regular consumers of coarse grains had a lower risk of diabetes (adjusted Hazard Ratio (HR), 0.88) and ischemic stroke (adjusted HR, 0.86), but not hemorrhagic stroke or major coronary events. Each 100 g/day increase in the usual intake of coarse grains was associated with a 14% lower risk of diabetes and a 13% lower risk of ischemic stroke.

Conclusion: Using data from the prospective China Kadoorie Biobank, researchers found that the consumption of coarse grains was associated with a lower risk of ischemic stroke and diabetes.

Yang, J., et al. Coarse Grain Consumption and Risk of Cardiometabolic Diseases: A Prospective Cohort Study of Chinese

SERUM BIOMARKERS AND FUNCTIONAL OUTCOME AFTER TRAUMATIC BRAIN INJURY

Traumatic brain injury (TBI) is a leading cause of death worldwide and a major and increasing health burden. This study assessed the incremental prognostic value of six serum biomarkers (S100 calcium-binding protein B [S100B], neuron-specific enolase, glial fibrillary acidic protein [GFAP], ubiquitin C-terminal hydrolase L1 [UCH-L1], neurofilament protein-light [NFL], and total tau [t-tau]) for predicting functional outcome, six months after TBI.

Data were obtained from the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) observational, cohort study. Participants were 14 years of age or older with a median age of 51 years. Extracted data included demographic, clinical, biomarker assays, CT results, and outcomes. The primary outcome measure was the Glasgow Outcome Scale-Extended (GOSE-E) at six months. The GOSE-E scores were divided into clinically relevant endpoints, including mortality (GOSE 1), unfavorable outcome (GOSE $\leq$ 4), and incomplete recovery (GOSE $<$ 8).

Data were complete for 2,283 patients. At six months, 12% had died, 26% had an unfavorable outcome, and 63% had an incomplete recovery. Increased levels of several biomarkers were associated with worse six-month GOSE-E outcomes, and were strongest for UCH-L1, NFL, S100B, t-tau, and GFAP. The levels of UCH-L1 had the greatest incremental prognostic value. Adding biomarkers to the established prognostic models resulted in a relative increase in R^2 of 48-65% for the IMPACT test and 30-34% for the CRASH prognostic models.

Conclusion: This study found that serum biomarkers can improve the prognostic accuracy of established prognostic models.

Helmrich, I., et al. Incremental Prognostic Value of Acute Serum Biomarkers for Functional Outcome after Traumatic Brain Injury (CENTER-TBI): An Observational Cohort Study. **Lancet Neurol**. 2022, September; 21(19): 792-802.

TRAUMATIC BRAIN INJURY AND SUBSEQUENT CARDIOVASCULAR DISEASE

It is estimated that 20% of military veterans who served in Iraq and Afghanistan since 9/11/2001, have sustained at least one traumatic brain injury (TBI). As prior data have suggested an association between TBI and stroke, this study evaluated the association between TBI and cardiovascular disease (CVD) among a group of military veterans.

Military data collection sites were explored for veterans with a diagnosis of TBI, and a control group with no history of TBI. Data were extracted for age, sex education, rank, deployment history, combat exposure, and medical comorbidities. The primary outcome was cardiovascular disease (CVD), a composite of coronary artery disease, stroke, peripheral artery disease and CVD death.

Data were completed for 1,559,928 veterans with a TBI and 1,258,759 with no TBI (N-TBI). Compared to the n-TBI group, CVD was more likely among those with mild TBI ($p<0.001$), moderate to severe TBI ($p<0.001$), and penetrating TBI ($p<0.001$). All categories of TBI were significantly associated with stroke, PAD, and CAD. Death from CVD was more likely among those with mild TBI ($p<0.001$), and moderate to severe TBI ($p<0.001$). Stroke was also more likely among those with TBI ($p<0.001$), with this being more pronounced among those with severe TBI with a hazard ratio (HR) ranging from 2.53 for mild TBI to 12.15 for penetrating TBI.

Conclusion: This large study of military veterans suggests that traumatic brain injury is independently associated with the risk of cardiovascular disease.

Stewart, I., et al. Association Between Traumatic Brain Injury and Subsequent Cardiovascular Disease Among Post-9/11-Era Veterans. **JAMA Neurol**. 2022, Sep 6; e222682. Online ahead of print.

VESTIBULAR OCULAR MOTOR SCREENING AFTER CONCUSSION

In populations with mild traumatic brain injury (mTBI) and persistent dizziness and imbalance, vestibular ocular motor screening may be useful for clinical subtyping. This study compared self-reported Vestibular Ocular Motor Screening (VOMS)

symptom scores in adults with mTBI to matched controls.

This cross-sectional study was completed across three separate sites between June 2019 and September 2020. Participants were 18 to 50 years of age without medical conditions that may affect balance. Subjects reported an mTBI with symptoms persisting beyond three weeks. The patients were compared to 57 healthy controls. All were tested with the VOMS, with post-item symptom scores recorded. The subjects were also tested with the Dizziness Handicap Inventory (DHI), as well as for clinical balance, and gait assessments. For the VOMS, patients were assessed for smooth pursuit, horizontal saccades, vertical facades, near point convergence, horizontal vestibular ocular reflex, vertical vestibular ocular reflex and visual motion sensitivity. The DHI, a self-reported symptom questionnaire, was given at baseline and follow-up. Balance was assessed, and gait speed was determined using the one-minute walk test at a comfortable self-selected pace between two lines six meters apart. Higher level mobility was assessed using the Revised High-Level Mobility Assessment Tool (HiMAT-R) and the modified (narrowed) Illinois Agility Task (mIAT).

Compared to the control group, the mTBI group reported significantly more symptoms following each item of the VOMS, and a further near point of convergence. Strong positive relationships were found between the DHI self-reported symptoms and scores and VOMS symptom scores ($p < 0.001$ for all comparisons).

Conclusion: This study of patients with mild traumatic brain injury found significantly more symptoms on the vestibular ocular motor screening test, with these correlated with scores on the Dizziness Handicap Inventory.

Parrington, L., et al. Exploring Vestibular Ocular Motor Screening in Adults with Persistent Complaints After Mild Traumatic Brain Injury. *J Head Trauma Rehabil.* 2022, Sept/Oct; 37(5):E346-E354.

AEROBIC VERSUS RESISTANCE EXERCISE FOR CHRONIC WHIPLASH ASSOCIATED DISORDER

Whiplash injury is a common following motor vehicle accidents, with up to 30% developing chronic, moderate to severe pain-related

disability. As exercise is a common treatment recommendation after such injuries, this study compared the efficacy of resistance to aerobic exercise in patients with chronic whiplash associated disorder (WAD).

The subjects were patients with chronic WAD Grade II, with neck pain intensity as a primary complaint. Patients were assessed with a Short Form 36 questionnaire, and a Godin-Shepherd Leisure Time Physical Activity questionnaire. Using a single case experimental design, participants were randomly allocated to receive aerobic or resistance exercises, with three exercise sessions per week for eight weeks with each session lasting 30 to 60 minutes. The aerobic group had a target intensity of 40-60% of their maximum heart rate. The strengthening group exercised at 40-60% of their one repetition maximum with two to three sets per exercise with one session typically consisting of 10 to 15 exercises. Patients were assessed at baseline and follow up with the Neck Disability Index (NDI).

At follow-up all eight patients in the aerobic group showed a decrease in pain intensity and pain bothersomeness. The average improvement in the 100-point VAS scores was 7.95 in the aerobic group and 2.12 in the resistance training group.

Conclusion: This small pilot study of patients with chronic whiplash associated disorder found that aerobic exercise had a greater effect on pain and disability than did resistance training.

deZoete, R., et al. The Effectiveness of Aerobic Versus Strengthening Exercise Therapy in Individuals with Chronic Whiplash Associated Disorder: A Randomized Single Case Experimental Design Study. *Disability Rehabil.* 2022. DOI:10.1080/09638288.2022.2127937.

LONG TERM POSTURAL CONTROL AMONG ELITE ATHELETES

After a mild traumatic brain injury (mTBI), symptoms typically subside within 14 days. Recent studies of patients with persistent post concussive syndrome (PPCS) have found that many suffer from vestibular symptoms. This study was designed to determine whether a mTBI affects postural stability and motor learning through sensory motor adaptation.

Subjects were elite athletes in a variety of sports, who had terminated their sports career due to neck and head injuries. All had symptoms persisting for more than six months. Postural stability was measured by posturography, under four conditions; eyes open, eyes closed, during quiet rest, and when perturbed. Force plates measured the energy used to maintain balance. Perturbations were produced by vibrators strapped over the calf muscles, with conditions including both a high and a low frequency vibration.

Data were complete for 20 elite athletes with mTBI and PPCS and a control group of 12 athletes with no history of sports related concussion. During the perturbation trial, compared to controls, the TBI group used 143% more energy ($p = 0.004$). During the vision trial with eyes closed, the mTBI group used 222% more energy ($p = 0.003$). With repetitions of the perturbation trials the mTBI group demonstrated less improvement than did the control group.

Conclusion: This study of elite athletes with persistent post concussive syndrome, found that these patients have worse postural stability than controls, during quiet stance, with eyes closed and with postural perturbations.

Al-Husseini, A., et al. Long-Term Postural Control in Elite Athletes Following Mild Traumatic Brain Injury. *Frontiers Neurol- Open.* 2022, September 12. doi.org/10.3389.

THROMBECTOMY SIX TO 24 HOURS AFTER BASILAR ARTERY OCCLUSION

Previous trials which focus on patients with acute stroke due to large vessel occlusion (LVO) have often excluded those with basilar artery occlusion. The Basilar Artery Occlusion Chinese Endovascular (BAOCHE) trial was designed to assess the efficacy and safety of endovascular thrombectomy, in conjunction with medical therapy, as compared with medical therapy alone, in patients with acute ischemic stroke due to basilar-artery occlusion.

Subjects were 18 to 80 years of age with an occlusion of the basilar artery or of both vertebral arteries within six to 24 hours of symptom onset. Those patients were randomly assigned in a 1:1 ratio to undergo thrombectomy plus standard medical care (thrombectomy group) or standard medical care alone (control

group). The primary outcome variable was a good functional outcome, defined as a modified Rankin Scale (mRS) score of zero to three at 90 days.

Data were analyzed for 218 patients with a median age of 65 years and a median time from symptom onset of 663 minutes. Intravenous alteplase was administered to 18% in the thrombectomy group and 21% in the control group. Good functional outcomes were seen in 46% of the thrombectomy group and 24% of the control group ($p < 0.001$). An mRS score of zero to two was achieved by 39% in the thrombectomy group and 14% in the control group. Symptomatic intracranial hemorrhage occurred in six percent of the thrombectomy group and one percent of the control group.

Conclusion: This study of patients with a basilar artery occlusion and a symptom onset of six to 24 hours found that those who underwent a thrombectomy had a significantly greater chance of a good outcome as compared to those receiving medical treatment alone.

Jovin, T., et al. Trial of Thrombectomy Six To 24 Hours after Stroke Due to Basilar Artery Occlusion. *N Engl J Med*. 2022, October 13;387(15): 1373-1384.

FISH CONSUMPTION AND STROKE RISK

Studies of the relationship between fish consumption and the risk of stroke have produced contradictory results. Most of the longitudinal studies of the association between fish consumption and the incidence of stroke have been carried out in the United States, Japan, and Europe. This prospective cohort study analyzed the association of fish consumption with the incidence of stroke among adults in Shanghai.

Data were obtained from the Shanghai Suburban Adult Cohort and Biobank (SSACB) study and a cohort study in Minhang district, Shanghai. A total of 62,841 participants were recruited at baseline. All attended face-to-face interviews, with exams including blood and urine samples. Fish consumption was determined by a food frequency questionnaire at baseline and divided into four categories (less than 300 grams/week, 300-450 grams per week, 450-600 grams per week and over 600 grams per week). Follow-up was

performed through linkage to health information systems.

Data were complete for 57,701 adults with a median age of 59 years. During a median follow-up of 4.56 years, 807 new stroke events were identified, including 664 ischemic, 113 hemorrhagic and 30 unspecified strokes. In an adjusted analysis, compared to those who consumed <300 grams per week, participants who consumed 300-450 g per week of fish had the lowest incidence of total stroke (Hazard Ratio (HR) 0.78) and ischemic stroke (HR 0.70). No significant correlations were found between fish consumption and hemorrhagic strokes.

Conclusion: This Chinese prospective cohort study found that the fish consumption of 300 to 450 g per week reduced the risk of total stroke and ischemic stroke as compared to the consumption of under 300 g per week.

Cui, S., et al. Fish Consumption and Risk of Stroke in Chinese Adults: A Prospective Cohort Study in Shanghai, China. *Nutrients*. 2022, October; 14(20): 4239.

PROPHYLACTIC LEVETIRACETAM IN THE ACUTE PHASE OF INTRACEREBRAL HEMORRHAGE

The incidence of early seizures after intracerebral hemorrhage (ICH) is estimated at 30% when subclinical seizures are diagnosed by continuous EEG. As current guidelines do not recommend prophylactic anti-seizure medication in this setting, this study assessed the effect of levetiracetam in patients with an acute ICH.

This double-blind, randomized, placebo-controlled, phase three trial included adults presenting within 24 hours of a nontraumatic ICH. The patients were randomly assigned to receive intravenous levetiracetam every 12 hours or a matching placebo, with treatment continuing for six weeks. Continuous EEG was started within 24 hours and recorded over 48 hours. The primary endpoint was the occurrence of at least one clinical seizure within 72 hours of inclusion.

Data were collected for 50 patients with mild-to-moderate severity ICH. During the first 72 hours, a clinical or electrographic seizure was observed in 16% of the treatment group and 43% of the placebo group ($p = 0.043$). All seizures in the first 72 hours were electrographic only. Neurological deterioration due to the intracerebral

hemorrhage occurred in one patient in the levetiracetam group and four in the placebo group.

Conclusion: This small, randomized, controlled trial suggests that levetiracetam may be effective for preventing acute seizures in patients with nontraumatic intracerebral hemorrhage.

Peter-Derex, L., et al. Safety and Efficacy of Prophylactic Levetiracetam for Prevention of Epileptic Seizures in the Acute Phase of Intracerebral Hemorrhage (PEACH): A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial. *Lancet Neurol*. 2022, September; 21(9): 781-791.

CERVICAL FACET INJECTIONS FOR CERVICOGENIC HEADACHE

Cervicogenic headache (CGH) is generally defined as a headache referred from upper cervical joints and spinal nerves of C1-C3, bony structures or soft tissue of the neck. Currently, first line treatment recommendations for these headaches include education, support and therapy. This systematic review and meta-analysis was designed to better understand the efficacy of intraarticular cervical facet steroid injections for the treatment of CGHs.

A systematic review was conducted for publications including adult patients diagnosed with CGH, presenting with axial cervical pain or headache, with neck involvement, refractory to physical therapy or medication. From this search, three studies were included which reported the effects of a corticosteroid joint injection under fluoroscopy, with outcomes measured by visual analog scale (VAS) scores of pain.

From the literature review, three studies with a total of 64 patients met the inclusion criteria. The VAS pain scores improved significantly in all studies. In the pooled analysis, the mean improvement in VAS pain scores from baseline to follow-up was 3.299/10 ($p < 0.001$).

Conclusion: This literature review and meta-analysis of studies of patients with treatment resistant cervicogenic headaches found that steroid injections at the cervical facet joints were effective for decreasing pain.

Appeadu, M., et al. The Effectiveness of Intraarticular Cervical Facet Steroid Injections in the Treatment of Cervicogenic Headache: Systematic

REPETITIVE NEUROMODULATION FOR MEMORY IN OLDER ADULTS

Previous studies have found differential contributions to memory of the dorsolateral prefrontal cortex (DLPFC) and the inferior parietal lobe (IPL). This trial explored the hypothesis that the modulation of theta rhythms in the IPL can improve auditory-verbal working memory (WM), and that modulation of gamma rhythms in the DLPFC can improve auditory-verbal long-term memory (LTM), in adults 65 to 88 years of age.

This randomized, double-blind study comprised two sham-controlled experiments. In experiment one, 60 participants were randomized to receive sham or actual stimulation, including DLPFC gamma (60 Hz) or IPL theta (4 Hz) stimulation. Each subject underwent eight sessions of transcranial alternating current (tACS), 20 minutes per day for four consecutive days. Five runs of a recall task were performed during the 20 minutes sessions. In each run, the subjects encoded a list of 20 words, and were asked to immediately recall the words at the end of the presentation of the list. Memory was examined as a function of the serial position of the presented words. In the second experiment, the protocol was repeated with theta and gamma frequency targets reversed.

Compared to the sham group, significant improvement in memory was noted for the primary word cluster (LTM) in the DLPFC gamma group ($p < 0.001$), with significant improvements noted on day two, three, four and at one month. Compared to the sham group, the IPL theta group had better WM on day three and four, and at one month ($p < 0.001$). In experiment two, with the stimulation frequencies reversed, no changes were noted in WM or LTM. The sustainability of the memory improvements at one month was correlated to the speed of memory improvement during the four-day intervention.

Conclusion: This study demonstrates that transcranial alternating current stimulation for 20 minutes four times a day using theta rhythms in the IPL and gamma rhythms in the DLPFC can improve working memory and long-term memory in older adults.

Grover, S., et al. Long-Lasting, Dissociable Improvements in Working Memory and Long-Term Memory in Older Adults with Repetitive Neuromodulation. **Nat Neurosci.** 2022, September; 25(9): 1237-1246.

LOW-INTENSITY TRANSCRANIAL ULTRASOUND AND HAND MOTOR FUNCTION

Studies have demonstrated that neuromodulation techniques can induce neuroplasticity and have been successfully used for the rehabilitation of injuries to the central nervous system. This study explored the effects of transcutaneous ultrasound (TUS) on motor function and cortical excitability in healthy adults.

This double-blind, randomized, controlled study recruited 20 healthy volunteers, randomized to receive the sham intervention (S) or TUS, provided for 10 minutes. All of the participants received TUS and sham stimulation on separate days, in random order. At baseline and follow-up, the patients were assessed for motor function using a tapping test, based on the Quiq 2.0 APP software, and for the motor evoked potential (MEP) at the abductor pollicis brevis. The primary outcome variables were the change from baseline in the tapping score and the MEP.

After the 10-minute session, compared to the sham group, the TUS group had significantly higher scores on the tapping test ($p = 0.002$), shorter MEPs ($p < 0.001$), and increased MEP amplitudes ($p < 0.01$). Also, the MEP latency was significantly shorter in the sham condition than in the TUS condition ($p < 0.001$).

Conclusion: This study of healthy adults found that ten minutes of transcranial ultrasound stimulation can improve hand motor function.

Zang, M., et al. Low-Intensity Transcranial Ultrasound Stimulation Facilitates Hand Motor Function and Cortical Excitability: A Crossover, Randomized, Double-Blind Study. **Front Neurol.** 2022, September; 13: 926027. doi: 10.3389/fneur.2022.926027.

HAND OSTEOARTHRITIS IN POSTMENOPAUSAL WOMEN

Osteoarthritis of the hand (HOA) is one of the most prevalent forms of OA. The lifetime risk of symptomatic HOA at age 85 has been estimated to

be 50% in women and 25% in men. This study assessed the prevalence of HOA and the disability associated with this condition among older women.

The Qualite Osseuse Lyon ORleans (QUALOR) study is a perspective cohort of postmenopausal women 55 years of age or older. All underwent a clinical evaluation, with assessments including the Australian/Canadian Osteoarthritis Hand Index (AUSCAN), the Cochin Rheumatoid Hand Disability Scale, measurement of grip strength using a dynamometer, and radiographs.

Radiographic osteoarthritis (ROA) was defined as at least two radiographically positive joints among 30 without any HOA symptom. Symptomatic osteoarthritis (SHOA) was defined using the ACR criteria.

Data were complete for 1,189 participants with a mean age of 71.7 years. Radiographic osteoarthritis was observed in 68.5%. The distal interphalangeal joints were the most frequently affected. Radiographic signs of OA of the thumb base were present in 37.8% of the right and 39.5% of the left hands. In addition, symptomatic HOA was found in 40.5%, with erosive arthritis detected in 11.8%. In addition, 17% of patients with symptomatic HOA had moderate to severe disability.

Conclusion: This study of women 55 years of age or older found that 28% had asymptomatic radiographic osteoarthritis of the hand and 40.5% had symptomatic osteoarthritis of the hand.

Aroux, M., et al. The Disability Associated with Hand Osteoarthritis is Substantial in a Cohort of Postmenopausal Women: The QUAYLOR Study. **Osteoarthritis Cartilage.** 2022, November; 30(11): 1526-1535.

EARLY AXONAL LOSS AND LONG-TERM DISABILITY IN CIDP

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an immune-mediated condition associated with variable degrees of clinical disability. Recent studies have shown that axonal damage occurs early in CIDP. This study was designed to assess whether the amount of external loss before the initiation of treatment is predictive of long-term disability.

Eligible patients were diagnosed at the Departments of Neurology and Clinical Neurophysiology,

Rigshospitalet, between 1990 and 2015. The patients underwent electrodiagnostic testing and were subsequently treated with immune-modulating therapy. All were examined clinically and electrophysiologically at follow-up. Disability was evaluated with the Rasch-built Overall Disability Scale (I-RODS), for immune-mediated peripheral neuropathies. Neurologic impairment was assessed with the neuropathy impairment score (NIS). Isokinetic strength was assessed at the wrist and ankle with isokinetic dynamometry scores (IKS).

Data were completed for 30 patients. The average time between diagnostic and follow-up studies was 13.4 years. The initial axonal Z scores were correlated with scores on the I-RODS, NIS, and IKS. The amount of axonal loss at diagnosis correlated significantly with the amount of axonal loss at follow-up. A multivariate regression analysis found that the initial axonal Z score was predictive of follow-up I-RODS scores ($p=0.02$) as well as follow-up IKS ($p=0.04$).

Conclusion: This study of patients with chronic inflammatory demyelinating polyneuropathy found that pretreatment axonal loss at diagnosis in chronic inflammatory demyelinating polyneuropathy is predictive of long-term disability.

Al-Zuhairy, A., et al. Axonal Loss at the Time of Diagnosis as Biomarker for Long-Term Disability in Chronic Inflammatory Demyelinating Polyneuropathy. *Muscle Nerve*. 2022. doi.org/10.1002/mus.27722.

LONG-TERM CANNABIS USE AND AGING

While cannabis use is often characterized as an activity of the young, those who began consuming cannabis in the 1970s have a long-term use that warrants investigation. This longitudinal study of a population-representative cohort of 1,037 individuals in New Zealand who, over time, displayed long-term cannabis use.

The participants were born between April 1972 and March 1973 and followed until the age of 45 years. All were assessed for cannabis, tobacco, and alcohol use at ages 18, 21, 26, 32, 38, and 45 years. Biological aging and health, financial and social preparedness for old age were assessed at 45 years. Biological aging was assessed with five outcomes, including the pace of

aging, brainAGE (the difference between chronological age and estimated age based on multiple MRI-derived measures of structural brain integrity), the volume of white matter hyperintensities, gait speed, and facial age.

Of the 997 alive at age 45, 938 were available for follow-up. Standardized mean differences between long-term cannabis users and non-users were large for biological aging ($p<0.0001$), health preparedness ($p<0.0001$), financial preparedness ($p<0.0001$), and social preparedness ($p<0.0001$). In an adjusted analysis, those with long-term cannabis use demonstrated worse social preparedness in midlife ($p=0.017$) but did not demonstrate accelerated biologic aging, worse health, or worse financial preparedness.

Conclusion: This study demonstrates that long-term cannabis use is not associated with accelerated biologic aging or worse health but does correlate with worse social preparedness in midlife.

Meier, M., et al. Preparedness for Healthy Aging and Polysubstance Use and Long-Term Cannabis Users: A Population-Representative Longitudinal Study. *Lancet Healthy Longev*. 2022, October 1; 3(10). e703-e714.

MARIJUANA USE AFTER ANTERIOR CERVICAL DISCECTOMY AND FUSION

Anterior cervical discectomy and fusion (ACDF) is the most common surgical intervention for the management of cervical radiculopathy and/or myopathy. As medical marijuana is gaining popularity as an alternative analgesic, this study investigated the effect of preoperative marijuana use on the clinical outcomes following ACDF.

All patients ≥ 18 years of age who underwent primary one- to four-level ACDF between 2012 and 2021, with documented marijuana use were identified. A 3:1 propensity match was performed between those not using marijuana (controls) and documented marijuana users, controlling for age, sex, body mass index, construct length, smoking status, Charlton Comorbidity Index (CCI), diabetes, kidney disease, liver disease, and congestive heart failure. Surgical complications were recorded, including all spine reoperations within three years.

Sixty patients using marijuana,

and 180 matched controls were included in the analysis. The 90-day all-cause readmission rates were 8.3% in the marijuana group and 1.1% in the control group ($p=0.012$). Patients who used marijuana had a greater rate of spine reoperations (21.7%) than patients who did not (5.00%, $p<0.001$). The rate of revision for adjacent segment disease (10.0% vs. 2.22%, $p=0.018$) and pseudarthrosis (10.0% vs. 2.78%, $p=0.031$) were also significantly higher for the marijuana group.

Conclusion: This retrospective study found that patients who used marijuana at the time of cervical spine surgery had higher complication and revision rates than did controls.

Lambrechts, M., et al. Marijuana Use and Its Effect on Clinical Outcomes and Revision Rates in Patients Undergoing Anterior Cervical Discectomy and Fusion. *Spine*. 2022, November 15; 47(22):1558-1566.

FREQUENCY OF PURE VASCULAR COGNITIVE IMPAIRMENT

The diagnoses of multi-infarct dementia and vascular dementia were developed to delineate dementia caused by vascular origins from dementia caused by Alzheimer's Disease (AD). This study was designed to identify individuals without neurodegenerative pathologies to determine the extent to which cerebral vascular disease pathologies are associated with cognitive impairment.

The patients were enrolled in either the Religious Orders Study (ROS) or the Rush Memory and Aging Project (MAP). The inclusion criteria for both studies were age ≥ 65 years, without known dementia, agreeing to annual evaluations, as well as a postmortem evaluation. Annual neuropsychological tests were used to diagnose incident mild cognitive impairment or dementia.

Of the 2,096 participants who died, 1,767 had a complete postmortem pathological examination. Neurodegenerative pathologies that were identified included those for AD, TDP-43, Lewy bodies, and hippocampus sclerosis. The postmortems were categorized into three subgroups. The vascular subgroup included 369 (20.9%) without significant levels of neurodegenerative brain pathology. The neurodegenerative subgroup was composed of 407 (23%) without significant cerebrovascular disease

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pathology. The mixed subgroup included the remaining participants (56.1%). Cognitive impairment was present before death in 78% of the mixed-pathology group, 68% of the neurodegeneration group, and 43% of the vascular group.

In the vascular subgroup, macroinfarctions (Odds Ratio (OR) 2.05) and atherosclerosis in the basal ganglia (OR 1.35) were associated with cognitive impairment. In the mixed model, only macroinfarctions were associated with a faster cognitive decline in the vascular subgroup ($p < 0.001$). The results demonstrate that it is mainly white matter disruptions in the frontal lobe and, to a lower extent, parietal lobe that are associated with cognitive decline in pure VCI.

Conclusion: This study of older adults without known dementia found that cerebral vascular disease, specifically macroinfarctions were associated with higher odds of cognitive impairment and dementia and a faster rate of cognitive decline.

Oveisgharan, S., et al. Frequency and Underlying Pathology of Pure Vascular Cognitive Impairment. **JAMA Neuro.** 2022. doi.org.proxy.library.emory.edu/10.1001/jamaneurol.2022.3472.

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