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ABSTRACT BOOK

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The Interactions between Biomolecules and Amyloid Degrading Enzymes

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Abstract:

Various amyloidogenic proteins have been suggested to be involved in the onset and progression of neurodegenerative diseases (ND) such as Alzheimer's disease (AD). Particularly, the aggregation of misfolded amyloid- β (A β) and hyperphosphorylated tau (pTau) are linked to the neurodegeneration and pathogenesis of AD. In order to care these diseases, multiple small molecules have been developed to regulate the aggregation pathways of these amyloid proteins. In addition to controlling the aggregation of amyloidogenic proteins, maintaining the levels of the proteins in the brain by amyloid degrading enzymes [ADE; neprilysin (NEP), insulin degrading enzyme (IDE), and matrix metalloproteinases (MMPs)] is also essential to cure AD. Therefore, numerous biological molecules and chemical agents have been investigated as either inducer or inhibitor against the levels and activities of ADE. Although the side effects of enhancing the activity of ADE could occur, the removal of amyloidogenic proteins could result in a relative good strategy to treat AD. Furthermore, since the causes of AD are diverse, various multi-functional (multi-target) chemical agents have been designed to control the actions of multiple risk factors of AD, including A β , metal ions, and/or reactive oxygen species (ROS). Many of them, however, were invented without considerations of regulating ADE levels and actions. Incorporation of previously created molecules targeting A β , metal ions, and/or ROS with the chemical agents handling ADE could be a promising way to treat AD. This presentation introduces the relationships between ADE and molecules capable of modulating the activity and expression of ADE.

Comparison of Adaptive Socialization Skills and Brain Volumes in a Prospectively Gathered School-age Sample of DS and ASD

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Abstract:

Background: Children with Down Syndrome (DS) have a 15-fold increased likelihood of receiving a co-diagnosis of autism spectrum disorder (ASD) than the general population. Few studies have compared cortical and subcortical brain volumes in DS to ASD.

Methods: Children (mean age = 9.9 years, SD = 5.8) participated in the multi-site Infant Brain Imaging Study (IBIS; PIs: Piven, Hazlett) across four diagnostic groups: DS (DS, n=26), high-risk ASD (biological sibling with ASD and an ASD diagnosis; HR+, n=26), high-risk non-ASD (HR-, n=103), and low-risk controls (LR, n=77). Cognitive functioning, social communication, and adaptive behaviors were assessed. MRI scans were conducted on a 3T Siemens Prisma. Analyses were conducted to compare behavioral and neuroimaging markers across groups using an alpha threshold of 0.01 to account for multiple comparisons.

Results: Communication and Daily Living skills were lower in the DS group (DS<LR=HR-=HR+). DS and ASD did not significantly differ in the socialization domain (DS=HR+<LR=HR). The DS group displayed consistently smaller cortical and sub-cortical volumes than the other groups (DS<LR=HR-=HR+; p<0.001). Significant associations between socialization skills and right hippocampal volumes were found for the HR- group only (r²=0.099; p=0.009). Larger left and right grey matter cerebellar volumes were associated with higher socialization scores in the HR- group only (r²= 0.129; p=0.002, r²=0.119; p=0.004, respectively).

Discussion/Significance: Children with DS have deficits in socialization like children with ASD. While children with DS generally have significantly smaller brain volumes, there are unique brain-behavior relationships, specific to genetic risk status, which highlight potential mechanistic differences across groups.

Cognitive and Behavioral Domains that Differentiate between Normal Aging and Alzheimer's disease Dementia in Down Syndrome

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Abstract:

Down syndrome (DS) is predominantly caused by the triplication of chromosome 21 and is highly associated with the development of Alzheimer disease (AD). Dementia screening in primary care settings is essential for preventative care and ongoing management of AD, but screening for AD in people with DS is particularly difficult due to their pre-existing intellectual disability. A comprehensive evaluation is not feasible in the primary care setting and most physicians do not

have extensive training in administering neurocognitive assessments to patients with DS. Our group has developed an abbreviated neurobehavioral battery that is effective in screening for AD dementia in patients with DS and one that can be used by community practitioners. Using principal components analysis (PCA), we found that the combined abilities of being able to answer questions verbally and to do everyday tasks differentiated between those with and without AD dementia (sensitivity of 80%, specificity of 70%). Using classification and regression tree (CART) analyses, we found two informant-report scores to effectively classify AD dementia status (sensitivity of 100%, specificity of 81%). Furthermore, the *Dementia Questionnaire for People with Learning Disabilities* - Sum of Cognitive Scores and the *Vineland Adaptive Behavior Scales, 2nd Edition* - Community score were better classifiers than performance-based neurocognitive measures. The importance of caregiver ratings when screening for AD dementia in adults with DS will be discussed, as well as differential diagnosis when a patient's cognitive abilities cannot be directly assessed due to motor, sensory, or speech and language impairments, or limited cooperation.

The Black Widow Matrix

Charles Williams

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Abstract:

In the incidences of concussion and CTE in sports where the ravages of CTE are at an alarming rate in the 90th percentile after brain death evaluation. Athletes are at a greater risk for mental health problems, including Chronic Depression and Suicide ideations/attempts. CTE and Concussion and associated syndromes (such as Alzheimer's and Dementia), as it stands is considered the number one personal, economic, and social burden in the world. Researchers around the globe have stated that athletes who have incidences of concussion, their quality of life deteriorates at such a rapid rate before death therein more difficult to treat psychologically and medically. Specific to the individuals we extract exosomes through patented nanotechnology which determines biological signatures in the blood analysis developed in our wet lab. Findings: The basic tenets performed at team's hospital referrals and team medical facilities were to look at the distribution of information derived by either a Neuropsychological test, CAT, or MRI to determine the extent of the concussed athlete.

My team and I focused our attention on the impact of neuronal leakage; thus, biological signatures of TAU, PTSD, APOE3/4, in the exosomes, as well as the injury, degradation, and the associated accordion style death of neurons. Dr. Williams and Dr. Sugaya have been developing new approaches to cross the blood brain barrier via liver LDC-DHA (mfsd2A) artificial intelligence packaging distribution, to deliver blended Citicoline, EPA/DHA/DPA to the brain; thus, reducing the inflammation, to resuscitating the impacted neurons; thus, creating amplification of the entire brain.

How does breathing polluted air compares with breathing fresh air in causing a stroke in adults: Overview of reviews

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Abstract:

Objective: To review the present body of systematic reviews on the connection between air pollution and stroke and to produce evidence to enable policymakers to make decisions.

Method: For the six systematic reviews involving over 150 case crossovers, time series, and cohorts totaling over 50 million participants, experts, and websites were consulted. Unpublished material was discovered in Prospero and InPlasy. We used the keywords "air pollution" and "stroke" to search Google Scholar, Epistemonikos, Lilac, PubMed/Medline, Cochrane Library, grey literature, and the Global Burden of Disease website between January 2012 and January 2022. 34 duplicates were removed from the 224 articles chosen for abstract screening. Finally, 190 abstracts were screened, with 171 being rejected for noncompliance. Full-text retrieval was requested for 19 documents. Six of the 19 articles could not be retrieved because they did not contain free-full texts. Six published full-texts and one unpublished protocol were eventually reviewed. A table was created to keep track of which articles were excluded and why. We used a PRIOR flowchart to demonstrate study screening, selection, and identification (Preferred Reporting of Items in Overview of Reviews).

Abstracts were entered into the Covidence tool by two independent authors. Covidence was used by two independent authors to code and abstract data (IRR 80 percent). Teams met once a week to discuss norms and to learn about data collection and management tools. RevMan was used to assemble data and assess publication bias.

We conducted a thorough search for missing data. We examined the primary studies table and contacted the authors of the Systematic review about missing data. We used overlap criteria to weed out articles that didn't fit our definition of a systematic review.

Minor discrepancies existed among the included systematic reviews due to the omission of post-review epidemiologic papers. The primary study citation matrix values in our review reached 17%. Data from studies with similar subgroup analyses were pooled using the random effect model to overcome overlap. This was done to prevent overemphasis on one study and to address heterogeneity. Sensitivity analysis was not possible due to the small number of studies in each subgroup.

The included reviews were highly heterogeneous. Each systematic review was assessed using the JBL and AMSTAR 2 checklists. We tabulated the qualitative data. This overview was written using the PRIOR reporting guidelines.

Results: The forest graph shows that air pollution has little or no effect on the risk of a stroke event occurring. Publication bias was minimal in our overview.

We provided summary stats. We conclude that PM 2.5 increases ischemic stroke risk, PM 2.5 increases cumulative stroke events up to 2 days post-increment in its levels, NO₂ increases hospital admission and deaths to stroke, and SO₂ increases hospital admissions to stroke. But the risk is only marginally elevated. In spite of this, the exposure is widespread. Individual cases may be multiplied by the small increase in risk.

PI3K Gene Therapy for Axon Regrowth and Functional Improvement after Spinal Cord Injury

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Abstract:

The ability of the spinal cord to regenerate largely disappears during development. After injury in adulthood, we don't observe much new growth of axons that would make meaningful connections, which is a key prerequisite for restoration of movement. Here, we use a PI3K isoform gene therapy and compare two promoters to show that we are able to stimulate corticospinal projecting neurons to regenerate their axons and improve behavioural outcomes. PI3K produces PIP₃, a key signaling lipid, which affects motility, protein translation, transport/trafficking and epigenetic controls. In mature neurons many axon growth molecules are excluded from axons, and PI3K expression enables anterograde transport of developmentally restricted molecules, such as the integrins, which has been shown to promote growth. We used a model of C4 dorsal column lesion and injected the right motor cortex at 4 sites concurrently with a total of 2 µl of viral vector mixture of AAV1-CAG-PI3K + AAV1-CAG-eGFP or AAV1-CAG-eGFP alone and compared it with AAV1-hSYN-eGFP + AAV1-hSYN-PI3K or AAV1-hSYN-eGFP only. We allowed rats to survive for 6, 9, 12 or 16 weeks before transcardial perfusion. Using fluorescent immunohistochemistry, we evaluated levels of PI3K and GFP in 40 µm frozen floating brain sections and were able to reach over 80% co-expression when we used vectors with hSYN as soon as 6 weeks after transduction. We only observed approximately 20% at 6 weeks and 40% at 9 and 12 weeks when we used the CAG promoter. In addition to excellent co-expression levels, we discovered that PI3K strongly upregulated the GFP signal when compared to controls which would be in line with its identified role in the upregulation of protein synthesis. Subsequently, we manually counted GFP labelled axons of the hSYN group in 20 µm spinal cord cross sections above lesion sites and every other 20 µm longitudinal section of lesioned spinal cords. With hSYN promoter, we observed around 1000 GFP-labelled axons above the lesion with the best outcome of over 3000 at 12 weeks after brain injections and SCI. Vector mixtures transducing neurons with PI3K and GFP with either promoter elicited growth of axons past lesion sites, but we observed many more when we used neuron specific

hSYN promoter where up to 750 axons extended past the lesion with some reaching at least 1.3 cm below lesion. Moreover, rigorous weekly behavioural testing revealed functional improvements in skilled paw reaching, grip strength and ladder crossing in rats treated with PI3K compared to GFP controls. From our results, we conclude that the use of hSYN promoter in the brain is superior to CAG and provides high co-expression levels. Moreover, PI3K acted as booster of GFP production and its overexpression in cortical motor neurons lead to robust axon regeneration that resulted in function restoration.

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Treating Elevated Lp(a) and Ischemic Cerebral Vascular Events with Lipoprotein-apheresis

Patrick M. Moriarty*

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Abstract:

Background: Stroke is the third leading cause of death in the western world and remains the primary cause of death in China. Ischemia, due to CVD risk factors, is the most common pathology associated with strokes. However, cryptogenic strokes account for almost 40% of all ischemic strokes for patients under 55 years old. A good percentage of these idiopathic strokes may relate to Lipoprotein(a) [Lp(a)] levels.

Methods: Discuss potential mechanisms of action of Lp(a) levels and stroke. Demonstrate the clinical data connecting Lp(a) levels with strokes. Describe present and future therapies on the lowering of Lp(a) levels and CVD, in particularly strokes.

Results: Lp(a) contains an LDL-like moiety bound to apoprotein a with atherosclerotic, pro-thrombotic, and pro-inflammatory properties. The BIOSIGNAL trial found elevated Lp(a) [$>40\text{mg/dL}$] was independently associated [adjusted ratio 2.40, 95% CI 1.05-5.47] with large artery atherosclerotic stroke etiology and risk of recurrent cerebrovascular events among primarily Caucasian individuals aged <60 years. Presently, Lipid-apheresis is the only FDA-approved therapy for elevated Lp(a) levels and CVD. Based on case studies and the German Lipid Apheresis Registry (GLAR) Lipid-apheresis lowers the risk of CVD, including stroke, by 90% for CVD patients with an elevated Lp(a) ($>60\text{mg/dL}$). Pharmacotherapy, such as statins and ezetimibe, have no effect on Lp(a) levels. Future therapy may include drugs, such as antisense antibodies or siRNA to Lp(a), that lower Lp(a) levels by $>90\%$.

Conclusion: Increased Lp(a) is significantly associated with stroke. Lipid-apheresis treatment lowers CVD events. Future Lp(a) lowering medications look promising in reducing Lp(a) levels and CVD.

Remote Patient Monitoring

Marc Fischer and John Mavraides*

Dogtown Media and National Institutes of Health, USA

Abstract:

NeuFun is a mobile app developed in partnership with the National Institutes of Health that reproduces most aspects of a neurological examination for telemedicine assessment of subjects with neurological disorders or neurological symptoms. NeuFun consists of fifteen tests that measure cognitive, motoric, cerebellar and sensory functions that can be self-administered by patients. Clinical testing performed by NIH has demonstrated statistically significant correlations between selected neurological functions measured by trained clinicians and the machine learning optimized outcomes derived from NeuFun. Physicians can prescribe all of the tests, or any subset based on the patient's abilities. Patient's test results are displayed in the app after each test and are compared to their personal best score as well as to age-related normative results. All patient data from testing is streamed to a cloud-based platform and can be viewed remotely by a clinician / administrator or can be downloaded for further analysis.

Hiccup Severity and Prevalence in U.S. Cancer Populations: A Nationwide Survey of Healthcare Professionals

Carol Lipshultz

Meter Health, USA

Abstract:

Background and objective: Hiccups are a common, often transient event with minimal effect on the average person. This breathing pattern is defined by the involuntary contraction of diaphragmatic and thoracic musculature, causing a sharp, high-volume “hic” inspiration that interrupts the eupneic respiratory pattern. Current consensus describes the neurological mechanism of hiccups activation in the three-part “hiccup reflex arc”. This includes the afferent limb (phrenic nerve, vagus nerve, and sympathetic chain), central processing (midbrain and brainstem), and the efferent limb (motor fibers of phrenic nerve, recurrent laryngeal branch of the vagus nerve, and motor neurons of the diaphragm, glottis, and intercostal muscles). Despite their typical transience, hiccup longevity and severity in vulnerable patient populations can lead to significant quality of life (QoL) degradation and poor health outcomes. Meter Health has defined clinically significant hiccups (CSH) as those that last greater than 48 hours or occur incident to certain medical conditions and drug treatments.

A specific subset of chemotherapy patients receiving treatment with dexamethasone experience prolonged and debilitating CSH. They require intervention to reset the eupneic breathing pattern and improve patient quality of life. Current treatment options are limited to home remedies and the off-label use of drugs that often induce significant, undesirable side-effects. While CSH are associated with more than 100 medical conditions, Meter Health aims to elucidate the burden of CSH to identify a key part of oncological palliation that remains underdiagnosed and insufficiently treated.

Survey and results: Meter Health conducted a survey of 90 oncology healthcare professionals. Questions pertained to the incidence, severity, and QoL consequences of hiccups in chemotherapy patients. Notably, stress/anxiety and fatigue were marked as severe for most patients experiencing CSH. Comments described the demoralizing effects of seemingly unending, intense hiccups. As compared to patient experience of nausea and vomiting, 77.8% of healthcare professionals asserted that hiccups were equal or greater in severity.

Conclusion: Hiccups represent an under-researched and under-reported impact at the interface between oncological treatment and neurologic effects. Clinically significant hiccups can pose a high risk for medically relevant populations, yet their occurrence is neither well-acknowledged nor their severity addressed in the currently available palliative care. Establishing a validated patient-reported outcome (PRO) to assess hiccups alongside new treatment regimens could aid in the diagnosis and palliation of CSH in oncology. In addition, advancing our understanding of the hiccups mechanism of action could extend hiccup palliation to other disease states and conditions, thereby widely improving patient QoL and health outcomes.

Use of Optokinetic Chart Stimulation to Reduce Chronic Spasticity in people with Stroke and Traumatic Brain Injuries: A Retrospective Case Series

Benjamin Chitambira

Neurorestorative and Neurorehabilitation Solutions Ltd, UK

Abstract:

Background and Purpose: Spasticity after stroke and traumatic brain injuries often leads to pain and severe activity limitations. The aim is to report reduction of spasticity and restoration of voluntary movements in chronic strokes and traumatic brain injuries.

Design and setting: Retrospective case series in the community. Participants with chronic spasticity who had 0/5 on the Oxford scale in at least one segment of their affected upper limb were eligible for the study.

Methodology: Participants looked at the OKCS app 3 times daily. They had the OKCSIB protocol upper limb active-assisted anti-gravity extensor exercises carried out by a therapist once weekly. The Wilcoxon test was used to analyse before and after intervention spasticity and voluntary movement scores. The Modified Ashworth Scale and the Oxford Scale for manual muscle strength was a secondary outcome measure. Informed written consent was obtained from all participants.

Results: Out of 25 participants who had been treated for spasticity of the upper limb, only 11 participants were eligible for this study. Physiotherapy records of the 11 participants were retrospectively obtained for before intervention and after intervention outcomes. The spasticity scores improved significantly with $p < 0.05$. Importantly the spasticity resolved to transition to recovery of voluntary movements instead of just improvement in the spasticity scores and passive range of motion with $p < 0.05$.

Conclusions: The OKCSIB protocol led to statistically significant and clinically significant reversal of chronic spasticity to the point of making participants regain voluntary movements.

10 Years Retrospective Study of ADHD in Children Aged 3 to 7 Years in Our Clinic

Neena Shilen* and Renjini Raghavan

Sunrise Institute of Medical Sciences, Cochin, India

Abstract:

Randomized study of 1500 cases of ADHD in children aged 3 to 7 yrs. was studied and compared to age and sex matched 1500 controls attending well child clinic. The study was conducted to determine the incidence of adenotonsillar hypertrophy, obstructive sleep apnea, enuresis, cognitive impairment, speech and language defects and sleep problems in these children. About 33.8% had adenotonsillar hypertrophy vs. 11.2% in controls, 26.4% had obstructive sleep apnea vs. 0.3% controls, 5.3% had Enuresis vs. 0.1% controls, 18.2% had speech and language problem vs. 1.6% in controls, 42% had cognitive difficulties vs. 4.8%, sleep disturbances in 78% Vs. 31% controls. TonsilloAdenoidectomy was done in 28%, ABA was done in 93% and Medication was required in 17% cases.

A Case Reflection – Thallium Poisoning

Simeon Zou* and Eric Ashman

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Abstract:

Thallium poisoning results in devastating systemic and neurological complications. However, its clinical presentation is non-specific and not well recognized in common neurology practice, which may lead to delayed recognition and diagnosis, eventually prolonged poisoning and irreversible dose-dependent systemic neurological morbidity and mortality. Here we report a thallium poisoning case which highlights the clinical course, clues that lead to diagnosis, clinical management and outcome.

Decreased Interactions between Calmodulin and A Mutant Huntingtin Model Might Reduce the Cytotoxic Level of Intracellular Ca²⁺: A Molecular Dynamics Study

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Abstract:

Mutant huntingtin (m-HTT) proteins and calmodulin (CaM) co-localize in the cerebral cortex with significant effects on the intracellular calcium levels by altering the specific calcium-mediated signals. Furthermore, the mutant huntingtin proteins show great affinity for CaM that can lead to a further stabilization of the mutant huntingtin aggregates.

In this context, the present study focuses on describing the interactions between CaM and two huntingtin mutants from a biophysical point of view, by using classical Molecular Dynamics techniques. The huntingtin models consist of a wild-type structure, one mutant with 45 glutamine residues and the second mutant with nine additional key-point mutations from glutamine residues into proline residues (9P(EM) model). Our docking scores and binding free energy calculations show higher binding affinities of all HTT models for the C-lobe end of the CaM protein. In terms of dynamic evolution, the 9P(EM) model triggered great structural changes into the CaM protein's structure and shows the highest fluctuation rates due to its structural transitions at the helical level from α -helices to turns and random coils. Moreover, our proposed 9P(EM) model suggests lower interaction energies when compared to the 45Qs-HTT mutant model, this finding being in good agreement with the 9P(EM)'s antagonistic effect hypothesis on highly toxic protein-protein interactions.

Inhibiting EZH2 is Neuroprotective after Stroke in Aged Mice

Fan Bu, Jia-wei Min, Ahmad El Hamamy, Yan Xu, Li Qi, Edward Koellhoffer, Louise D. McCullough and Jun Li*

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Abstract:

Ischemic stroke results in activation of microglia, which may polarize towards a pro-inflammatory (M1) phenotype and/or an anti-inflammatory (M2) phenotype. Enhancer of zeste homolog (EZH) 2 is a histone-lysine N-methyltransferase enzyme, a key modulator of microglia polarization. We here investigated whether microglial-specific deletion of EZH2 leads to a beneficial protective effect in stroke and microglial over-expressing microglial EZH2 exacerbates stroke outcome in vivo. Aged male mice were subjected to 60-minutes middle cerebral artery stroke. Tamoxifen administration was started 30 days prior to stroke to induce genetic deletion of microglial EZH2 in CX3CR1-creER/EZH2-floxed mice. Microglial EZH2 over-expressing was performed using lentiviral vectors. Mice were sacrificed for immunohistochemistry and crystal violet staining (brain infarct assay) after behavior tests at 3 days after stroke. The expression of microglial EZH2 was significantly abrogated with tamoxifen injection in KO mice compared to the control floxed mice. EZH2 deletion reduced brain infarct volume and improved functional outcome assayed by adhesive removal test. Mechanistically, microglial EZH2 deletion led to a decrease in expression of M1 marker iNOS, an increase in M2 marker Arg1 co-stained in microglia (Iba1). We additionally found over-expressing EZH2 in microglial cells exacerbated stroke outcome including performance in adhesive tape removal and hang-wire tests 3 days after stroke. We observed decreased Arg1 and increased iNOS in stroke mice with over-expression of EZH2. Genetic deletion of EZH2 in microglia improved stroke outcome in aged while overexpression of EZH2 exacerbated stroke outcome.

Rehabilitation of Persistent Headache and Neurocognitive Deficits Following Concussion in a 38-year-old Female: Case Study

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²American College of Functional Neurology, USA

³Carrick College, USA

Abstract:

Objective: To demonstrate decreased headache symptomatology and neurocognitive deficits following a multimodal, functional neurology approach to neurorehabilitation.

Background: This case study presents a 38-year-old female who began experiencing new daily persistent headaches (NDPH) and neurocognitive deficits following a concussion. Her symptoms remained after independently receiving physical therapy and medication, causing her to file for disability.

Design/Methods: The patient was prescribed 23 treatment sessions over two consecutive weeks at an outpatient neurorehabilitation center specializing in functional neurology. The C3Logix neurocognitive assessment and graded symptom checklist were utilized at intake and discharge. Multimodal treatment interventions included transcranial photobiomodulation, non-invasive neuromodulation of the lingual branch of the trigeminal nerve, hand-eye coordination training, vestibular rehabilitation utilizing a two-axis whole-body off-axis rotational device, and cognitive training.

Results: On intake, their composite symptom score was reported as 55/162, Trail Making Test Part A was 39.5 milliseconds, Trail Making Test Part B was 54.4 seconds, and Digit Symbol Matching was 51 matched symbols in 2 minutes. On discharge, the patient experienced a 7% in self-reported symptoms, Trail Making Test Part A improved to 17.6 seconds (+55.44%), Trail Making Test Part B improved to 38.7 seconds (+28.86%), and Digit Symbol Matching was 63 matched symbols in 2 minutes (+19.05%).

Conclusions: The present case study results demonstrated meaningful improvements in both self-rated concussion symptoms and neurocognitive performance for this patient. The authors suggest further investigation into multi-modal, neurological rehabilitation to decrease chronic postconcussion symptoms and improve neurocognitive assessment scores.

A Novel, Multimodal, Rehabilitative Approach to Improve Stability in People with Multiple Sclerosis

Emily Kalambaheti^{1,2,3} and Shaun Kornfeld^{*1,3}

¹Plasticity Centers, USA

²Carrick College, USA

³American College of Functional Neurology, USA

Abstract:

Introduction: Multiple sclerosis (MS) is characterized by autoimmune-mediated lesions involving the nerve fibers and myelin of the central nervous system resulting in various neurological challenges. Balance issues is a commonly reported consequence of MS.

Design/Methods: A neurological rehabilitation clinic treated 13 patients between the ages of 43 years and 77 years (average 62.8 years) with MS (5 males; 6 females) and subsequent balance challenges. Each participant enrolled in a program consisting of 10 treatment sessions over 5 days. Each treatment was multimodal, consisting of transcranial photobiomodulation, repetitive electrical neuromodulation, neuromuscular reeducation, vestibular rehabilitation, orthoptic exercises, and full body rotation in yaw, pitch, or roll separately or combined. Two participants enrolled in a second rehabilitation program of 10 treatments two years after their initial program. Two participants were excluded due to an inability to stand unassisted, and one participant was excluded due to complications of an unrelated medical condition.

Discussion: On intake, balance was assessed using the Computerized Assessment of Postural Systems® (CAPS) with an average stability score of 38.24% (SD 17.57%). Upon discharge, CAPS was readministered with an average stability score of 47.71% (SD 20.64%) and average percent change of 25.59%. These results indicate an improvement in balance following the multimodal neurological rehabilitative program. The authors hypothesize the improvements in balance may be due to the hemodynamic effects and neuroplasticity induced by the frequency and intensity of the administered modalities.

Conclusion: The authors suggest further investigation into multi-modal, neurological rehabilitative approaches to increase stability scores in people with MS.

Characteristics of Neuronal Responses of the Somatosensory Cortex in WAG/Rij Rats to Vibrissa Stimulation Area

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Abstract:

The functioning of the somatosensory system was studied in WAG/Rij rats genetically predisposed to absence epilepsy (AE) and demonstrating depression-like behavior, during the periods when AE had not been formed yet (2–3 months of age) and when this pathology was already well pronounced

(6–7 months). Healthy Wistar rats served as a control. The responses of single somatosensory cortical neurons to single-pulse electrical stimulation of the vibrissal area (whiskers) were recorded extracellularly. The evoked unit activity of somatosensory cortical neurons in response to afferent stimulation, regardless of age and rat strain identity, was found to include four components: primary (short-latency) excitation and inhibition and secondary (long-latency) excitation and inhibition. In 2–3-month-old WAG/Rij rats, in contrast to Wistar rats, the number of short-latency inhibitory responses was significantly smaller, while the number of long-latency inhibitory responses was significantly larger. It was postulated that the imbalance of varied inhibitory mechanisms in WAG/Rij rats may underlie the development of both AE and depression. In 6–7-month-old WAG/Rij rats the secondary excitatory response to afferent stimulation was mainly represented by a multicomponent high-frequency phasic reaction (alternation of short-term discharges with inhibitory periods). In Wistar rats of the same age, the secondary excitation was represented by a tonic reaction. The frequency of phasic discharges is compatible with that of spike-wave activity, which is an electroencephalographic sign of AE. It is assumed that the phasic response may be considered as a neuronal equivalent of epileptic activity, while the spike-wave activity in WAG/Rij rats may be provoked by vibrissal afferentation.

Care for Older Adults with Dementia: PACE Day Care or Residential Dementia Care Units?

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Abstract:

Persons with dementia (PwD) are at greater risk for various adverse health outcomes, and the best care model remains to be determined. We initiated a case-control study aiming to compare the physical and neurocognitive performance of PwD in the Program of All-inclusive Care for the Elderly (PACE) (PC group) and residential dementia care units (RC group). Demographic characteristics, physical function, cognition, mood, and behavioral and psychotic symptoms of dementia (BPSDs) were assessed every 3-6 months in both groups, while frailty and Timed Up-and-Go Test (TUGT) were assessed every 6 months in the PC group only. Overall, 96 participants (mean age: 86.4 ± 6.8 years) were enrolled with the median follow-up period of 43.6 weeks. Lower incidence of hospital admissions was noted in the PC group (0.52 ± 1.12 vs 1.38 ± 2.49 admissions/1,000 person-days, p=0.023), even though the PC group had higher multimorbidity and more severe BPSDs. During the study period, the PC group showed a significant improvement in body mass index, less physical dependence, better cognitive performance and reduced depressive mood. In addition, the PC group showed improvement in frailty, leisure hour activities, and TUGT results. However, participants in the PC group were more likely to experience BPSD deterioration (β coeff.: 0.193, 95% CI: 0.121-0.265). In conclusion, the PACE services significantly reduced unexpected hospital admissions of PwD, facilitated the maintenance of physical independence,

and improved cognitive performance and mood status. Further randomized controlled studies are needed to determine the most appropriate care model for PwD.

Fecal Microbiota Transplantation for the Treatment of Alzheimer's disease

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Abstract:

Alzheimer's disease (AD) is a progressive neurodegenerative disease of the brain that is characterized by memory impairment and cognitive dysfunction. Pathological hallmarks of AD include the formation of extracellular amyloid beta (A β) plaques and intracellular neurofibrillary tangles. The accumulation of these proteinaceous deposits induces synaptic dysfunction, oxidative damage and neuroinflammation, resulting in neurodegeneration. Neuroinflammation, triggered by the glial cell response to A β , exacerbates the toxic milieu in the AD brain and contributes to further A β genesis. Therapeutics targeting these proteinaceous deposits are at the forefront of research and drug discovery. However, the near-impenetrable blood-brain barrier excludes more than 99% of effective therapeutics from entering the central nervous system. Based on unfavorable clinical trial data, focus is shifting to repurposing medicines and identifying alternative routes at addressing different aspects of the disease. Fecal microbiota transplantation (FMT) is a safe and reliable therapeutic for the treatment of diseases such as *Clostridium difficile* infection, ulcerative colitis and irritable bowel syndrome among others. Recent studies have shown it to be effective in reducing dysbiosis and has demonstrated efficacy in symptom reduction of neurodegenerative diseases such as Parkinson's. Employing the 5xFAD mouse model of Alzheimer's, we provide evidence that fecal microbiota transplantation (FMT) significantly and effectively reduces amyloid plaque burden in the transgenic mouse brain. We also provide evidence that FMT significantly improves cognitive function of treated mice compared to non-treated littermates. Our results provide evidence of the feasibility of employing FMT for the treatment of Alzheimer's disease.

Study on the Effect of Health Qigong on Improving the Difficulty of Nighttime Sleep Maintenance in Patients with Parkinson's disease

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Abstract:

Background and Purpose: Parkinson's disease is an incurable degenerative neurological disease, nearly 95% of patients suffer from varying degrees of sleep distress, in which maintenance sleep

difficulties have a serious impact on the quality of life of patients with PD. The objective of this study was to assess the effect of health qigong on sleep maintenance in patients with Parkinson's disease through a year-long traditional exercise intervention.

Methods: 40 patients with Parkinson's disease were randomly divided into experimental and control groups, with 20 people in each group. The Parkinson's Sleep Scale (PDSS) is used to compare indicators of sleep maintenance before, during, and after interventions. Spss23.0 was used to repeatedly measure variance to determine differences between and within groups.

Results and Discussion: After one year of health Qigong intervention, the night sleep maintenance of Parkinson's disease patients was significantly improved, and the quality of life of patients was positively affected, indicating that fitness Qigong exercise can be promoted as a means of exercise rehabilitation for Parkinson's disease patients.

Conclusions: Health Qigong can effectively improve the sleep maintenance difficulties of Patients with Parkinson's disease at night, thereby improving the quality of life of patients with PD, and providing research directions for guiding the prevention and treatment of Parkinson's disease in the future.

Effect of Health Qigong Exercise on Flexibility of Upper Limbs in Patients with Parkinson's disease

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Abstract:

Background and Purpose: Parkinson's disease is accompanied by stiffness of hands and arms. Due to stiffness and slow movement, the range of motion will be limited. It seriously interferes with daily life activities and equipment activities; therefore, this study used Health Qigong exercise as a means to improve the flexibility of the upper limbs of Parkinson's patients.

Methods: Twenty patients with mild Parkinson's were randomly divided into Health Qigong intervention group and control group. The experimental group was subjected to a 16-week experimental intervention on the basis of conventional drug treatment. Three times a week, 60 minutes each time (preparation, Health Qigong exercise, and relaxation). The evaluation standard is the back grasp test.

Results and Discussion: The two groups had significant differences in the post-test. The back grasp test results of the experimental group were extremely significant (left shoulder: $p < 0.01$, right shoulder $p < 0.01$).

Conclusions: Health Qigong exercise has a positive effect on improving the flexibility of upper limbs of Parkinson's patients.

Effects of Health Qigong exercise on depression in patients with Parkinson's disease

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Abstract:

Background and Purpose: Parkinson's disease is one of the most common degenerative diseases of the nervous system, among which mood disorders are the most common non-motor symptoms, and the impact of Parkinson's disease on the quality of life is more important than the impact of motor characteristics. In addition to the main motor symptoms of Parkinson's disease (PD), approximately 42% of PD patients report depressive symptoms. This study aimed to determine the effect of Health Qigong as a potential complementary therapy for depression symptoms in Parkinson's disease (PD).

Methods: Twenty-six patients with PD recruited and randomly allocated into either Health Qigong exercise group (n=13) or control group (n=13). Health Qigong exercise was used for intervention, which is carried out 3-5 times a week for 12 weeks. Before the experiment and after the intervention, Hamilton Depression Scale (HAMD) was performed to evaluate the depression of patients with Parkinson's disease.

Results and Discussion: The results showed that Health Qigong exercise improved PD patients' mood better than the control group. After 12 weeks of the experiment, the score of Hamilton Depression Scale (HAMD) in the Health Qigong exercise group decreased by 80 percent compared with that before and after the experiment, and the difference was very significant ($P < 0.01$), while there was no statistical difference in the score change in the control group.

Conclusions: The present findings suggest that Health Qigong may provide benefits for improving depression in patients with PD.

Effect of Health Qigong Exercise on Gait of Patients with Parkinson's disease

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Abstract:

Background and Purpose: Gait disorder is one of the main clinical symptoms of Parkinson's patients (PD), and early PD mainly show bradykinesia, lower limb weakness, and lower range of activity. Drug treatment is ineffective, thus causing falls and other conditions. Studies have shown that physical exercise can relieve gait disorders in PD. Health Qigong, as a traditional Chinese health exercise, is simple, easy to learn, safe and effective. This study was designed to study the effects of gait in patients with mild and moderate PD through Health Qigong exercise intervention.

Methods: Twenty-four patients with mild and moderate PD were randomly divided into Health Qigong exercise group and control group. Patients completed 60-70 minutes of exercise intervention

(preparation, Parkinson's exercise therapy, relaxation) twice a week for 12 weeks. The assessment criteria included a gait (walking ability) test.

Results and Discussion: Under normal medication and lifestyle, after Health Qigong exercise, the step length, step frequency and step speed of the experimental group were significantly higher than those of the control group (step length: $P < 0.01$, step frequency: $P < 0.01$, step speed $P < 0.01$).

Conclusions: Health Qigong exercise has a positive effect on gait improvement of patients with mild and moderate PD.

Effects of Health Qigong on Functional Mobility in Patients with Parkinson's disease

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Abstract:

Background and Purpose: Parkinson's disease affects people ability to balance, transfer and walk, and they are at risk for falls. It also affects their normal life. This occurs when the patient is prone to falls during the most basic mobility activities such as standing up from the seat, walking, turning or sitting back in the seat. The purpose of this study was to evaluate the effect of Health Qigong on functional mobility in Parkinson's disease patients by a year of traditional health exercise intervention.

Methods: Twenty-six patients with PD were recruited and randomly allocated into either Qigong exercise group or control group with no intervention. The Qigong exercise involved 3 times each week in a year. Before and after exercise intervention, functional mobility was measured using the Timed Up and Go Test with the Two-way Repeated Measures ANOVA analysis of variance using SPSS version 23.0.

Results and Discussion: After a year of Health Qigong intervention, following Health Qigong exercise, functional mobility was improved by a significant reduction ($P < 0.05$).

Conclusions: The results show that qigong exercises have a positive effect on functional mobility. Health Qigong can be used as a long-term intervention and provide research direction for guiding the prevention and treatment of Parkinson's disease in the future.

Keywords: *Health Qigong, Parkinson's disease, Functional Mobility*

The Efficacy of Taijiquan Exercise in Mild to Moderate Parkinson Patients under Different Control Interventions: Meta-analysis

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Abstract:

Purpose: To explore the effects of Taijiquan Exercise on disease severity, balance and walking function of patients with mild to moderate Parkinson's disease (MMPD) under different control interventions.

Method: As of November 15, 2021, a literature search was carried out in PubMed and other four databases. Formulate the inclusion and exclusion criteria of literature, make the literature information form, and two experienced evaluators independently complete the literature screening and data extraction—Stata15.0 software used for heterogeneity test, subgroup analysis and other data processing.

Results: A total of 20 randomized controlled trials were included, including 986 subjects. The results showed that different control measures combined with Taijiquan(CT) had significant differences in the improvement of disease severity as a whole ([SMD=-1.196, 95%CI(-2.077,-0.316),P=0.008]), but compared with some control interventions, the CT intervention was not statistically significant (routine nursing vs CT[SMD=0.019,95%CI(-0.540,0.578),P=0.948], conventional drugs vs CT[SMD= -9.168,95%CI(-25.802,7.467),P=0.280]; At the same time, there was significant difference in the improvement of balance function in patients with MMPD compared with various control measures (P < 0.01); It also had a significant effect on the improvement of walking function in patients with MMPD([SMD = -0.531, 95% CI (- 0.738, - 0.323), P < 0.001]).

Conclusion: Taijiquan exercise intervention can significantly improve the severity, balance and walking function of patients with MMPD. Due to not necessarily significant differences in all kinds of control intervention CT, Taijiquan intervention should be treated according to the purpose (such as improving balance and walking function).

The Effect of Baduanjin Intervention on Patients with Mild to Moderate Parkinson's disease: Meta Analysis

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Abstract:

Purpose: To explore the effects of Baduanjin Exercise on depression and anxiety, motor ability, daily living ability, balance ability, walking ability and lower limb motor work in patients with mild to moderate Parkinson's disease.

Method: Literature is retrieved through search of CNKI, WANFANG, Web of Science, PubMed from inception up to 15 November 2021. The inclusion and exclusion criteria of literature are formulated, and the literature information form is made. Two evaluators independently reviewed

and selected articles based on predetermined selection criteria and assessed articles with Physiotherapy Evidence Based Database Scale (PEDro). Stata15.0 are used for heterogeneity test, data combination, subgroup analysis, draw forest plot and sensitivity analysis.

Results: A total of 12 empirical studies were included, including 8 randomized controlled trials with 1204 subjects. The results of meta-analysis showed that there were significant differences in the intervention effects of Baduanjin Exercise on patients with mild to moderate Parkinson's disease compared with the control group ($P < 0.01$) (depression and anxiety [SMD = -1.348, 95%CI (-1.893, -0.804)], exercise ability [WMD = -5.385, 95%CI (-8.937, -1.834)], activities of daily living [WMD = 9.009, 95%CI (4.477, 13.541)], balance ability [WMD = 3.920, 95%CI (1.603, 6.238)], walking ability [WMD = 21.891, 95%CI (10.987, 32.795)] and lower limb motor function [WMD = 5.403, 95%CI (2.720, 8.086)]).

Conclusion: Baduanjin Exercise Intervention can improve depression and anxiety, motor ability, daily living ability, balance ability, walking ability and lower limb motor function in patients with mild to moderate Parkinson's disease. It is suggested that patients with mild to moderate Parkinson's disease should actively carry out Baduanjin Exercise to improve their body ability and reduce the impact of the disease.

Effects of Health Qigong Exercise on Lower Limb Agility in Patients with Parkinson's disease

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Abstract:

Background and Purpose: Parkinson's disease is accompanied with lower limb stiffness, the range of movement may be limited or even interfere with daily living activities. As a traditional sport in China, Health Qigong has a unique way of keeping fitness. This study aims to determine the importance of Health Qigong exercise for the lower limb agility of patients with moderate to mild Parkinson's disease.

Methods: Twenty-six patients with mild Parkinson's disease were randomly divided into Health Qigong exercise intervention group and control group. Patients completed 60-70 minutes of exercise (preparation, Parkinson's motor therapy, relaxation) twice a week for 12 weeks. The test indicators were adopted reaction time of taking off from both feet.

Results and Discussion: After Healthy Qigong exercise, the two groups had significant differences in the post-test. The reaction time of the intervention group was significantly shorter than that of the pretest group ($P < 0.01$).

Conclusions: Health Qigong Exercise has a positive effect on lower limb agility in patients with Parkinson's disease.

Effects of Health Qigong Exercise on Clinical Motor Function in Parkinson's disease

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Abstract:

Background and Purpose: The clinical motor function of patients with Parkinson's disease is significantly lower, which affects the stability and balance of the body and increases the probability of falling. This study investigated the effect of 12-week Health Qigong exercise on clinical motor function in Parkinson's disease (PD) patients.

Methods: Thirty-one patients with mild and moderate PD were recruited and randomly divided into experimental group of 15 and control group of 16. Both groups were treated with basic neurology drugs and recorded, and the experimental group was additionally given Health Qigong exercise for 12 weeks, 5 times a week, 60 minutes each time, while the control group did not do any other regular exercise. Before and after the experiment, the motor function part of the Parkinson's Comprehensive Rating Scale (UPDRS III) was tested, and the results were analyzed by Two-way Repeated Measures analysis of variance using SPSS version 23.0.

Results and Discussion: After 12 weeks of Health Qigong exercise, the score of the third part of the motor function in the Parkinson's Comprehensive Rating Scale (UPDRS III) decreased significantly ($P < 0.01$), and the exercise ability was improved.

Conclusions: The results show that 12 weeks of Health Qigong exercise can effectively improve the clinical motor function of PD patients, which is beneficial to improve their quality of life. It can be used as an adjuvant therapy for sports rehabilitation in addition to drugs and surgery, and provides some new rehabilitation training ideas for researchers and clinicians.

Preterm Birth Compromises Development of the Cerebellum and Hippocampus: Evidence from A Large Animal Pig Model

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Abstract:

Infants born preterm have an elevated risk of compromised neurodevelopment, associated with motor and cognitive deficits. Imaging studies of human patients suggest that the cerebellum, a center of motor coordination, which is also involved in cognitive processing, and hippocampus, a center of learning and memory, are particularly vulnerable to adverse effects of preterm birth. The mechanisms that mediate brain pathology in preterm infants remain largely unknown, which prevents the development of treatment strategies to ameliorate neurodevelopmental deficits caused by precocious exposure to the extrauterine environment. We used the pig as a large animal translational model to study the cellular and molecular mechanisms of neural development

affected by preterm birth. We found that preterm birth affected both Bergmann glia and the proliferation of granule cell precursors in the cerebellum. Our gene expression and ex vivo rescue studies identified the secreted molecule Jag1 as a major molecular target affected by preterm birth. In the hippocampus of preterm pigs, we observed a reduced number of radial glial stem cells and intermediate progenitors, which was associated with reduced cell proliferation but normal apoptosis. Our ongoing experiments will identify the genes that mediate the phenotypes mentioned above.

The Effect of Eight-style Tai Chi on Improving the Balance Ability of Children with Moderate Intellectual Disabilities

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Abstract:

Background and Purpose: With the continuous development and growth of society, people have a more inclusive and broad vision than before, which also increases our sense of responsibility to the society, and makes us begin to pay more attention to the development of some minority groups and their physical and mental health. A group also includes people with intellectual disabilities. According to research, the main reason for the life expectancy of people with intellectual disabilities is shorter than the average life expectancy of the normal population. The lack of normal physical activity makes them more prone to the recurrence of some complications. Balance ability is the most normal and basic ability of physical activity. This paper mainly discusses the impact of Eight Style Tai Chi on improving the balance ability in children with moderate intellectual disabilities.

Methods: This paper mainly explores the effect of eight-style Tai Chi on improving the balance ability of children with moderate intellectual disabilities. A total of 24 children with moderate intellectual disabilities from special education schools were recruited, ranging in age from 9 to 12 years old, with an average age of (10.55±1.14) years old, they were divided into a control group of 12 and an experimental group of 12. The experimental group was given eight-style Tai Chi sports intervention activities for 12 weeks (3-5 times a week, 30-60 minutes each time), while the control group did not. For intervention, the BERG balance scale (BBS) was selected in this experiment to evaluate the balance ability of children with moderate intellectual disabilities before and after intervention. In this experiment, SPSS20.0 was used to analyze the differences between groups, and the significance level was set as 0.05.

Results and Discussion: There was no significant difference in the BERG scale score between the experimental group and the control group in the early stage of the experiment, but after 12 weeks of eight-style Tai Chi training, the BERG scale score of the experimental group was significantly higher than that of the control group [$F= 5.09$, $P<0.001$].

Conclusions: Eight-style Tai Chi has a significant effect on improving the static balance ability of children with moderate intellectual disabilities.

What is Cerebral Pulsy?

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Abstract:

The term “spastic diplegia” should be abandoned” – exhorted Colver and Sethumadhavan in 2003 in Arch Dis Child, but their flamboyant slogan has not been heard as yet. Our observation also suggests in favor of revision of classification of cerebral pulsy and its apprehension. We report the case of the two years old boy, with spastic diplegia and mental retardation; whose EMG detected decreased excitability of L 2 – S 2 spinal motoneurons, with no signs of neither spinal muscular atrophy, nor polyneuropathy nor myopathy. In addition, his MRI revealed spina bifida posterior S 1 – S 4.

The founder of cerebral pulsy teaching, Dr. Little W. J. wrote in 1861, that thorough postmortem examination reveals in this condition traumatic or/and vascular lesions either in brain or in spinal cord. However, why 30 years later his follower, great Sigmund Freud, when suggesting for this condition the new term – spastic diplegia, – looks in brain for explanation of this common spinal phenomena? He documented a poor correlation between clinical syndromes and neuropathologic lesions and was forced to elaborate the tricky theory of brain damage in pregnancy. Moreover, why nothing has changed since the Freud until our days? We still look for the origin of diplegia in brain, most often addressing it to cortex paracentral area lesions. The authors presume, that quality of postmortem examination of the newborns for unknown reasons had decreased after time of Dr. Little, and spinal cord is not studied such thoroughly as Dr. Little and his colleagues did.

A Missing Link, Regarding Central and Peripheral Neurophysiological Changes of Significant Importance for Better Understanding Recurrent Multiple Pain

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Abstract:

Background: Recurrent pain of stress etiology is a common, worldwide problem with impaired quality of life and decreased school attendance. Research show that pain of stress etiology, often called psychosomatic pain, often is a complex of multiple pains, other symptoms and augmented widespread muscular tension with a specific pattern of tender points (1).

Objective and Method: We will in a clinical context present electromyography (EMG) data, showing a novel and a missing link, regarding central and peripheral neurophysiological changes of significant importance for better understanding recurrent multiple pain.

Results: During high acoustic signals, the startle reaction was shown, via EMG, to be potentiated, more easily and more often elicited in several muscles related to the pain, in 19 children with recurrent stress related pain in the head, neck and abdomen, diagnosed according to strict defined criteria (2), and compared to 23 matched controls. Also, higher resting muscle activity was shown. We will also present data showing increased cortisol and decreased oxytocin, an imbalance between nociceptive omega-6 and antinociceptive omega -3 fatty acids and increased risk for developing fibromyalgia in children with psychosomatic pain.

Conclusion. Stressors potentiated the startle reaction with increased muscle activity in rest and increased excitability. These reactions and increased cortisol and decreased oxytocin in those children are in accordance with findings of the right dominance of stress in the bi-cameral brain (3). These neurophysiological facts can be of importance for the understanding of clinical manifestation of recurrent pain and must be heeded in the treatment of patients with pain related to stress.

Therapeutic Effect of Novel Antipsychotic Drugs Acting at Receptors of Neurotransmitters and Neuropeptides

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Abstract:

Major depression is a frequent psychiatric disease, which is mainly treated by different antidepressant drugs. However, one third of the depressive patients remain treatment-resistant. In major depression, in the brainstem, hippocampus and prefrontal cortex, alterations of neurotransmitters and neuropeptides and the belonging neural networks are updated. Starting from these findings, novel antidepressant drugs and combination of different antidepressant drugs are suggested. In the prefrontal cortex, glutamatergic neurons, which receive a postsynaptic excitatory potential from D2 dopaminergic neurons, exert a presynaptic inhibition upon M1 muscarinic cholinergic neurons via NMDA receptors. Medium spiny GABAergic/somatostatin neurons, which receive projections from M1 muscarinic cholinergic neurons, presynaptically inhibit D2 dopaminergic neurons via GABAA/somatostatin1 receptors. The combination of an NMDA receptor antagonist, for example ketamine with an M1 muscarinic cholinergic receptor antagonist, for example scopolamine, exert a rapid, long-lasting antidepressant effect. In preclinical studies, the antidepressant effect of orvepitant, an NK1 receptor antagonist, has been demonstrated: this antagonist reaches a complete antagonism of NK1 receptors. In clinical studies, the combination of an NMDA receptor antagonist with an M1 muscarinic cholinergic receptor antagonist should be investigated in depth. In clinical studies, the antidepressant effect of a triple reuptake inhibitor should be examined and compared to current antidepressant drugs. The superior therapeutic effect of antidepressant drugs like venlafaxine, a selective noradrenaline and serotonin reuptake inhibitor and bupropion, a selective dopamine and norepinephrine reuptake inhibitor and their adverse effects will be pointed out. Non-pharmacological measures to enhance the antidepressant effect will also be discussed.

Green Tea Suppresses Brain Aging

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Abstract:

Since the aging population is growing worldwide, the prevention of brain aging is a universal problem. In particular, the number of elderly people is increasing rapidly in Japan, with the highest percentage of elderly people in the world. Epidemiological studies have demonstrated that the intake of green tea is effective in reducing the risk of dementia. The most important component of green tea is epigallocatechin gallate (EGCG). Both EGCG and epigallocatechin (EGC) have been suggested to cross the blood–brain barrier (BBB) to reach the brain parenchyma, but EGCG has been found to be more effective than EGC in promoting neuronal differentiation. It has also been suggested that the products of EGCG decomposition by the intestinal microbiota promote the differentiation of nerve cells and that both EGCG and its degradation products act on nerve cells with a time lag. Based on the BBB permeability of catechins and their degradation products, several cups of green tea, or approximately one bottle of catechins, may reduce the age-related decline in cognitive function.

Effect of Healthy Qigong Intervention on Cognitive Function in Middle-aged and Old Age

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Abstract:

Objective: To observe the effect of Health Qigong on cognitive function in middle age and old age. In the process of pathology and physiological aging, the treatment of chronic diseases such as neurodegenerative diseases are limited. Health Qigong, as a traditional Chinese exercise, combines the adjustment of body, breath and mentality. In the form of motion, need to fully mobilize the visual, auditory, movement center and body muscles in a short period of time, so that the combinational motion and control is constantly changing and accurate, to promote the human forecourt system, ontological sense, vision system and nervous system integration function. In breathing coordination, mindfulness-based cognitive therapy is required to regulate mood and relieve stress through breathing and meditation. This shows that the traditional Chinese Qigong can prevent cognitive decline ahead of time, and has certain application prospects.

Methods: 68 middle-aged and elderly were randomly divided into Qigong group (34 people) and control group (34 people). Qigong group under the guidance of specialized researchers, for 12 weeks, 2 times a week, each 90 minutes of Qigong exercise, control group to maintain the normal lifestyle unchanged and do not participate in Qigong exercises. Use the Simple Mental State Scale (MMSE) to test before and after the experiment. There was a significant difference after the experiment compared with before the experiment ($P=0.029$, $P<0.05$).

Conclusion: Health Qigong can effectively delay and improve cognitive function in middle age and old age, and reduce the risk of Alzheimer's disease to a certain extent.

Study Effects of Health Qigong Baduanjin Exercises on the Inhibitory Ability of Executive Function in the Elderly

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Abstract:

Cognitive deterioration is becoming one of the health threats in an aging society. Inhibitory Ability, a core component of the executive functions, is the individual's ability to inhibit irrelevant stimuli or intentionally and actively inhibit dominant responses when performing a task. To provide a theoretical basis for effectively alleviating Cognitive Function in the elderly through physical exercise methods, this study used Health Qigong Baduanjin exercise as an entry point to investigate its effect on the inhibitory ability of the elderly; 32 eligible elderly people were randomly divided into the control group and the experimental group. The experimental group was given lasts for 12 weeks' intervention of 60 minutes of Health Qigong Baduanjin Exercises three times a week. The control group did not participate in fitness activities. Before and after the experiment, both groups implemented Franker test. Use SPSS 23.0 to carry out research on the obtained information. Results: 1. The experimental group showed significant differences in the reaction time before and after ($p=0.017 < 0.05$); 2. In the inconsistency task, the post-test time was significantly lower in the experimental group than the control group ($p=0.046 < 0.05$); In the consistency task, the two groups showed significant differences in time ($F=9.418, p=0.005$), and the post-test time was significantly lower than the pre-test time, but the post-test was more significant in the experimental group ($p=0.004 < 0.01$); 3. In conversion cost, the experimental and control groups showed a significant difference ($F=7.129, p=0.012$), the post-test scores of the experimental group were lower than pre-test ($p=0.036 < 0.05$). Conclusion: 12-week Health Qigong Baduanjin exercise can improve the Inhibitory Ability and can prevent the development of cognitive disorders in the elderly effectively.

Health Qigong Exercising Effects of Middle-aged and Elderly Women's Execution Function: A Randomized Controlled Trial

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Abstract:

Purpose: This research to explore the effect of Health Qigong exercise to the Execution Function (EF) of middle-aged and elderly women, and whether it can be used as a cognitive disorder preventive method for daily exercise.

Patients and methods: Randomized controlled trial compared Health Qigong exercise intervention with the normal life and sports habits. The primary outcome was the three sub-functions of EF (Inhibition, Shifting, Updating) that were measured by its common research paradigms (Flanker, More-odd shifting, 2-back). All experimental group(EG) were conducted a ten-week (weekly for 3 times) Health Qigong exercise intervention that consisted of 60 minutes: warm-up, Health Qigong combined with Tibetan dance, aerobic exercise and cool-down all of them in each time. All women maintained the normal life habits. We calculated these reaction-time (RT) and error rate(ER) using repeated measurement ANOVA.

Results: From July to September 2021, 33 women were randomized: Middle-age groups (N=18, Eight women in the Middle-age EG and 10 in the Middle-age control group) and Elderly groups (N=15, 7 in the Elderly EG and 8 in the Elderly control group). Middle-age EG's Flanker RT significantly decreasing (P=0.015); Elderly EG's Flanker ER significantly reducing (P=0.012); Elderly groups EG's 2-back RT significantly reducing (P=0.041). Other sub-function factors had positive changes to varying degrees in EG but were not significant. These data were not significant change in all control group.

Conclusion: Health Qigong exercise has positive effects on middle-aged and elderly women, especially in Inhibition and Updating. It is exercise method that can prevent cognitive disorder.

The Desensitization of the Transient Receptor Potential Vanilloid 1 by Nonpungent Agonists and Its Resensitization by Bradykinin

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Abstract:

Transient receptor potential vanilloid type-1 (TRPV1) channels have crucial roles in inflammatory hyperalgesia. Different inflammatory mediators can modulate TRPV1 sensitization. Bradykinin is an algogenic substance released at the site of inflammation. The aim of the present study is to investigate the desensitization of TRPV1 receptor by nonpungent agonists and to determine how bradykinin and prostaglandin E2 receptors (EP3 and EP4) modulate the resensitization of TRPV1 receptor after being desensitized by nonpungent agonists. Tail flick test was used to investigate capsaicin-induced thermal hyperalgesia and the desensitization of TRPV1 by the nonpungent agonists (olvanil and arvanil) in male BALB/c mice weighed (22–25g). Resensitization of TRPV1 by bradykinin and the role of prostaglandin receptors in mediating sensitization of TRPV1 were also investigated. Intraplantar injection of capsaicin (0.3µg) produced a robust thermal hyperalgesia in mice, while olvanil (0.3µg) or arvanil (0.3µg) produced no hyperalgesia, emphasizing their lack of pungency. Olvanil and arvanil significantly attenuated capsaicin-induced thermal hyperalgesia in mice. Bradykinin significantly reversed the desensitizing effects of arvanil, but not olvanil. EP4 but not EP3 receptors mediate the sensitization of TRPV1 By bradykinin in vivo. The present study provides evidence for a novel signaling pathway through which bradykinin can regulate the TRPV1 ion channel function via EP4 receptor

New Detection Technology Based on Fiber Optic Nanogold-Linked Immunosorbent Assay for Rapid Glial Fibrillary Acidic Protein (GFAP) Determination in Stroke Patients

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Abstract:

In acute stroke, one or more biomarkers not only can differentiate true stroke patients from stroke mimicking conditions but also distinguish the difference between ischemic stroke (IS) and intracerebral hemorrhage (ICH). One of the stroke biomarkers, glial fibrillary acidic protein (GFAP) in acute stroke has been studied extensively in recent years. Several studies demonstrated a rapid increase of GFAP in blood samples of ICH patients compared to slow release in ischemic stroke. As the concentration of GFAP in blood is very low, the detection is challenging. In this research, a rapid (averaged 15 min analysis time), high analytical sensitivity and selectivity method based on fiber optic nanogold-linked immunosorbent assay (FONLISA) technology is developed.

The technology is based on the interaction of an analyte with a surface-immobilized capture antibody and a gold nanoparticle-labeled detection antibody to form a sandwich-like complex on a fiber core surface. The LOD for GFAP is 2.81 fg/mL with the linear dynamic range from 10 fg/mL to 1 ng/mL. On clinical GFAP detection with serum samples, totally 10 positive and 3 negative samples which checked by CT method are used. For ten positive samples, results from the FONLISA method are highly correlated (correlation coefficient, $R = 0.98$) with that from the ELISA method. For three negative samples, ELISA has one false-positive result, leading to a diagnostic specificity of 75%, while the specificity for FONLISA is 100%. In addition, the positive predictive value and test efficiency are 90.9% and 92.3% for ELISA, respectively, and 100% and 100% for FONLISA, respectively.

Dysregulated OGF Serum Levels in Multiple Sclerosis and Animal Models of Experimental Autoimmune Encephalomyelitis Correlate with Disease

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Abstract:

Multiple sclerosis (MS) is a progressive demyelinating disorder of the CNS that presents as early as the third decade. MS is autoimmune in nature, and results in CNS lesions and eventual motor and cognitive dysfunction. Women and those living in the northern hemispheres are at higher risk. Current therapies are not completely effective, are costly, and many require medical intervention. Validation of non-invasive biomarkers to detect the onset and progression of disease are warranted.

Endogenous opioids, specifically opioid growth factor (OGF), chemically termed [Met5]-enkephalin, and its receptor, OGF_r, are altered in the serum of patients with MS, and animals with experimental autoimmune encephalomyelitis (EAE), the mouse model of MS. OGF is an inhibitory growth factor that targets cyclin dependent inhibitory kinases and limits cell replication. Reduced serum and tissue levels of OGF may impede modulatory mechanisms needed during autoimmune attacks. Clinical studies have demonstrated that MS patients with decreased OGF levels also have increased IL-17 and TNF α , along with changes in IL-6 throughout the course of disease. Serum ELISA data from individuals with various disease-modifying treatments revealed that OGF values were not responsive to any preferred treatment. Animal studies have documented that prophylactic treatment with OGF suppressed lymphocyte and neutrophil proliferation, leading to improved behavior in the EAE mice. Serum levels were elevated following treatment with OGF or LDN. Another endogenous peptide, β endorphin, was not altered in humans or animals with MS or EAE supporting the concept that OGF may be a novel biomarker that could be used to effectively track disease progression and response to therapy. Research was supported in part by the Shockey Family Foundation.

The Role of Creative Tasks in Neurorehabilitation after A Severe Coronavirus Disease

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Abstract

The aim of the work is to assess the role of creative tasks in neurorehabilitation after a severe coronavirus disease.

Material and methods: 32 patients with verified post-COVID syndrome and MCI were examined. They were invited to participate in art therapy sessions. Consent to participate in the program was given by 19 patients who made up the main group. The remaining 13 patients were included in the control group. The average age was 46.1 \pm 6.9 years for the patients of the main group, 49.2 \pm 5.9 years for the control group. The gender ratio in the groups was 1/1.29 with a predominance of women.

All patients of the main group underwent session for teaching painting and modeling skills, the session time was 30 minutes, 20 lessons per course. Before treatment and 3 months after the therapy, all patients were tested using the MMSE and TMT scales.

Results: At the time of the initial visit, all patients had a moderate decrease in cognition. The MMSE score was 25.6 \pm 0.9 points, the execution time for TMT (A) was 49.2 \pm 5.8 s, TMT(B) was 135.6 \pm 9.7 s. After the art therapy, there were 26.9 \pm 1.0 points on the MMSE scale, TMT(A) - 39.1 \pm 6.7 s, TMT(B) - 119.7 \pm 11.3 s in the main group. For comparison, in the control group, MMSE scores were 26.1 \pm 1.3 points, TMT (A) execution time - 48.8 \pm 6.2 s, TMT(B) - 132.4 \pm 10.9 s ($p < 0,05$).

Conclusions: Carrying out art therapy in the neurorehabilitation program after a severe coronavirus disease significantly improves visual attention and task switching.

Key words: neurorehabilitation, art-therapy, post-covid syndrome

Cognitive Dysfunction in Patients with Postcovid Syndrome: The Role of Stenotic Changes in the Carotid Arteries

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Abstract:

The aim of the work was to evaluate the role of asymptomatic carotid stenosis (ACS) in the development of cognitive dysfunction in patients with post-COVID syndrome.

We examined 69 reconvalescents after a coronavirus infection who had signs of cognitive dysfunction. The average age of the patients was 50.5 ± 8.3 years. All patients were examined using a battery of tests: MoCA, TMT, Schulte tables. Additionally, all patients underwent duplex scanning of brachiocephalic vessels.

Results: Manifestations of stenotic changes in the carotid arteries were registered in 28 (40.6%) patients. Small (up to 29%) carotid stenoses prevailed. None of the patients had a history of TIA and stroke. All examined patients complained of poor memory, impaired planning functions and executions. The average score on the MoCA scale was 22.1 ± 1.8 points in patients with ACS and 25.2 ± 2.1 points in those who did not have any carotid stenosis. The results of the TMT test were 74.4 ± 2.6 s and 69.3 ± 3.2 s, respectively, the time to fill in the Schulte tables was 155.6 ± 4.2 s and 138.3 ± 4.8 s ($p < 0.05$).

Conclusions:

1. The presence of ACS exacerbates the risks of cognitive dysfunction in patients with post-COVID syndrome.
2. Prophylactic administration of statins in patients with hyperlipidemia and ACS may be part of the complex therapy of patients who have had a coronavirus infection

Keywords: *cognitive dysfunction, post-COVID syndrome, asymptomatic carotid stenosis.*

Delayed Anastomotic Occlusion after Direct Revascularization in Adult Hemorrhagic Moyamoya Disease

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Abstract:

Delayed anastomotic occlusion occurred in a considerable part of hemorrhagic moyamoya disease (MMD) patients undergoing direct revascularization. This study aimed to investigate the predictors and outcomes of delayed anastomotic occlusion in adult hemorrhagic MMD. The authors retrospectively reviewed 87 adult hemorrhagic MMD. Univariate and multivariate logistic regression analyses were performed. After an average of 9.1 ± 6.9 months angiographic follow-up,

the long-term graft patency rate of 79.8%. Occluded group has significantly worse angiogenesis than non-occluded group ($P < 0.001$). However, the improvement of dilated anterior choroidal artery-posterior communicating artery were similar ($P = 0.090$). After an average of 4.0 ± 2.5 years clinical follow-up, the neurological statuses and postoperative annualized rupture risk were similar between the occluded and non-occluded group ($P = 0.750$; $P = 0.679$; respectively). In the multivariate logistic regression analysis, collateral circulation Grade III (OR, 4.772; 95%CI, 1.184-19.230; $P = 0.028$) and preoperative computed tomography perfusion (CTP) Grade I-II (OR, 4.129; 95%CI, 1.294-13.175; $P = 0.017$) were independent predictors of delayed anastomotic occlusion. Delayed anastomotic occlusion in adult hemorrhagic MMD might be a benign phenomenon. Good collateral circulation (Grade III) and compensable preoperative intracranial perfusion (CTP Grade I-II) are independent predictors for this phenomenon. Moreover, the delayed anastomotic occlusion has no significant correlations with the long-term angiographic and neurological outcomes except neoangiogenesis

Cognitive Impairment and Social Cognition Impairment in Patients with Multiple Sclerosis

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Abstract:

Cognitive impairment is prevalent in all types of multiple sclerosis (MS), including radiologically-isolated syndrome (RIS), clinically-isolated syndrome (CIS), relapsing-remitting multiple sclerosis (RRMS), primary progressive multiple sclerosis (PPMS) and secondary progressive multiple sclerosis (SPMS). However, the incidence and the rate of cognitive impairment progression is higher among patients with SPMS. Several clinical studies found an association between cognitive impairment progression and disability progression which could potentially signal a relapse or the conversion of CIS to MS. Although different types of the disease are associated with different domains affected, all disease types are associated with executive function deficits. Recent studies examined the integrity of social cognition in patients with MS presenting with and without cognitive impairment. According to the results, patients with MS who presented with cognitive impairment showed significant social cognition impairment, particularly in the recognition of negative facial expressions, compared with patients with MS without cognitive impairment and healthy adults. The severity of social cognition impairment was greater in patients presenting with the progressive types of the disease, particularly in those with the SPMS type, and seemed to be associated with the degree of physical disability. Although social cognition impairment is thought to be an outcome of cognitive impairment, some patients with MS without cognitive impairment and lesions in amygdala presented with social cognition impairment, leading to the hypothesis that lesions in amygdala could be used a predictive factor for social cognition impairment. Social cognition impairment affects the interpersonal relationships of the patients and is associated with higher unemployment rates.

The Impact of The Pandemic on Demented Patients

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Abstract:

Worldwide studies revealed that the mortality rate amongst demented infected individuals was significantly higher compared with the rate of infected patients without dementia and several studies were conducted to examine the factors that contributed to that. Since severely demented patients cannot live independently, they often reside in nursing homes which were heavily attacked by COVID-19. During the first wave of the pandemic, nursing home residents accounted for 40% of all deaths in the United States, even though nursing home population may be less than 1% of the total population. Additionally, demented patients are usually older than 65 years old and they suffer from various comorbidities which make them prone to severe infection and death. Moreover, in the absence of fever and cough, COVID-19 may initially present with atypical symptoms in these patients, such as agitation, disorientation, and confusion. Other factors include increased drug interactions between the treatment for dementia and the drugs used for the treatment of COVID-19, as well as the exclusion of demented patients from the ICU, since severely infected patients of younger age are prioritized. On the other hand, clinical studies revealed that demented patients showed significantly accelerated rate of disease progression during the pandemic. Factors that contributed to that include decreased physical and social activity, as well as the interruption of cognitive therapy and physiotherapy programs, due to confinement. Additionally, the pandemic itself acted as a major stressor. In conclusion, the pandemic of COVID-19 disease had a significant impact on the life of demented individuals overall.

Oligodendrocyte Precursor Cells Response after Focal Cerebral Ischemia

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Abstract:

Ischemic stroke is the second cause of mortality and the first of long-term disability worldwide. The only approved treatment is reperfusion, which are not suitable for all patients and not reduces subsequent neurodegeneration. Although glial response to ischemic damage is poorly understood, glial cell-related therapies are progressively overcoming inefficient neuron-centered approaches. Oligodendrocyte response after ischemia is the least known, but due to its potential re-myelination function, makes them a good candidate to take into account after stroke. The oligodendrocytes response to ischemia is time-dependent. At short-term, they get injured inducing axon demyelination, that aggravate neuronal damage. However, at long-term, they increases in number at ischemic region. The role of these newly generated oligodendrocytes is not totally understood, although get considered they could be part of a cerebral neuroprotective self-response. Recently, our group has demonstrated in an *in vivo* model of stroke (permanent medial cerebral artery occlusion; pMCAo), that after 5-21 days of pMCAo oligodendrocytes that colonize damaged area, present high levels of 3R-Tau isoform (3R-Tau⁺). This fact occurs in parallel with neurological improvement of rats.

The aim of this work is ascertain if 3R-Tau⁺ cells are oligodendrocytes precursors cells (OPCs). Our results shows that at short-term OPCs increases in ischemic area and at long-term a reduction occurs. These variations in OPCs distribution occurs in parallel with morphological changes, which leads us to propose that OPCs could differentiated into mature oligodendrocytes at long-term. Finally, using co-localization analysis we can conclude that OPCs are not the 3R-Tau⁺ oligodendrocytes previously observed.

Impact of COVID-19 Stroke Epidemiology and Clinical Stroke Practice at UTMB

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Abstract:

Introduction: Since the beginning of the COVID-19 pandemic, studies have shown a reduction in the number of stroke hospitalizations in the US and around the world. Several studies note fear of exposure as a contributing factor for this decline and concerns regarding stroke care. This study investigated the impact of the COVID-19 pandemic on stroke epidemiology and care of stroke patients in the UTMB Health System.

Methods: UTMB Stroke Program data was used to evaluate the following categories: modes of transportation, time to intravenous thrombolytic therapy (tPa), duration of hospital stays, and pre/post discharge modified Rankin scores (mRS). Two-tailed Paired Sample T-tests were conducted to extrapolate trends prior/during the COVID-19 pandemic and/or the rise of the delta variant specifically.

Results: The analysis indicated a significant increase in EMS from home/scene transports ($P < 0.0001$) during the COVID-19 pandemic compared to pre-pandemic, and higher pre-mRS prior to the rise of delta variant cases in Texas ($P < 0.0001$).

Conclusion: A rise in EMS transports rather than private/taxi transports may be indicative of limited means of transportation in Galveston County and/or the reluctance of individuals to travel to the hospital due to fear of exposure. Such fear may increase total hospital visits, as symptoms become more severe before medical attention is sought, which was shown. A significant decrease in pre-mRS and no difference in time to IV tPa, duration of hospital stay, or post-mRS may indicate optimal stroke care despite challenges imposed by COVID-19 variants.

Ubisol-Q₁₀ and Ashwagandha Root Extract Target Multiple AD-associated Biochemical Mechanisms Ameliorating AD Pathologies

Darcy Wear*, Caleb Vegh, Lauren Culmone, Hasana Jayawardena, Gabrielle Walach, Subidsa Srikantha, Iva Okaj, Rachel Huggard, Mathew Gagnon, Sezen Eren, Jerome Cohen and Siyaram Pandey

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Abstract:

Alzheimer's disease (AD) is a progressive neurodegenerative disorder currently affecting approximately 6.5 million Americans, with the number expected to double by 2050. The development of amyloid-beta plaques and neurofibrillary tangles directly result in the loss of hippocampal and cortical neurons as well as severe memory impairment. Unfortunately, current treatments solely provide symptomatic relief, rather than targeting the biochemical mechanisms responsible for the development of AD pathologies; namely mitochondrial dysfunction, elevated oxidative stress, neuroinflammation, impaired astroglia activation, and autophagy impairment. Previous work has shown Ubisol-Q₁₀, a water-soluble formulation of coenzyme-Q₁₀, stabilizes mitochondria, reduces levels of oxidative stress, and resumes autophagy in-vitro and in-vivo. It also cleared amyloid-beta plaques and ameliorated memory deficits in transgenic AD mice. Alternatively, ashwagandha root extract (ASH) has been used in Ayurveda as a tonic for memory impairment and has been shown to reduce neuroinflammation, oxidative stress, and memory issues in transgenic mice. We hypothesized that a combination of Ubisol-Q₁₀ and ASH will more effectively diminish AD pathologies through targeting multiple biochemical mechanisms. Indeed, this combined treatment effectively reduced amyloid-beta plaque accumulation while reducing oxidative stress levels, stabilizing mitochondria, enhancing autophagy, and blocking pro-inflammatory microglia activation. Interestingly, another potential anti-inflammatory pathway was observed in AD mice whereby untreated mice displayed pro-inflammatory astroglia activation while mice given the Ubisol-Q₁₀/ASH combination had anti-inflammatory astroglia activation. These results suggest that targeting these major biochemical mechanisms via Ubisol-Q₁₀ and ASH can ameliorate common pathologies and may inhibit the progression of AD.

Anti-inflammatory and Neuroprotective Effects of A Novel Water-soluble Formulation of Coenzyme-Q10 and Ashwagandha Root Extract in a Paraquat Induced Rat Model of Parkinson's disease

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Abstract:

Parkinson's disease (PD) is the most common movement disorder and second most common aging neurodegenerative disorder. PD is characterized by progressive loss of dopaminergic neurons in the substantia nigra resulting in impaired movement coordination. There is no cure and current therapies only provide symptomatic relief but result in adverse side effects over long term use. There are several biochemical mechanisms implicated in PD which include oxidative stress, mitochondrial dysfunction, impaired autophagy, and inflammation. Two nutraceuticals, ubisol-Q10, a water-soluble coenzyme-Q10 formulation and ashwagandha root extract have shown neuroprotective effects in models of PD when used separated by various PD biochemical mechanisms (Ubisol-Q10 targets oxidative stress, mitochondrial dysfunction, and autophagy impairment; ashwagandha targets oxidative stress and inflammation). We evaluated the neuroprotective efficacy of these two agents combined versus alone in a paraquat induce rat model of PD. We found the combination treatment was more effective at preserving dopaminergic neuron morphology/numbers, reduced oxidative stress, increased autophagy, inhibited pro-inflammatory microglia/astroglia, and activated pro-survival astroglia. While Ubisol-Q10 and ashwagandha were effective antioxidants, ashwagandha acted as the primary reducer of inflammation and Ubisol-Q10 was the primary autophagy activator. Increased neurotrophic factor expression was also observed in animals given ashwagandha. Paraquat treated animals given Ubisol-Q10, ashwagandha, or both showed increased expression of apoptosis/inflammation regulator, CARP1. Furthermore, using the same water-solubilizing technology in Ubisol-Q10, were able to reduce the effective therapeutic dose of ashwagandha extract. These exciting pre-clinical results suggest this treatment, composed of nutraceuticals, has potential to developed into a well-tolerated therapy for PD.

Human Amniotic Epithelial Cells Recover Mouse Model of Parkinson's disease mainly by Anti-oxidative and Anti-inflammatory Factors

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Abstract:

Human amniotic epithelial cells (hAECs) have been reported to be neuroprotective for Parkinson's Disease (PD) in animal models. However, the mechanism is not fully understood. Here, we report that specific growth factors from hAECs contribute to the recovery of dopaminergic neurons. First, hAECs transplanted into the striatum of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced PD mice prevented the loss of nigral dopaminergic neurons, and promoted the survival of nigral dopaminergic neurons and outgrowth of their neurites and striatal axon fibers in PD mice. In addition, the grafts also decreased microglial activation, inflammatory factor levels and MPTP-induced excessive reactive oxygen species (ROS) levels. When hAECs were co-cultured with mesencephalic dopaminergic neurons insulted with 1-methyl-4-phenylpyridine (MPP⁺), the survival of dopaminergic neurons and the outgrowth of their neurites were significantly enhanced. Moreover, the conditioned medium (CM) of hAECs (hAEC-CM) also exhibited a similar pro-survival role for lesioned dopaminergic neurons. Furthermore, analysis of an antibody array of 507 soluble proteins from hAEC-CM showed high levels of many neurotrophic factors, growth factors, neuronal CAM (NrCAM), and anti-inflammatory. Moreover, an antibody neutralization assay revealed that BDNF and CNTF, OSM, GM-CSF and NrCAM secreted by hAECs significantly enhanced dopaminergic neuronal survival and their neurite outgrowth. More importantly, anti-inflammatory factor Il-1ra, IL10 and IL13 also augmented the survival of dopaminergic neurons. Our findings demonstrate for the first time that an anti-oxidative and anti-inflammatory role of hAECs in PD mice and reveal a novel molecular mechanism of hAECs for the treatment of PD.

Computational Analysis of the Wrist: Benefits of A Gyroscope in Terms of Reducing Tremor in Parkinson's disease Patients

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Abstract:

Parkinson's disease (PD) is one of the most common neurodegenerative diseases in the elderly with tremor being the most commonly associated motor symptom. While neuromodulation and medications can reduce this symptom, they pose significant side effects. Wearable devices, however, can counteract tremor with minimal risks. The present study used multibody dynamic simulations to investigate the benefits of the gyroscopic devices in terms of (i) reducing tremor in hands of individuals with different anthropometric dimensions, as well as (ii) determining whether there is any correlation in terms of the device placement. These factors were systematically altered to simulate a total of 36 scenarios (3 hand sizes and 6 device placements, with and without the device activated). The results indicated that the gyroscopic device alleviates tremor magnitudes. The mean angular velocity, or resting tremor, showed most significant reduction when placed centrally over the hand at a greater distance from the skin (0.02 vs 0.002 m). The findings of this study will enable future biomechanical and therapeutic efforts to improve the efficacy of non-invasive treatments for the reduction of tremor through wearable devices.

The Influence of Biological Molecules on the Actions of Amyloid Degrading Enzymes

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Abstract:

In an aging society in the world, dementia leads pain to patients and their families has become a common disease in our lives. Among dementia, Alzheimer's disease (AD) is the most commonly shown disease. Various causes of the disease have been proposed and amyloid hypothesis insists that the toxic amyloid- β ($A\beta$) species could be the major risk factor of the onset and progression of AD. In this perspective, clearance of $A\beta$ species from the brain by regulating the activity of amyloid degrading enzymes (ADE), including neprilysin and matrix metalloproteinases, could be a potent treatment for AD. Therefore, the structures and functions of these enzymes along with the interactions with biological molecules in the brain would be important to understand the pathogenesis of AD and develop an effective medication for the disease. In this presentation, multiple ADE with biological molecules which could affect the activities and/or expression of the enzymes are presented.

Asymptomatic Idiopathic Basal Ganglia Calcification with Severe Cerebral Atrophy: A Unique Case Report on Fahr's Syndrome

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Abstract:

Idiopathic basal ganglia calcification (IBGC), previously referred to as Fahr disease, is a rare neurological disorder identified on radiological studies with a wide variety of clinical presentations. Here we discuss the case of an 84-year-old female patient that was admitted for abdominal pain indicative for diverticulitis. During her hospital stay, she complained of neck pain and was subsequently found to have extensive cerebral atrophy with incidental findings of bilateral calcifications affecting the cerebellum, thalami, dentate nuclei, and basal ganglia. While our patient was asymptomatic, it is worth describing the appropriate workup necessary in the case of IBGC not only on physical examination but also including laboratory investigations and radiographic studies to identify rare neurological disorders.

Two Cases of MOG Antibody-associated Demyelinating Diseases Preceded by Epstein-Barr Virus Infection

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Abstract:

Introduction: Myelin oligodendrocyte glycoprotein (MOG) is a glycoprotein expressed on the outermost surface of the myelin sheath and on the membrane of oligodendrocytes. The role of MOG in the central nervous system is not clearly understood, but anti-MOG have been detected in immune-mediated conditions that lead to demyelination including, but not limited to, monophasic acute disseminated encephalomyelitis (ADEM) and longitudinally extensive transverse myelitis (LETM). The underlying pathophysiology remains discreetly undefined but infectious processes may play a significant role. Our study reports two cases of anti-MOG ADEM and anti-MOG LETM, preceded by symptomatic infection with Epstein-Barr virus (EBV) infection.

Case presentations:

Case 1: A 59-year-old right-handed female with no significant history developed acute onset of ascending bilateral lower extremity numbness, weakness, and urinary retention four days before presentation. The patient was diagnosed with EBV mononucleosis two months prior to onset of these symptoms.

Case 2: A 23-year-old right-handed female with no significant past medical history developed urinary retention, gait instability, numbness and tingling in her hands, and difficulty ambulating two days before presentation. She reported having an upper respiratory tract infection one month before onset of symptoms and serologies revealed EBV.

Discussion: To our knowledge, cases 1 and 2 are the second and third reports of MOG antibody-associated demyelinating disease preceded by EBV infection. There are similarities, as well as differences between our cases to the first case reported. Overall, additional studies are needed to help determine prognostic and therapeutic factors in anti-MOG immune mediated conditions preceded by EBV.

Augmenting Psilocybin Assisted Psychotherapy with Brain Stimulation (rTMS) for Chronic PTSD: Proof of Concept Study

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Abstract:

Background: Post-Traumatic Stress Disorder (PTSD) is often a chronic, difficult to treat and

debilitating mental illness that affects up to 8.3% of U.S. individuals in their lifetime and has many serious comorbidities including suicidality^{1,2}. Current first-line treatments can take up to 36 weeks for their effects and have high non-response rates (~55%)². Given the poor response to pharmacotherapy alone, combining medication with other interventions can potentially enhance the robustness and/or durability of response while possibly needing lower dosage of medication, thus mitigating the side-effects². In particular, non-invasive stimulation of the right dorsolateral prefrontal cortex at high frequencies using (rTMS) has been shown to significantly reduce PTSD symptoms³. MDMA, a schedule-I agent, has been recently FDA-approved as a breakthrough therapy for PTSD as a result of multiple studies showing its clinical and sustained efficacy in PTSD^{4,5}. Due to similar neurobiological mechanisms, rapid and persistent action, minimal side-effects and efficacy in chronic depression and anxiety, psilocybin has been proposed as another treatment for PTSD⁵.

Methods: This proof-of-concept study intends to investigate the efficacy of psilocybin assisted psychotherapy augmented with rTMS in patients with chronic PTSD. We hypothesize that psilocybin assisted psychotherapy augmented by rTMS will produce a quick and robust decrease in PTSD symptoms as well as enhance the rates and durations of remission as compared to an active comparator (methylphenidate) augmented by active or sham rTMS.

Key words: PTSD, novel treatments, psychedelics, psilocybin, brain stimulation, rTMS.

'Everything is as Before, But Nothing is as it was'—A Phenomenological-Hermeneutic Study of Meaningfulness in Adult Refractory Epilepsy Patients' after Interdisciplinary Epilepsy Rehabilitation

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Abstract:

Background: Interdisciplinary Rehabilitation aimed at adults with Refractory Epilepsy (RE) establishes scientific evidence of higher health-related QoL, including improved self-worth and increased self-awareness as outcomes. Yet there is very little research-based knowledge of how life transforms itself after the rehabilitation program from the patients' perspectives.

Aim: The aim of this study was to identify and describe how – from the patient perspectives - life transforms itself after rehabilitation among adults with refractory epilepsy, focusing on the meaningfulness of interdisciplinary rehabilitation.

Method: Nine patients; six women and three men; 26-58 years old (mean 39), who all participated in an Interdisciplinary Rehabilitation Program in an Adult Epilepsy Clinic, were interviewed between six months and two years after rehabilitation. Nine interviews were recorded, transcribed verbatim and analyzed as described by the phenomenological method 'Reflective Lifeworld Research'.

Findings: The essence of the phenomenon was revealed as life as a struggle for a dignified existence with RE as a navigating life companion. Through the clusters of meaning, four constituents emerged from the phenomenon:

1) To accept the limitations of body and mind; 2) To be on a journey toward your inner self; 3) To be quietly understood; 4) To fight for renewed hope and recognition during transition.

Conclusion: The patients consider it meaningful to know their own bodies with the constraints that this involves. This knowledge helps them make decisions that not only have a positive effect on their epilepsy, but also raise their self-esteem and give them renewed hope and courage to face life. However, the struggle for a dignified life is continuously hard, and it comes to a head in patients' transition from 'patient to citizen', where asymmetries arise. These asymmetries leave considerable marks on the patients' worlds and challenge their renewed hope for a dignified existence.

Sub-components of Reading and Their Effects on Recovery in Left-stroke Patients

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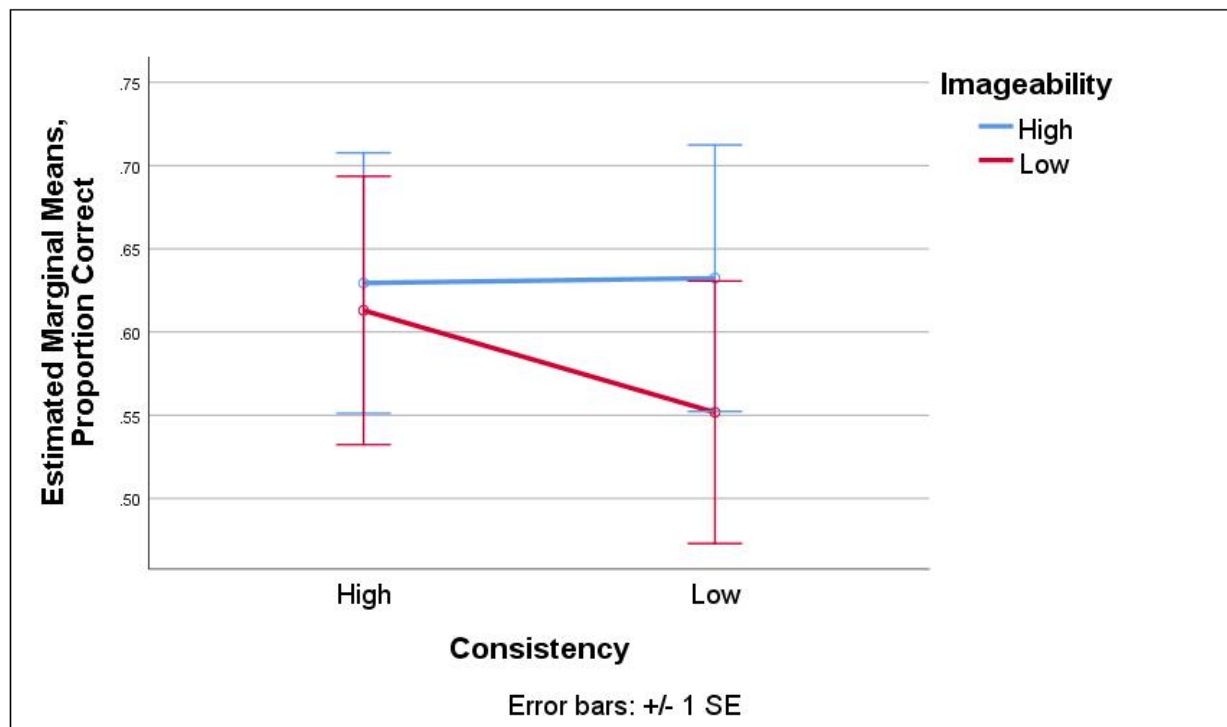
Abstract:

Better understanding of reading mechanisms after stroke can help develop effective treatments that alleviate acquired reading deficits. In a longitudinal study, we characterized reading accuracy of 17 left-stroke patients (8 women; 9 men; ages 29-81; $M=61.53$; $SD=14.68$) during subacute (<5 weeks) and chronic (>3 months, $N=8$) post-stroke period. We hypothesized that words that easily evoke an image (high-imageability), are frequent (high-frequency), and follow spelling-sound correspondence rules (high-consistency) would be read more accurately. We also predicted that reading real words would be more accurate than reading readable nonwords, and that accuracy would improve from subacute to chronic period.

Consistent with these predictions, reading accuracy improved from subacute to chronic period and was higher for real words than nonwords (M words/acute=.61, $SD=.30$; M nonwords/acute=.40, $SD=.33$; M words/chronic=.82, $SD=.16$; M nonwords/chronic = .59, $SD=.30$, all $p<.05$). While some degree of recovery is evident, our data suggest that reading deficits, especially problems in letter-to-sounds mapping for unfamiliar words, persist chronically. During the subacute period, participants read high-frequency words more accurately than low-frequency words ($F(1,16)=8.63$, $p<0.05$, $\eta_p^2=.35$). There was a marginally significant imageability by consistency interaction ($F(1,16)=4.02$, $p=0.062$, $\eta_p^2=.20$), such that words of low imageability and low consistency were read less accurately (Fig.1). Chronically, in addition to the main effect of frequency ($F(1,7)=5.65$, $p<0.05$, $\eta_p^2=.45$), there was a main effect of imageability ($F(1,7)=7.03$, $p<0.05$, $\eta_p^2=.5$).

Our results suggests that different sub-components of reading may be important at different stages of recovery, offering important insight into stimulus selection for speech and language therapies.

Figure 1:



Effects of Combination of Baduanjin with Different Control Measures on Motor Function and Balance Ability of Stroke Patients

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Abstract:

Purpose: To explore the effect of different control measures and combined with Baduanjin(CB) intervention on the motor function and balance ability of stroke patients.

Methods: As of November 15, 2021, a literature search was carried out in four databases including PubMed. Develop literature inclusion and exclusion criteria, and two experienced reviewers will independently complete literature screening and data extraction. Use Stata15.0 software to perform data processing such as heterogeneity test and subgroup analysis.

Results: A total of 18 randomized controlled trials were included, and 1398 subjects were included. The results showed that the combined intervention of different control measures and Baduanjin had significant differences in the improvement of motor function (conventional rehabilitation exercise VS (CB)[SMD=1.406,95%CI(0.448,2.365),P=0.004], Conventional treatment VS (CB)[SMD=0.539,95%CI(0.116,0.962),P=0.013], health education VS (CB) [SMD=0.744, 95%CI (0.329,1.158),P<0.001], conventional treatment and conventional rehabilitation training VS (CB)[SMD=0.507,95%CI(0.188,0.826),P=0.002], balance training VS (CB)[SMD=1.265,95%CI(0.718,1.812),P<0.001]); At the same time, there are significant differences in the improvement of balance ability (conventional rehabilitation treatment VS (CB)

[SMD=0.880,95%CI(0.509,1.251),P<0.001], healthy Education VS (CB)[SMD=0.802,95%CI (0.385,1.218),P<0.001], conventional treatment and balance training VS (CB)[SMD=1.759, 95%CI(1.217,2.301), P<0.001]), but compared with Bobath treatment, the results of the study were not statistically significant (P>0.05]).

Conclusion: The traditional treatment plan (CB) intervention can promote the motor function and balance ability of stroke patients. However, whether Baduanjin will be more effective for targeted rehabilitation techniques such as Bobath still needs to be more effective. Deep research.

Effect of Perceived Sleep Quality on Subjective and Objective Working Memory Performance among Veterans with mTBI

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Abstract:

Veterans with mild traumatic brain injury (mTBI) history often report deficits in subjective working memory performance (SWM) and sleep quality (SQ). However, SWM does not reliably align with objective working memory performance (OWM). The present study examines the relationship between SWM and OWM among Veterans with mTBI history who report poor sleep quality.

Method: Participants included 40 Veterans (6.25% Female; age $M = 46.91$, $SD = 14.28$; years of education $M = 14.84$, $SD = 1.78$) with a history of mTBI. Thirty-two Veterans met criteria for poor SQ (Pittsburg Sleep Quality Index Score cutoff of ≥ 5). SWM was measured by Behavioral Inventory Rating of Executive Functioning (BRIEF) and OWM by the Wechsler Adult Intelligence Scale (WAIS-IV) working memory index score. A Pearson correlation was used to analyze the relationships between (1) SWM and SQ, and (2) OWM and SQ. Regression analyses were conducted to determine the predictive value of SQ on SWM and OWM.

Results: SWM was significantly correlated with SQ ($p < 0.05$, $r = 0.664$, Cohen's $d = 5.19$). The regression analysis indicated that SQ significantly predicted SWM ($p < .001$, $R = 0.594$, $R^2 = 0.353$). There was no significant relationship between SQ and OWM ($p = .79$).

Conclusions: Veterans with mTBI history who reported poor SQ were more likely to report WM difficulties. However, OWM was not correlated with SQ or SWM performance. This disconnect highlights the need for therapeutic interventions targeting SQ to enhance perceived cognitive functioning and quality of life.

Evaluation of National Disparities in Access to Neurosurgical Care

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Abstract:

Background: When neurosurgical care is needed, the distance to a facility staffed with a neurosurgeon is critical. This work utilizes geospatial analysis to analyze access to neurosurgery in the Medicare population and relevant socioeconomic factors.

Methods: CMS billing and demographic data from 2015-2019 was combined with national NPI registry data to identify the average travel distance to reach a neurosurgeon. This was merged with USA Department of Agriculture data to capture 31 socioeconomic attributes. Moran's I statistic was calculated across counties. Socioeconomic variables were compared using ANOVA.

Results: Hotspots with highest neurosurgeon access (0.59 ± 0.77 neurosurgeons per 1000 Medicare members, $p < 0.05$) were predominantly located in the Mid-Atlantic region, central Texas, and southern Montana. Coldspots (0.0 ± 0.01 neurosurgeons per 1000 Medicare members, $p < 0.05$) were found in the Great Plains, Midwest, and southern Texas, with an average distance to a neurosurgeon of 63.6 ± 39.7 miles. There were statistically significant differences ($p < 0.05$) between high- and low-access counties, including: prevalence of strokes (3.9% to 3.12%), percent with a college degree (33.15% to 19.33%), poverty (11.25% to 16.35%), median household income (\$66,551.12 to \$47,167.56), and total population density (1355.34 to 44.36 people per square mile). There were no statistically significant differences in race or ethnicity.

Conclusions: There exist statistically significant clusters of decreased neurosurgery access within the United States, with varying sociodemographic characteristics between access hotspots and coldspots.

Identifying Neural Patterns and Biomarkers of ASD Through Multi-phase Resting-state Functional MRI Analysis

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Abstract:

Autism spectrum disorder (ASD) is a neurological disorder impacting communication and social interaction. The CDC estimated that approximately 1 in 44 children had ASD in 2021 with prevalence nearly tripling since 2002. Yet the current diagnosis process is based on subjective clinical developmental and behavioral observations. As a result, early diagnosis, which is necessary to develop treatment targeted towards a person's specific needs at the right developmental stage, is often missed. Through the application of deep learning to functional magnetic resonance imaging (fMRI), this is the first study to address the specific research gap by systematically evaluating deep learning ASD classification based on fMRIs through multi-site, multi-atlas, gender and age

demographics segmentation, and feature and functional connectivities analysis, outperforming state-of-art accuracy, specificity, sensitivity of 70%, 67%, and 73% respectively in 10 iterations of 10-fold cross-validation, despite site-to-site variability in Autism Brain Imaging Data Exchange (ABIDE) database. More importantly, this research identifies neural patterns and biomarkers of ASD that emerged in the classification study. In particular, specific ROIs and functional connectivity pairs were identified as most reliable for ASD classification including the pairs originating from right Thalamus, left Angular Gyrus, left and left and right front Superior frontal Medial. Further, the top 25 % of the functional connectivities between regions of interest (ROIs) determine the ASD classification performance. Through this research, understanding of ASD and objective identification of neural patterns and biomarkers for earlier diagnosis and timely treatment is pushed one step forward.

A Tripartite Memory Systems Model of Neurodegenerative Disease

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Abstract:

Extensive preclinical research on multiple memory systems has reveal detailed neurobehavioral profiles of cognitive memory (S-S), simple habit (S-R) and higher-order habit [(S-S)-R] associative functions of the hippocampus, dorsolateral striatum/putamen and the dorsomedial striatum/caudate nucleus, respectively (Devan, McDonald, & White, 1999; Devan, Hong, & McDonald, 2011; Devan & White, 1999; McDonald et al., 2005). Experimental and clinical studies in humans converge with the animal research, suggesting that the three memory systems show early and selective vulnerability in different neurodegenerative conditions (AD, PD and HD, respectively). We propose that early assessment to develop comprehensive neurobehavioral profiles well before any disease onset will provide highly sensitive, temporally specific, multilevel biomarkers to target systems-level intrinsic cellular and molecular processes in advance of disease onset. This approach has the potential to correctively restore and prevent neurodegenerative processes, that once initiated, lead to inevitable decline that palliative therapies may only slow symptom progression in a prolonged management of care and extended state of ill-health among our elders, rather than attenuate or even prevent disease onset. Consequently, the approach of identifying predictive biomarkers for early intervention may provide significant improvements in healthcare, increasing the quality of life in our elders and their loved ones, and reducing the societal burden based on slow progressive dysfunction that is both emotionally and financially untenable going forward in biomedical advancement rather than remaining stagnant for several more decades to come.

Increased Incidence of Stroke in Multiple Sclerosis: Shared Genes between The Two Diseases

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Abstract:

Recent clinical studies on patients with multiple sclerosis (MS) have revealed an increased incidence of any type of stroke compared to the general population, with ischemic stroke (IS) being the most encountered. Large-scale GWAS have examined the genetic component of several neurological disorders, including MS and IS to identify potential risk genes. So far, several risk genes associated with the predisposition to MS and IS have been revealed accordingly. Since the current available treatments used for MS do not seem to protect the patients from stroke, the need to create new targeted treatments that will be more effective emerges and therefore, the identification of any shared genes between the two diseases is crucial. Until recently, the only shared gene between MS and IS identified was SLC44A2, due to limited available data. Lately, the meta-analysis of Li et al. (2019) revealed 220 shared genes between MS and IS, the vast majority of which plays a key role in pathways associated with immune system regulation. Moreover, the meta-analysis of Tian et al. (2020) identified 5 shared genes which present significant difference in their translation patterns between patients with MS who have suffered a stroke and those who have not. Both MS and IS are disabling neurological disorders which have a tremendous impact on the quality of life (QoL) of the patients and their caregivers, but also affect the society and the economy overall. The development of new targeted treatments protecting the patients with MS from stroke is essential.

Mild Cognitive Impairment and Social Cognition Impairment in Parkinson's disease

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Abstract:

The incidence of mild cognitive impairment (MCI) is high amongst patients with Parkinson's disease (PD). Patients with PD may present with MCI already at the diagnosis, later on the course of the disease or even before the diagnosis. The presence of PD-MCI before the occurrence of motor symptoms is associated with hallucinations, REM sleep behavior disorder and autonomic nervous system dysfunction. Clinical studies have revealed that PD-MCI is highly associated with older age at disease onset and the postural instability and gait disorders (PIGD) subtype, whereas there is little association between PD-MCI and the tremor-dominant (TD) subtype. PD-MCI is typically characterized by visuospatial deficits which affect execution function and attention. Several clinical studies examined the integrity of social cognition in patients with PD with and without MCI. Patients with PD-MCI presented with greater impairment in social cognition compared with the patients with PD without cognitive impairment and healthy adults, by exhibiting greater difficulty in the recognition of negative facial expressions, particularly anger, and the scanning of the face by spending greater amount of time in the center of the face and less time in the exploration of the mouth and the rest of the face. Although patients with PD-MCI presented with greater cognitive impairment, patients with PD without cognitive impairment performed worse than healthy adults which signifies the impact of oculomotor deficits in patients with PD overall. Social cognition impairment is associated with MCI and its integrity is crucial for the interpersonal relationships of the patients with other people.

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