Society For Neurochemistry, India (SNCI) 2020

34TH ANNUAL MEETING(VIRTUAL)

11TH - 13TH DEC 2020

Brain Diseases, Injuries and Infections: Emerging Challenges and treatment strategies

Spotlights

- Neuro-infections
- Cell death mechanisms
- nervous system diseases
- Cognitive Neuroscience
- Current aspects of aging studies
- Demyelination in CNS and PNS

Organisers

Prof. Prakash Babu Phanithi
School of Life sciences
University of Hyderabad,
Hyderabad, Telangana state, INDIA

Dr. M. Varalakshmi
School of Medical Sciences
University of Hyderabad,
Hyderabad, Telangana State, INDIA

Mechanistic Studies of Neuro-degenerative Diseases

Dr. Rita Christopher NIMHANS, Bengaluru

Plasma microRNA as potential biomarkers for the diagnosis of cerebral small vessel disease

IIT Kharaghpur **Dr. Nihar Jana**

Huntington's Disease, Genetics and pathogenic mechanisms

Prof. Anita Jagota School of Life Sciences UOH, HYDERABAD

Therapeutic effects of hydro-alcoholic leaf extract of Withania somnifera on age-induced Neurodegeneration in SCN

BHU UOH **Prof. S. K. Trigun**

Sirtuin1 (SIRT1) as epigenetic hot spot in pathogenesis of an excitotoxic brain disorder

Prof. Pravir Kumar DTU, Delhi

Post-Translational Modification in neuro generative disorders

Therapeutic Approaches or Interventions for recovery and Neuro - Regeneration

Dr. Gurucharan Kaur Guru Nanak Dev University, Amritsar

Tinospora Cordifolia-Journey from ayurvedic folk medicine to preclinical neurotherapeutic role

Jamia Hamdard, New Delhi **Dr. Suhel Parvez**

Pramipexole provides mitochondrial-mediated neuroprotection after traumatic brain injury

Dr. Anirban Basu NBRC, New Delhi

Modulation of Neural Stem/Progenitor Cell response following Japanese Encephalitis Virus infection

NCCS, PUNE **Nibedita Lenka**

Wnt-DUB link dictating early neurogenesis

Sarada Subhramanyam NIMHANS, Bengaluru

Tau-Centric Therapeutic approaches to Alzheimer's Disease

Mechanistic Studies of Neuro-degenerative Diseases

Dr. Amit Nayak CIIMS, Nagpur

Peripheral biomarker panel for prognosis of acute ischemic stroke: translational challenges and approaches

UOH, Hyderabad **Dr. Madhu Babu**

Mechanism of Tau and Fyn mediated Neurodegeneration in Alzheimer's Disease

Dr. Prasad Tammineni UOH, Hyderabad

Crosstalk between Autophagy and Endo-lysosomal pathways in Alzheimer's Disease

North East Hill University, Shillong **Dr. Dinesh Bhatia**

Study the cognitive behavioral changes in children with disability employing repetitive transcranial magnetic stimulation and Neurofeedback tools

D. Harikrishna Reddy Central University of Punjab, Bathinda

Neuro-Behavioural and Histopathalogical facets after Brain Stroke

Cognitive Neuroscience

Prof. Sukala Prasad BHU, Varanasi

Modulation of AMPA receptor trafficking/scaffolding proteins expression by Bacopa monnieri extract during cognitive impairment in mice

JSS College of Pharmacy, Mysuru **Dr. Saravana Babu**

Demystifying the link between sleep and cognition

Dr. M. Varalakshmi School of Medical Sciences, UOH, HYDERABAD

Protective function of Physical activity on Cognitive and Mental Health Outcomes; Activity and Wellbeing among older adults

Central University of Punjab, Bathinda **Dr. Debapriya Garabadu**

Abeta 42 down regulates adenosine - 2b receptor with impairment in mitochondrial and cholinergic function in memory-sensitive rat brain regions

Dr. Akash Gautam UOH, Hyderabad

The critical role of Arc/Arg3.1 in the object recognition memory

Molecular aspects of brain tumours and Neuro-infections

Dr. Rajpal Singh Kashyap CIIMS, Nagpur

IL 10 importance in Neuro-infections

KIIMS, Hyderabad Dr. Y.B.V.K Chandrasekhar

Role of Fluorescent dyes in Neurosurgery practice at a tertiary care centre

Dr. M. Janiki Kurnool Medical College

Neuro-infections

NIMHANS, Bengaluru Dr. Nandakumar DN

Advances in role of glutamate receptors and their crosstalk in growth and redox status of glioblastoma

Dr. Trupti Trivedi GCRI, Ahmedabad

Dissecting Molecular Profiling for Management of Glioblastoma Patients

Therapeutic Approaches or Interventions for recovery and Neuro - Regeneration

Dr. Sumana Chakravarty IICT, Hyderabad

Sex difference in zebrafish brain proteome profile indicates the critical role of H3K9me3 in recovery from acute hypoxia

PSJ College of Pharmacy, Coimbatore **Prof. M. Ramanathan**

Tribulus Terrestris Extract in the treatment of Neuropathic pain-preclinical studies

Dr. Sudip Paul NEHU, Shillong

Efficacy of gaming therapy for oral motor and cranial nerve disorders

NIMHANS, Bengaluru **Dr. Ravish**

Molecular Signature of the Immune Response to Yoga Therapy in Stress-related Chronic Disease Conditions: An Insight

Prof. Rashmi Ambasta Delhi University, Delhi

Therapeutic role of bone marrow derived mononuclear cells in diabetic neuropathy

Goa University, Goa **Dr. Shanti N. Dessai**

Frontiers and Tools to Study Developmental Neurogenesis

Dr. Omkumar RV Scientist G, Rajiv Gandhi Centre for Biotechnology Kerala

Multi-target directed drugs for neurological disorders

Symposium

Mechanisms of Post-stroke Brain Damage

Dr. Krishna Veeravalli
Associate Professor,
Dept. of Cancer Biology & Pharmacology,
University of Illinois, Peoria, IL

Silencing t-PA after ischemic stroke mitigates brain damage and promotes recovery

Dr. Saif Ahmad
Assistant Professor,
Barrow Neurosurgical Institute,
Phoenix, AZ

Role of complement C3a receptor in vascular cognitive impairment and disease

Dr. Venu Venna
Assistant Professor,
Dept. of Neurology,
University of Texas, Houston, TX

Age related gut microbial dysbiosis and stroke recovery

Prof. Raghu Vemuganti
Professor and Vice Chair,
Dept. of Neurological Surgery,
Univ. of Wisconsin, Madison, WI

Role of epitranscriptomics in ischemic brain damage

Symposium

Different Shades of Huntington's disease

Dr. Puneet Kumar Central University of Punjab, Bathinda

Chemicals induced animal models:
Insight into the pathogenesis of Huntington's disease

Assistant Professor,
BITS- Pilani, Hyderabad, India **Dr. Pragya Komal**

Vitamin D intake enhances Vitamin D receptor expression in the striatum and rescues memory and motor dysfunction in mouse model Huntington's disease

Dr. Ana Christina Rego Professor,
University of Coimbre,
Portugal

Strategies of rescuing mitochondrial dysfunction in Huntington's disease

Professor,
McGill University,
Canada **Dr. David Stellwagen**

Tumour necrosis factor-alpha alters the function of striatal synapses in YAC128 mouse model of Huntington's disease

Symposium

Myeloid-lymphoid activity to understand brain injury

Prof. Krishnan M Dhandapani
Dept. of Neurosurgery,
Medical College of Georgia, Augusta University,
Augusta, GA, USA

Immunometabolic dysregulation initiates progressive neurodegeneration after brain injury

Department of Anatomy & Neurobiology
University of Tennessee,
Memphis, TN, USA
Dr. Tauheed Ishrat

TXNIP: a Potential Therapeutic Target for Brain Aging and Alzheimer's Disease

Prof. Babak Baban
Dept. of Oral Biology and Diagnostic Sciences,
Dental College of Georgia, Augusta
University, Augusta, GA, USA

Innate Lymphoid Cells (ILCs) and Brain Injury

Dept. Of Molecular and Biochemical Pharmacology,
Universidad Católica de Santa María,
Arequipa, Peru
Dr. Pallavi Shrivastava

Mystery of Fate of Microglia: Progenitor to Adult microglia priming in CNS disorders

Symposium

Modern Interventional tools for persons with disability

Dr. Sucheta Sahu Institute of Neuroscience, Kolkata, India

Rehabilitation Robotics: From Disability to Ability

NIMHANS, Bangalore, India **Dr. K Udupa**

Advances in Non-invasive brain stimulation in Neuropsychiatric disorders

Prof. R. Sharma AIIMS, Delhi, India

QEEG: A tool to assess brain function in neurodevelopmental disorders

Sendai, Tohoku University, Japan **Prof. K Tsutsui**

Dr. Archana Chaudhary Department of Biosciences, Faculty of Science, SGT University, Gurugram

Cognitive behavior:
An Environmental interventional tool affecting Human Psychology

Symposium

Bilingualism and cognition : Recent developments

Suvarna Alladi NIMHANS, Bangalore, India

Bilingualism and dementia: Implications for the concept of cognitive resilience

Indian Institute of Technology Guwahati, India **Bidisha Som**

Investigating complexity in 'the bilingual experience' and its role in adaptive control

Veeky Baths Birla Institute of Technology & Sciences, Goa campus, India

Alzheimer's Detection Using Speech Analysis

University of Hyderabad Hyderabad **Ramesh Kumar Mishra**

Bilingual language control and interaction in the social world

Niels O. Schiller Leiden University Centre for Linguistics (LUCL) & Leiden Institute for Brain and Cognition (LIBC), The Netherlands

What grammatical characteristics of words may tell us about our mind and cognition: Cross-linguistic evidence on the selection of lexico-syntactic features

Symposium

C20s in the Brain - Eicosanoids in Neuronal Health and Disease

Dr. Ritushree Kukreti

Senior Principal Scientist CSIR -
Institute of Genomics & Integrative Biology (IGIB),
Mall Road, Delhi, India;
Professor, Academy of Scientific and Innovative Research (AcSIR),
Ghaziabad, India

Cyclooxygenase-2 (COX-2) in Epilepsy: Potential Mechanisms and New Therapeutic Strategies

Senior Assistant Professor,
South Asian University,
New Delhi, India

Ravi Shankar Akundi

Purinergic Modulation of Prostaglandin E2 Release in Activated Immune Cells

Dr. Undurthi Das

MD, DSc, FAMS, FRSC UND
Life Sciences 2221 NW 5th St,
Battle Ground, WA 98604, USA

Inflammation Resolution Deficiency in Some Neurological Disorders and it's Clinical and Therapeutic Implications

Associate Professor,
University of Florida College of Medicine,
Gainesville, Florida, USA

Dr. Eduardo Candelario Jalil

Role of Cyclooxygenase-2 in Neurovascular Injury following Ischemic Stroke

MECHANISTIC STUDIES OF NEURO-DEGENERATIVE DISEASES

SPEAKERS:

1. **Dr. Rita Christopher,** NIMHANS, Bengaluru
   Title: Plasma microRNA as potential biomarkers for the diagnosis of cerebral small vessel disease

2. **Dr. Nihar Jana,** IIT, Karagpur
   Title: Huntington's Disease, Genetics and pathogenic mechanisms

3. **Prof. Anita Jagota,**School of Life Sciences, UOH, HYDERABAD
   Title: Therapeutic effects of hydro-alcoholic leaf extract of *Withaniasomnifera*on age-induced Neurodegeneration in SCN

4. **Prof. S. K. Trigun,** BHU
   Title: Sirtuin1 (SIRT1) as epigenetic hot spot in pathogenesis of an excitotoxic brain disorder

5. **Prof. Pravir Kumar,** DTU, Delhi
   Title:POST-TRANSLATIONAL MODIFICATION IN NEURODEGENERATIVE DISORDERS

Plasma microRNA as potential biomarkers for the diagnosis of cerebral small vessel disease

Dr. Rita Christopher

Department of Neurochemistry, NIMHANS, Bengaluru

Cerebral small vessel disease (SVD) is the primary cause of cognitive dysfunction and vascular dementia in the elderly, in India. Diagnosis of SVD requires both clinical expertise and neuro-imaging studies and there are no blood-based markers to identify this disorder. Plasma microRNAs (miRNAs) have been proposed as diagnostic biomarkers in various disorders. We examined the miRNA profile in the plasma of patients with SVD to identify differentially expressed miRNAs which could serve as diagnostic biomarkers for SVD.

We performed plasma miRNA profiling byquantitative polymerase chain reaction(qPCR) in patients with SVD and age and gender-matched healthy subjects and found that 44 miRNAs were differentially expressed in SVD patients ($p< 0.05$ with a fold change of <2 and >2). We further validated a set of 7 highly differentially-expressed miRNAs in a cohort of 200SVD casesand 204 controls.Receiver operating characteristic (ROC) curve analyses showed that a panel of 4 up-regulated miRNA (miR-32-5p, miR-502-3p, miR-486-5p miR-451a, miR-363-3p) had a predictive value of 0.857 (95% CI 0.795–0.920; P<0.0001) and a panel of 2 downregulatedmiRNA (miR-409-3p, miR-376-3p) had the highest predictive value, with an AUC of 0.881 (95% CI 0.827–0.936; P< 0.0001). The expression of 3 plasma up-regulated miRNA(miR-363, miR-486 and miR-451a) were significantly negatively correlated with degree of cognitive decline as assessed using HMSE score.KEGG pathway analysis showed that these miRNAs target major pathways involved in cerebrovascular pathology including transforming growth factor-beta (TGF-β) signaling and aldosterone-regulated sodium reabsorption pathway. We conclude that plasmamiRNA could serve as blood-based biomarkers for the early identification of SVD. Further validation of the biomarker potential of these differentially-expressed miRNAs is warranted.

Huntington's disease: genetics, pathogenic mechanisms and therapeutic targets

Dr. Nihar Ranjan Jana

School of Bioscience, IIT Kharagpur, Kharagpur

One of the common neuro-pathological hallmarks of most age-related neurodegenerative disorders including Huntington's diseases (HD) is the accumulation of the abnormal disease protein as inclusion bodies. HD iscaused by abnormal extension of CAG triplet repeat in the coding region of *IT15* or *HD* gene. In the normal individual, CAG repeat length varies from 6-35, while the disease phenotype is associated with more than 36 CAG repeats and there is an inverse correlation between CAG repeat length with disease onset and severity. After the discovery of the HD gene in 1993, there have been remarkable progresses in understanding the disease pathogenic mechanisms. Wide-ranging studies using cellular and animal models as well as post-mortem HD brain samples discovered multiple abnormalities of specific neuronal function that are linked to the progression of HD. Appearance of aggregates of the misfolded mutant huntingtin indicate that neurons are unable to efficiently degrade them, and failure of clearance over time leads to the severe disturbance of the neuronal protein quality control system. Based on these findings,we hypothesized thatboosting up of the neuronal protein quality control system could decrease the load of aggregated huntingtin that eventuallymight prevent neuronal dysfunction and neurodegeneration. In my talk, I shalldiscussabout our journey in identifying Ube3a as cellular protein quality control ligaseand how this ligase is involved in the progression of HD. At the end, I shall talk about our identification of a novel inducer of Ube3a that significantly delay the disease progression in HD mouse model.

Therapeutic effects of hydro-alcoholic leaf extract of *Withaniasomnifera*on age-induced Neurodegeneration in SCN

Prof. Anita Jagota

Department of Animal Biology, School of Life Sciences, University of Hyderabad

Aging is associated with changes in several basic parameters of circadian timing system (CTS) in mammals leading to circadian dysfunction. The suprachiasmatic nucleus (SCN) in hypothalamus contains a light-entrained circadian clock. It is involved in regulation of neuronal, endocrine and behavioral rhythms through the expression of various clock genes. It regulates the rhythmic production and release of melatonin (messenger of darkness) from pineal gland involving close interaction of core circadian machinery with a network of interconnected transcriptional and translational feedback loops.

To understand the age induced stoichiometric alterations in interactomes of daily chronomics in neurodegenerative changes in the functional integrity of CTS, daily rhythms in various parameters in SCN at variable time points (Zeitgeber time (ZT) - 0, 6, 12 and 18) in three age groups (3 (adult), 12 and 24 months) of maleWistar rats maintained in light–dark conditions (LD 12:12). We report here, the age-induced change in interactions between various 5-HT metabolism components by middle age (12 m) changing further by 24 m. The m-RNA expression for clock genes such as *bmal1, per1, per2, cry1, and cry2* was rhythmic in SCN of adult rats.However in 12 and 24 m, the phases of expression of these genes were significantly altered with abolition of daily rhythms of *rCry1, rCry2* and *rBmal1* in 24m. Differential alterations with aging in the levels and chronomics of 2-D protein profiles and locomotor rhythms were observed.

Therapeutic differential restoratory effects of administration of withanolides and alkaloidsfrom*Withaniasomnifera* (Ashwagandha) on aging and neurodegeneration were studied on age induced Circadian dysfunction and desynchronization in various molecular parameters.

This work may prove useful towards targeting novel treatments for circadian dysfunction, good health and longevity.

Sirtuin1 (SIRT1) as epigenetic hot spot in pathogenesis of an excitotoxic brain disorder

Prof. Surendra Kumar Trigun, ArchitaKhanna

Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi

SIRTUINS, a group of class III protein deacetylases, are known to regulate epigenetically most of the normal cell functions. Out of the seven known homologues, SIRT-1 is considered to be the most critical one due to its epigenetic roles in regulating transcriptional activities of many genes. We speculated that SIRT-1 could be functionally associated with the NMDAR over activation led neuroexcitotoxicity. To investigate this evolving concept, we have studied the glu-NMDAR-apoptosis pathway via a visarborization pattern of hippocampal CA1 pyrimidal neurons and profile of SIRT1 vs SIRT1 activation led modulations of these parameters in the neurobehavioral characterized moderate grade hepatic encephalopathy (MoHE) rat model of excitotoxicity. MoHE was induced by administration of 100 mg/kg b.w of thioacetamidei.p. for 10 days. In comparison to the control group rats, correlative increases in TNF-α &NfkB profiles and a transition from a neuroprotective NR1/NR2A NMDAR composition towards a neurodegenerative NR1/NR2B combination could coincide with a significant decline in SIRT1 level and atrophied hippocampus CA1 pyrimidal neurons. The MoHE associated all these aberrant patterns could, however, be reversed back to the normal level due to the treatment of those MoHE rats, with 10 mg/Kg b.w. RSV (a Sirt-1 activator). Such a reversible pattern was further consistent with the RSV dependent deacetylation status of certain key SIRT1 nuclear targets; FOXO3a, p53, NfkB. The findings suggest that SIRT1 activation evidently reverses MoHE associated deranged neuroarchitectural, neuro-chemical and neurobehavioral derangements by deacetylating critical nuclear factors.

POST-TRANSLATIONAL MODIFICATION IN NEURODEGENERATIVE DISORDERS

Prof. Pravir Kumar, M.Sc. (BHU), PhD (Germany); PDF/Faculty (USA)
Professor, Department of Biotechnology, Delhi Technological University, Delhi

Accumulation of aggregated or non-functional protein is one of the important factors in the progression of neurodegenerative disorders, especially in Alzheimer's and Parkinson's disease. Post-translational modifications (PTMs) are an essential regulator of non-functional protein aggregation in the pathogenesis of NDDs. Any alteration in the post-translational mechanism and the protein quality control system, for instance, molecular chaperone, ubiquitin-proteasome system, autophagy-lysosomal degradation pathway enhances the accumulation of misfolded protein, which causes neuronal dysfunction. Post-translational modification plays many roles in protein turnover rate, accumulation of aggregate and can also help in the degradation of disease-causing toxic metabolites. Post-translational modifications such as acetylation, glycosylation, phosphorylation, ubiquitination, palmitoylation, SUMOylation, nitration, oxidation, and many others regulate protein homeostasis, which includes protein structure, functions and aggregation propensity. Different studies demonstrated the involvement of PTMs in the regulation of signaling cascades such as PI3K/Akt/GSK3β, MAPK cascade, AMPK pathway, and Wntsignaling pathway in the pathogenesis of NDDs. Further, mounting evidence suggests that targeting different PTMs with small chemical molecules, which acts as an inhibitor or activator, reverse misfolded protein accumulation and enhances neuroprotection.

THERAPEUTIC APPROACHES OR INTERVENTIONS FOR RECOVERY AND NEURO-REGENERATION

SPEAKERS:

1. **Dr. GurucharanKaur,** Guru Nanak Dev University, Amritsar
   Title: TinosporaCordifolia-Journey from ayurvedic folk medicine to preclinical neurotherapeutic role

2. **Dr. SuhelParvez,** JamiaHamdard, New Delhi
   Title: Pramipexole provides mitochondrial-mediated neuroprotection after traumatic brain injury

3. **Dr. AnirbanBasu,** NBRC, New Delhi
   Title: Modulation of Neural Stem/Progenitor Cell response followingJapanese Encephalitis Virus infection

4. **NibeditaLenka,** NCCS, PUNE
   Title: Wnt-DUB link dictating early neurogenesis

5. **SaradaSubhramanyam,** NIMHANS, Bengaluru
   Title: Tau-Centric Therapeutic approaches to Alzheimer's Disease

Pramipexole provides mitochondrial-mediated neuroprotection after traumatic brain injury

Mohd. Salman and Dr. Suhel Parvez*

Department of Medical Elementology and Toxicology, School of Chemical and Life Sciences, New Delhi.

Background: Traumatic brain injury (TBI) is the major cause of death and disability worldwide occurs when an external mechanical force damages the brain. Currently, no therapeutic drug is available that could potentially inhibits the neuronal death and dysfunction following TBI.

Objective: This study aimed to investigate the potential neuroprotective effects of pramipexole (PPX) in TBI model and explore the underlying mechanisms.

Materials and methods: In this study, male Wistar rats were divided into four groups: Sham, TBI, TBI+PPX (0.25 mg/kg, i.p.), and TBI+PPX (1.0 mg/kg, i.p.). Behavioral experiments were performed after 2 days of post-injury and animals were sacrificed to evaluate biochemical and molecular changes. The injured brain hemisphere was used for the estimation of oxidative stress parameters. The expression of Bax/BCl2 ratio and cytochrome c release were evaluated using western blot analysis. Additionally, we checked the mitochondrial ROS and mitochondrial membrane potential.

Results: PPX treatment was able to mitigate the oxidative damage and mitochondrial perturbation in experimental rats.

Conclusion: These results indicate that PPX can significantly attenuate the oxidative stress and mitochondrial dysfunction after traumatic injury, which provides potential therapeutic benefits against TBI.

Keywords: Pramipexole,Brain injury, Oxidative damage, Mitochondrialdysfunction, Neuroprotection

Modulation of Neural Stem/Progenitor Cell response following Japanese Encephalitis Virus infection

Dr. Anirban Basu
National Brain Research Center, Manesar, Haryana

Japanese encephalitis virus (JEV), a common cause of encephalitis in humans, especially in children, leads to substantial neuronal injury.We hypothesize that depletion of neural progenitor cells (NPCs) by the virus culminates in neurological sequelae in survivors of Japanese encephalitis (JE). We utilized both *in vivo*model of JEV infection and *in vitro*neurosphere cultures to study progressive JEV infection. JEV leads to massive loss of actively proliferating NPC population from the subventricular zone (SVZ). The ability of JEV infected subventricular zone cells to form neurospheresis severely compromised. JEV suppresses the cycling ability of these cells, preventing their proliferation. This arrested growth and proliferation of NPCs might have an effect on the neurological consequences in JE survivors.

We have further showed, with mass spectrometry based quantitative proteomic study, the impact of virus on the stem cells at protein level. Our aim was to perceive the stem cell proteomic response upon viral challenge. We performed a 2-DE based proteomic study of the human neural stem cells (hNS1 cell line) post JEV infection and found that 13 proteins were differentially expressed. The altered proteome profile of hNS1 cell line revealed sustained endoplasmic reticulum (ER)stress which deteriorated normal cellular activities leading to cell apoptosis. The proteomic changes found in hNS1 cell line were validated*in vivo* in the subventricular zone of JE infected BALB/c mice. Congruent alterations were also witnessed in multipotent neural precursor cells isolated from human foetus and in autopsy samples of human brain clinically diagnosed as cases of JE patients. ER resident chaperone GRP78, mitochondrial protein Prohibitin (PHB)and heterogeneous nuclear ribonucleoproteinhnRNPC (C1/C2) have been shown to interact with viral RNA. Hence it is proposed that these are the principle candidates governing ER stress induced apoptosis in JEV infection. All these may attribute to the fact that survivors of JEV infection have severe cognitive impairment, motor and behavioral disorders.

Wnt-DUB link dictating early neurogenesis

Nibedita Lenka

National Centre for Cell Science, Ganeshkhind, Pune

The complex event of neurogenesis is orchestrated through precise and fine-tuned modulation by genetic and epigenetic players. Alteration in the same results in neurodevelopmental defects. We have been interested in unraveling the intricate cell fate decision machinery operational during early neurogenic proceedings using embryonic stem cells (ESCs) as the model system, and delineating the guiding cues dictating the same. Accordingly, using candidate based approach we have been able to chalk out the temporal window of action of various neuromodulators. Wnt, a secreted glycoprotein, was detected as a major player that exerted its influence in a paracrine fashion. Although the activation time window of Wnt resided at the neural progenitor stage, it rather influenced neuronal differentiation. Moreover, a domineering pro-neuronal influence of Wnt was observed on overcoming Stat3 deficiency mediated impairment in neurite extension in LIF maintained clones. Further investigation led to identification of USP, a deubiquitinase (DUB), that acted downstream of Wnt to modulate differential fate specifications during ESCs differentiation. Further we have noticed direct interaction of this DUB with β-catenin indicating Wnt-DUB link in mediating the neurogenic progression. Moreover, the identified DUB could act on histone H2A and H2B reflecting to its chromatin modulatory effect. The ongoing studies in this context would shed light on the mechanistic basis underlying Wnt-DUB attributes and epigenetic modulations operational during early neurogenesis.

Tau-centric therapeutic approaches to Alzheimer's disease

Sarada Subramanian

Department of Neurochemistry, NIMHANS, Bangalore

Alzheimer's disease (AD) is an irreversible, progressive neurodegenerative disorder. AD is the leading cause of dementia, characterized by progressive loss of memory and other cognitive functions. Currently, more than 4 million people are affected by AD in India and it is forecast to double by 2050. Till date, no effective treatment for AD is available.

The cognitive impairment in patients with AD is closely associated with loss of synapses and the formation of neurofibrillary tangles (NFT) containing hyperphosphorylated tau in the hippocampus. Evidence from preclinical studies has suggested that the pathological tau based immunotherapy decreases the tau pathology and rescues the functional impairment.However, the potential side effect of current tau-based immunotherapy targeted primarily towards the central proline rich region and the positively charged C-terminal region is that it is prohibiting normal tau from performing its normal cellular functions. Given that there are multiple phosphorylations on tau, many of them have been reported to have pathological consequences; the identification and selection of the most therapeutically relevant phospho-epitopes is very essential. The N-terminal amino acid sequence of Tau (residues 1-137) harbours 14 potential phosphorylation sites in the form three clusters spanning the residues 18-50, 68-71 and 111-137. The possibility of the antibodies directed towards any one of these epitopes targeting specifically the pathological forms of phospho-tau allowing physiologically phosphorylated tau to continue to function will be elaborated.Further, the clinical value in terms of immunosassay development for quantitation of pathology associated pSer113 and pThr 123 in AD samples will be discussed.

SYMPOSIUM

MECHANISMS OF POST-STROKE BRAIN DAMAGE

ORGANISED BY,

Dr.RAGHU VEMUGANTI, Professor and Vice Chair

Department of Neurological surgery, University of Wisconsin, Madison, WI, USA.

SPEAKERS:

1. **Dr. Krishna Veeravalli,** University of Illinois, USA
   Title: Silencing t-PA after ischemic stroke mitigates brain damage and promotes recovery

2. **Dr. Saif Ahmad,** Barrow Neurosurgical Institute, Phoenix, Arizona, USA
   Title: Role of complement C3a receptor in vascular cognitive impairment and disease

3. **Dr. VenuVenna,** University of Texas, Houston, USA
   Title: Age related gut microbial dysbiosis and stroke recovery

4. **Prof. Raghu Vemuganti,** University of Wisconsin, Madison, USA
   Title: Role of epitranscriptomics in ischemic brain damage

Silencing t-PA after ischemic stroke mitigates brain damage and promotes recovery

Dr. Krishna Kumar Veeravalli, Associate Professor

Departments of Cancer Biology and Pharmacology, University of Illinois at Chicago, USA

Elevated brain levels of tissue-type plasminogen activator (t-PA) after ischemic stroke are postulated to have both beneficial and detrimental actions on the pathogenesis of stroke. Based on the mechanisms of post-stroke brain damage and the known molecular interactions of t-PA, we hypothesized that the potential deleterious effects of t-PA outweigh its beneficial actions, and therefore t-PA may worsen stroke. To test this hypothesis, we attenuated post-stroke t-PA expression and determined whether this treatment had a more favorable outcome on brain injury and neurological recovery. Young adult male Sprague-Dawley rats were subjected to transient focal cerebral ischemia using an intraluminal suture model of middle cerebral artery occlusion, followed by reperfusion. To achieve knockdown of t-PA, plasmids expressing shRNAs specific to t-PA (t-PAsh) were formulated as nanoparticles and administered intravenously to rats within 30 min after reperfusion at a dose of 1 mg/kg body weight. Appropriate cohorts of sham-operated, untreated and vehicle (scrambled control shRNA) or drug (t-PAsh)-treated rats were euthanized at different post-reperfusion time points and the collected brains were used in various analyses (TTC staining, real-time PCR, immunoblot, and Evans blue dye extravasation assay). To assess treatment effects on post-stroke neurological recovery, we performed the neurological severity score assessment as well as other functional tests (adhesive removal, beam walk, and Rotarod) at regular intervals, until 14 days after reperfusion. Consistent with our prediction, t-PAsh treatment attenuated the infarct volume and post-stroke neurological deficits, prevented the degradation of key tight junction proteins, such as claudin-5 and ZO-1, curtailed the blood-brain barrier disruption, and facilitated the post-stroke neurological recovery. Overall, these results indicate that t-PA predominantly has a deleterious effect on the ischemic brain and that its attenuation mitigates brain injury and promotes neurological recovery from stroke. Suppression of brain t-PA may represent a new treatment strategy for ischemic stroke.

Role of Complement C3a receptor in Vascular Cognitive Impairment and Dementia (VCID)

Dr. Saif Ahmad, Assistant Professor
Barrow Neurological Institute, Arizona, USA

Background: Chronic cerebral hypoperfusion results in cognitive impairment and vascular dementia known as vascular contributions to cognitive impairment and dementia (VCID). Reduction in cerebral blood flow (CBF) underlies neurovascular dysfunction, microglial activation, and white matter degeneration in VCID. Complement C3a receptor (C3aR) has been implicated in the pathogenesis of stroke and Alzheimer's disease (AD).We previously reported that genetic and pharmacologic C3aR inhibition protects the cerebrovasculature and improves outcome in murine stroke.

Hypothesis: We hypothesized that hypoperfusion activates the C3a/C3aR axiswhich exacerbates white matter degeneration and hippocampal atrophy, however C3aR deletion may beprotective in chronic VCID.

Methods: VCID was induced through bilateral carotid artery stenosis (BCAS) by using male wild-type (C57BL/6) and C3aR-KO mice. CBF was assessed using laser speckle and MRI. Neurocognitive outcome was assessed using Morris water maze (MWM) and novel object recognition (NOR) tests.Protein expression was evaluated using ELISA, immunohistochemistry and Western blot.

Results:WT-BCAS mice demonstrated reduced cerebral blood flow and impairment in spatial learning and memory by MWM and NOR tests. We also noted white matter degeneration after BCAS in WT mice using Luxol blue staining, as well as increased expression of C3a/C3aR and pro-inflammatory markers in plasma and hippocampus.We further observed decreased expression of myelin basic protein (MBP)and BBB integrity markersZO1 and occludinfollowing BCAS. C3aR-KO mice showed improvement in CBF and cognitive outcome and proteins expression following BCAS.

Conclusion:C3aR mediates white matter injury and neuroinflammation following BCAS and genetic deletion of C3aR improves long-term functional outcome and CBF in this model.Further work is necessary to understand the contribution of C3aR to the pathogenesis of VCID.

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Age-related gut microbial dysbiosiscontributes to impaired stroke recovery

Dr. Venugopal Reddy Venna, Assistant Professor

Department of Neurology, University of Texas, USA.

Recent studies have revealed that the inflammatory state of the gut microbiome has an important role in the outcome after stroke. Furthermore, aging is associated with a changes in gut microbial populations, or “dysbiosis” which has been implicated in several diseases. These findingsare especially significant,as stroke is an age-related disease, and both morbidity and mortality rise sharply in the elderly, often due to systemic complications such as sepsis rather than being directly attributable to the stroke itself. In this study, we altered the gut microbiome through fecal transplants in aged male mice (18–20 months) 3 days after experimental stroke to resemble that of young mice using either young donor biome (2–3 months) or aged biome (18–20 months) or direct enrichment of short-chain fatty acids (SCFAs) using selective SCFA-producing bacteria. Fecal transplantsfrom young donor elevated brain SCFA levels, improved gut inflammation after stroke. Our results indicate that young microbiome transplants improve post-stroke recovery in aged mice, by modulation of immunologic, microbial, and metabolomic profiles and play a key role in maintaining gut integrity.

Role of epitranscriptomics in ischemic brain damage

Prof. Raghu Vemuganti, Professor and Vice Chair

Department of Neurological Surgery, University of Wisconsin, USA

Recent studies showed that RNAs can undergo >170 types of chemical modifications that are called epitranscriptomic modifications. In mammals, formation of N^6-methyladenosine (m^6A; methylation of adenosine at N^6-position) is the most abundant of these modification.The m^6A methylation controls metabolism and functions of mRNA by modulating splicing, export, stability, translation, and degradation. The m^6A methylation is regulated developmentally and shows a very high abundance in brain.Furthermore, m^6A methylation is biased towards neuronal transcripts and alters due to neuronal activity.Using a mouse transient middle cerebral artery occlusion (MCAO) model of focal ischemia, we currently show that the global m^6A levels increased significantly at 12h and 24h reperfusion in the peri-infarct cortex compared with the sham (by 3.3 to 4.1 fold; $p<0.05$; n =5/group). This was observed in both male and female mice. Transcriptome-wide m^6A changes were profiled using immunoprecipitated methylated RNAs with microarrays (44,122 mRNAs and 12,496 lncRNAs).While 139 transcripts (122 mRNAs and 17 lncRNAs) were hypermethylated, 8 transcripts (5 mRNAs and 3 lncRNAs) were hypomethylated (>5-fold compared to sham) in the ischemic brain at 12h reperfusion. Gene Ontology (GO) analysis showed that Inflammation, apoptosis and transcriptional regulation are the major biological processes modulated by the post-stroke differentially m^6A methylated mRNAs. The m^6A writers were unaltered, but the m^6A eraser (fat mass and obesity-associated protein) decreased significantly after stroke compared to sham.Thus, our studies show that stroke alters the cerebral m^6A epitranscriptome, which might have functional implications in post-stroke pathophysiology.

SYMPOSIUM

MODERN INTERVENTIONAL TOOLS FOR PERSONS WITH DISABILITY

ORGANISED BY: Dr. DINESH BHATIA,

North Eastern Hill University, Shillong

SPEAKERS:

1. **SuchetaSahu,** Institute of Neuroscience, Kolkata
   Tile: Rehabilitation Robotics: From Disability to Ability

2. **Dr. K Udupa,** NIMHANS, Bengaluru
   Title: Advances in Non-invasive brain stimulation in Neuropsychiatric disorders

3. **Prof. R. Sharma,** AIIMS, Delhi
   Title: QEEG: A tool to assess brain function in neurodevelopmental disorders

4. **Prof. K Tsutsui,** Tohoku University, Japan
   Title:

5. **Dr. ArchanaChaudhary,** SGT University, Gurugram
   Title: Cognitive behavior: An Environmental interventional tool affecting Human Psychology

Rehabilitation Robotics: From Disability to Ability

Dr. Sucheta Saha, MBBS, DMRT, MD (Physical Medicine & Rehabilitation)
Department of Neurorehabilitation, Institute of Neurosciences Kolkata.

Disability is defined by World Health Organization (WHO) as- 'Any restriction or lack of ability to perform an activity in the manner or within the range considered normal for a human being'. 'Rehabilitation' means 'To make able again'. Rehabilitation physicians are working worldwide with a constant goal of making disabled people able again. 'Rehabilitation Robotics' is the most advanced tool in their hands, where neuroplasticity plays the pivotal role harnessing the principals of rehabilitation and technology.

Development of Rehabilitation Robotics started in early 1990s, and over the last few decades it has become a reliable treatment modality in various neurological and musculoskeletal disorders, which can prevent disability if applied early in the course of the disease. It can also slow down the progression of the disability or reverse the residual neuro-muscular deficits. It has been used in several neuro-muscular diseases, like- Cerebrovascular accidents, Traumatic brain injuries, Spinal cord injuries, Parkinsonism, Cerebral Palsy etc. and found to be beneficial for the patients in many clinical studies. A study done by the author herself showed that Robotic Therapy can be an effective adjunct to the conventional rehabilitation program in Stroke. That was the first published study in India on Rehabilitation Robotics. Robotic devices provide high-intensity, task-oriented training with performance feedback. All these stimulate the adaptive plasticity of brain and facilitate motor relearning. Many Robotic systems are available for rehabilitation separately for the upper and lower extremities. They are- Armeo, Lokomat, Rewalk and so on. There are also Robotic prostheses, which can replace the lost part of the body, like- Bionic hand, Luke Arm etc.

Rehabilitation Robotics is a promising new area in Rehabilitation to alleviate the disability of persons suffering from array of neuromuscular conditions. In India the scope of Robotics is still unexplored. Awareness about the newest technology used in rehabilitation among the disabled population and physicians, clinical trials and financial support to establish robotic systems can improve the scopes of Rehabilitation Robotics in India and decrease the burden of impairment, disability & handicap in the society.

Advances in Non-invasive brain stimulation in Neuropsychiatric disorders

Dr. Kaviraja Udupa,MD, PhD, Additional Professor
Departments of Neurophysiology, NIMHANS, Bengaluru.

There is expanding interest in various brain stimulation techniques such as non-invasive brain stimulation (NIBS): repetitive TMS and transcranial direct current stimulation (tDCS), transcranial alternating brain stimulation (tACS), transcutaneous auricular vagal nerve stimulation (taVNS) and electroconvulsive therapy (ECT) and invasive deep brain stimulation (DBS) in various neuropsychiatric conditions. Transcranial magnetic stimulation (TMS) has been utilized in the investigation and treatment of many neurological and psychiatric disorders for the last three decades. Unlike other brain stimulation techniques such asECT and DBS, TMS is shown to be non-invasive, safe and effective mode of investigation to explore the physiology of cortical circuits in health and disease. Generally, single or paired pulses of TMS could be used to investigate cortical excitability functions, which are altered in various neuropsychiatric disorders. rTMS and various patterns of stimuli delivered over length of time alters the excitability of stimulated region for extended period of time (so called plasticity effects) thus providing therapeutic utility especially in patients with neuropsychiatric disorders such as depression, cerebral palsy, Duchene muscular dystrophy (DMD) and autistic disorders.

Inongoing studies we are investigatingfactors affecting attention deficit hyperactivity disorders, the efficacy of dual stimulation of tDCS and high frequency rTMS in patients with Major depression (commonest mental health disability) and investigate the medical refractoriness in depression by using a comprehensive battery of clinical and investigative modalities of TMS. Further, we are investigating mechanisms of potential Ayurvedic add-on therapies in couple of projects involving patients with depression or DMD. In these projects we are exploring various neurochemical factors to understand the interaction between excitatory and inhibitory neurotransmitter systems using paired pulse TMS protocols and neurochemical investigations.

Although rTMS treatment has been successfully considered as add-on to physiotherapies in management of unilateral stroke, clinical depression and various other neurodevelopmental disorders, we are still lacking the clear understanding of their mechanisms of action in neurodegenerative conditions. Many studies involving clinical & behavior changes, imaging measures, molecular and animal models of neurological conditions have looked into various modes of mechanisms of action of these brain stimulation modalities.Further, newer protocols of stimulation, newer brain stimulation techniques,novel combination of various modes of brain stimulationand imaging (multi-modal TMS), are emerging in research and clinical practice of these neuropsychiatric conditions. These newer protocols or combination of brain stimulation techniques may potentially augment both understanding the pathophysiology as well as treatment strategies for various disabling neuropsychiatric disorders.

QEEG: A tool to assess brain function in neurodevelopmental disorders

Prof Ratna Sharma, Department of Physiology AIIMS, New Delhi

Assessment of resting state neural networks can help us understand the physiological (developmental/ behavioural) and pathological (diagnosis and prognosis of a disease) basis of Autism spectrum disorders (ASD), which are a group of complex and heterogeneous developmental disorders involving multiple neural system dysfunctions.

To understand the neurophysiological substrates and putative prognostics markers of ASD, dense array electroencephalography (EEG) studies using 128-channel offer a promising research approach that provides greater precision and accuracy in localizing the brain sources of EEG activity across 6239 voxels that are correlated directly to structures revealed by MRI. We propose that distinct patterns of brain electrical activity could be used to distinguish children with ASD from typically developing children (CTRL).

Therefore, our objective was to compare EEG spectral power, coherence and source connectivity of children with ASD to CTRL during resting (eyes open and eyes closed) condition.

Ninety nine Children with ASD, aged between 3-12 years diagnosed as per DSM-5 criteria and 51 age matched CTRL were recruited for the study. EEG datawere acquired using 128-channel HydroCel Geodesic Sensor Net (HCGSN). To create a 3D coordinate file of scalp electrode position, Geodesic photogrammetry system was used. For spectral power andcoherence,Fast Fourier Transform and Magnitude Squared Coherence were performed respectively in MATLAB. Further, source connectivitywas calculated and compared using the sLORETA software in seven frequency bands. Statistical comparison was done by using statistical non-parametric mapping (SnPM) test.

Increased **spectral power** during eyes closed condition in lower (theta, LA1) and higher (beta and gamma) frequency bands and during eyes open condition in lower (theta) frequency band were observed in children with ASD compared to CTRL. Decreased **coherence** during eyes closed condition in middle (LA1) and higher (gamma) frequency bands and during eyes open condition in lower and middle (delta, theta and LA1) frequency bands was observed in children with ASD compared to CTRL. Increased **source connectivity** in theta band between right posterior cingulate cortex and right primary somatosensory cortex was observed during eyes closed condition in children with ASD compared to CTRL.

To conclude, altered spectral power, coherence in specific spectral bands and dorsal attention network map could serve as biomarker to assess ASD. Further, enhanced cross talk in cingulate cortex, somatosensory cortex, Inferior parietal lobe and temporal lobe might lead to altered sensory, cognitive, social and emotional profile of children with ASD.

Cognitive behavior: AnEnvironmental interventional toolaffectingHuman Psychology

Dr.Archana Chaudhary,
Department of Biosciences, Faculty of Science, SGT University, Gurugram

The world is facing serious environmental problems related to, amongst others, global warming, urban air pollution, and scarcity of safe drinking water. These problems are, at least partly, rooted in human behavior, and can thus be managed by changing the relevant behaviors so as to promote environmental quality.The neglect of the environment and over emphasis of the organism was the major downfall of cognitive psychology. A number of research studies have attempted to explore the factors that contribute to the effectiveness of free-choice learning experiences in influencing the adoption of environmentally sustainable attitudes and practices. There are real world case studies, field experiments, and other evidence which provide insight in it and on concepts from social, cognitive and behavioral psychology. There are still lacuna in knowledge which indicates that current standard experimental procedures fail to view the organism and environment as complex and interacting systems.However, it puts behavior in the context of the religion, social, economic, institutional, and policy forces that shape it and emphasizes arenas where individual action makes a real difference to the natural environment. Theories such as Cognitive Continuum Theory (CCT), while still much in need of empirical assessment, offer a systems level treatment of organism-environment interaction that will be needed if psychology is to become a cumulative science and minimize future attribution errors. Cognitive behavior helps in establishing an important new links between environmental science and behavioral science. Cognitive behavior therapy may address issues about human behaviors that harm the environment along with arousing emotions, challenging beliefs and enhancing environmental conceptions. The physical sciences have reached substantial consensus on best practices for managing natural resources and ecologies, and the main obstacle is changing individual behavior and policy opinions. In this direction increasing pro-environmental behaviors such as conserving water in the form of ice stupas in Himalayan regions would bring massive public benefits.

MECHANISTIC STUDIES OF NEURO-DEGENERATIVE DISEASES

SPEAKERS:

1. **Dr.AmitNayak**, CIIMS, Nagpur
   Title: Peripheral biomarker panel for prognosis of acute ischemic stroke: translational challenges and approaches

2. **Dr. MadhuBabu**, University of Hyderabad
   Title: Mechanism of Tau and Fyn mediated Neurodegeneration in Alzheimer's Disease

3. **Dr. Prasad Tammineni**, University of Hyderabad
   Title: Crosstalk between Autophagy and Endo-lysosomal pathways in Alzheimer's Disease

4. **Dr. Dinesh Bhatia**, North East Hill University, Shillong
   Title: Study the cognitive behavioral changes in children with disability employing repetitive transcranial magnetic stimulation and Neurofeedback tools

5. **Dr. Harikrishna Reddy**, Central Unuversity of Punjab, Bathinda
   Title: Neuro-Behavioural and Histopathalogical facets after Brain Stroke

PERIPHERAL BIOMARKER PANEL FOR PROGNOSIS OF ACUTE ISCHEMIC STROKE: TRANSLATIONAL CHALLENGES AND APPROACHES

Dr. Amit R Nayak,

Central India Institute of Medical Sciences, Nagpur

Acute ischemic stroke (AIS) continued to be a leading cause of death & disability worldwide. The management of stroke patients is very poor in the absence of a specific therapeutic agent as well as a good diagnostic/prognostic marker. We evaluated a panel of biomarkers ITIH4, NSE-100, S-100BB, MMP-9 & cytokines (IL1A, IL1B, IL2, IL4, IL6, IL8, IL10, IL12, IL17A, INFy, TNFα, and GM-CSF), in the follow-up serum samples of the AIS patients collected at admission, 24hrs, 48hrs, 72hrs, 144hrs & discharged time, in case of an expired patient the last sample drawn was used as expired time sample. Serum ITIH4, NSE & S100bb & levels showed a distinct pattern of expression in the follow-up samples of AIS patients with improved and dependent/expired outcomes. ITIH4 also correlates ($p<0.05$) with NSE, S-100, and MMP-9. Among studied cytokines, only IL-2, IL-10, and TNF-α show differential expression in AIS patients with improved and dependent/expired outcomes & are in agreement with ITIH4. Similarly, in the animal study also, we observed differential expression of ITIH4 with the severity of ischemic damage after middle cerebral artery occlusion (MCAO) in the rat model & get normalized with improvement. In conclusion findings of our clinical as well as animal, studies suggest that serum level of ITIH4, NSE, & S-100 could be promising peripheral biomarkers for the prognosis of the AIS. Similarly, it also suggests that inflammatory cytokine IL-2, IL-10, and TNF-α may be used as a surrogate prognostic biomarker. However, need to work on the translational challenges and approaches work to bring this marker into actual practice.

Crosstalk between Autophagy and Endo-lysosomal pathways in Alzheimer's Disease

Dr. Prasad Tammineni,

Department of Animal Biology, University of Hyderabad, India

Autophagy plays a crucial role in cellular quality control by eliminating protein aggregates and damaged organelles, which is essential for maintaining neuronal homeostasis. Defective autophagy is associated with the pathogenesis of Alzheimer's disease (AD). In AD brains, autophagic vacuoles (AVs) accumulate massively within dystrophic neurites. This raises a fundamental question as to whether impaired autophagic clearance contributes to AD-associated autophagic stress. We recently revealed that AD neurons display defective retrograde transport and accumulation of amphisomes predominantly in axons and presynaptic terminals. Amyloid beta oligomers are enriched in axons and interact with dynein motors.This interaction interferes with the coupling of the dynein motor with its adaptor SNAPIN. Such deficits disrupt dynein-driven retrograde transport of amphisomes, thus trapping them in distal axons and impairing their degradation in the soma. Therefore, our study provides new mechanistic insights into AD-linked autophagic pathology, and builds a foundation for developing potential AD therapeutic strategies by rescuing retrograde transport of amphisomes.

Study the cognitive behaviouralchanges in children with disability employing repetitive transcranial magnetic stimulation and Neurofeedback tools

Dr. Dinesh Bhatia,

North Eastern Hill University, Shillong

Impairment of cognition is one of the biggest challenges for children with disability. Cognition could be defined as a mental process for acquiring knowledge and understanding the thoughts, experiences and sensory process. The cognition process encompasses domains such as attention, knowledge, working memory, judgment and logical reasoning. The aim of the present study was to evaluate the effective therapy for understanding different cognitive changes in children with disability. The results obtained suggest that r-TMS is a result oriented therapy for cognitive enhancement in the selected therapy groups. The cognitive brain training exercises were found to be the next most effective and cost-effective therapy for cognitive enhancement in brain-damaged children. These results could be employed for understanding the cognitive changes occurring in the children with CP for cognitive enhancement or other such population group.

Neuro-Behavioural and Histopathalogical facets after Brain Stroke

D. Harikrishna Reddy
Department of Pharmacology, Central University of Punjab, Bathinda.

Brain stroke still remains a second leading cause of death and disability worldwide. A vast number of studies are going on, to invent therapeutics for treatment of this devastating condition. But still no promising therapeutics was discovered except rtPA which is having many limitations in normal use. A keen understanding of what is going wrong after manifestation of cerebral stroke is anticipated. We observed neuro-behavioural, histopathologicalas well as brain volume changes in brain stroke animals and after using novel pharmacological therapeutics. Adult male wistar rats weighing 250±20g were used in the study. For neuro-behavioural defects sensorimotor functions like flexions, circling, paresis, walking pattern was assessed and histopathological observations and brain swelling for conformation. The results demonstrated striking improvement of neuro-behavioural, histological changes and brain swelling/volume changes after using novel pharmacological therapeutics.

COGNITIVE NEUROSCIENCE

SPEAKERS:

1. **Prof. Sukala Prasad,** BHU, Varanasi
   Title: Modulation of AMPA receptor trafficking/scaffolding proteins expression by *Bacopamonnieri*extract during cognitive impairment in mice

2. **Dr. SaravanaBabu**, JSS college of Pharmacy, Mysuru
   Title: Demystifying the link between sleep and cognition

3. **Dr. M. Varalakshmi**, School of Medical Sciences, University of Hyderabad
   Title: Protective function of Physical activity on Cognitive and Mental Health Outcomes; Activity and Wellbeing among older adults

4. **Dr. DebapriyaGarabadu**, Central University of Punjab, Bathinda
   Title: Abeta 42 down regulates adenosine – 2b receptor with impairment in mitochondrial and cholinergic function in memory-sensitive rat brain regions

5. **Dr. AkashGautam**, University of Hyderabad
   Title: The critical role of Arc/Arg3.1 in the object recognition memory

Modulation of AMPA receptor trafficking/scaffolding proteins expression by *Bacopamonnieri*extract during cognitive impairment in mice

Prof. S. Prasad, Ph.D

Biochemistry & Molecular Biology Laboratory, Banaras Hindu University, Varanasi

Cognitive function of the brain undergoes alterations due to several patho-physiological, environmental factors, etc. The most common factors that affect the cognition is aging, age- borne neurodegenerative diseases, metabolic disorders like diabetes mellitus type II (DMII) and scarce availability of oxygen to brain (hypoxia), etc. Our group has been working on above aspects using mice models mimicking above conditions and addressing underlying mechanisms of cognitive impairment and its amelioration by nootropic herbal neuromodulators such as bacosideA enriched specialized extract of *Bacopamonnieri*(BME). Several neurotransmitters signaling such as cholinergic, dopaminergic and glutamatergic pathways have been implicated in the establishment/impairment of learning and memory under various diseased conditions. To understand the molecular underpinnings of above, we have been investigating the expression patterns of glutamate signaling and its regulatory mechanisms. Glutamate, an excitatory amino acid (EAA), plays an important role in the consolidation of learning and memory via its signaling and homeostatic pathways. To successfully achieve learning and memory, the glutamate present in the synaptic cleft dynamically bind with its various receptors such as AMPA, NMDA and mGlu receptors present on the post synaptic density in the frontal cortex, hippocampus and other memory related areas of the brain. AMPA receptor-dependent pathway is an important pathway as its activation is gateway to for the functioning of other glutamate receptors for achieving memory. AMPA receptor population on the post synaptic density is not static rather they are under the dynamic control by means of alterations in the levels of its trafficking or scaffolding proteins, post-translational modifications or by its own genetic regulation. In the present talk, emphasis will be given on how the trafficking proteins such as SAP97, PSD 95, GRIP and PICK- 1 undergo alterations in their expression patterns, modulated by BME and altogether associated with the levels of AMPA receptors in the memory forming regions of the brain in cognitively compromised mice models of the aforesaid patho-physiological conditions and the relevance of the finding in the light of neuroprotective role of *Bacopamonnieri*extract will be discussed.

Demystifying the link between sleep and cognition

Dr. Saravana Babu Chidambaram, MPharm, PhD, FICS, FST, Associate Professor, Dept of Pharmacology, JSS College of Pharmacy, Mysore.

Sleep maintains the function of the entire body through homeostasis. Chronic sleep deprivation (CSD) is a prime health concern in the modern world. CSD has profound negative effects on brain vasculature at both the cellular and molecular levels, and that this is a major cause of cognitive dysfunction and early vascular ageing. Our lab is involved in studying the correlations among sleep deprivation (SD), brain vascular changes and ageing. We are extensively focussing attention to correlate the alterations in the major signalling molecules (BDNF, CREB, synaptic proteins - synapse-associated protein 97 (SAP97), synaptophysin, synapsin-1 and postsynaptic density protein-95 (PSD-95) expression) in SD and changes in brain vasculature, cognitive dysfunction and early ageing. The present connect SD-induced loss in the number of dendritic spines and their effects on alterations in synaptic plasticity, cognitive disabilities and early vascular ageing based on our laboratory investigation.

Protective function of Physical activity on Cognitive and Mental Health Outcomes; Activity and Wellbeing among older adults

Dr. M.Varalakshmi,
School of Medical Sciences, University of Hyderabad.

The world is greying fast with 10% of the world with aged population (65 years and above) (W.H.O). India is one of the rapidly ageing countries contributing to these global statistics. The estimated 104 million older adults aged 60 years and above (Census 2011) has been steadily increasing and is projected to 173 million by 2026 (UNPF). Physical inactivity is the fourth leading risk factor for mortality (WHO). About Eighteen percent of older adults experience mild cognitive impairment (MCI), and approximately 10%–15% of that dementia every year. Cognitive and functional health is crucial for independent living in ageing population. Promoting brain health and functional independence in ageing adults is a public health concern. Physical activity improves functioning, delays the onset of frailty and preserves independent living. Regular physical exercise is a cost effective lifestyle strategy that shows positive mental health outcomes besides physical benefits, determining brain and cognitive benefits. Pattern of exercise intervention remains difficult because of individual differences in tolerance, differences in risk factors, variation in health, attitudes of adherence. Study to understand the social and mental health among older adults, majority of the older women (82.5%), and men (70%) reported feeling insecure and 27% of them often felt isolated and 62% of them felt neglected and 29% of them were feeling lonely most of the time. Thirty six percent of them were with MCI and there is strong positive association between perceived happiness with physical activity and cognitive functions in older adults (Varalakshmi 2019).

Evidence determines the effectiveness of exercise program and the associated factors for functional, cognitive and mental health (unpublished data from the India Ageing Study pilot program 2019) examined the outcome of programmed exercise intervention on functional health and mental health outcome among adults (≥60 years), shows significant enhancement in the four measures for functional health, fall risk reduction (from60% to 40% (men) and 68% to 59% (women)) and positive association of exercise intervention on social engagement and mental health.

Older adults (92%) from the specific study agreed that the exercise program engaged them more socially and developed a sense of competence and self-respect, satisfaction with life, which are essential evaluative affective components of mental wellbeing. The findings are consistent with a study showing improvements in both emotional and eudemonic well-being dimensions with physical activity programs (Mack et al., 2017; AntonellaDelleFave et al, 2018). Conclusion: Multimodal interventions like combined physical activity, stimulating mental and social activities are protective for functional health, prevent or delay age associated diseases like depression and dementia.

Amyloid beta 42 down regulates adenosine-2b receptor with impairment in mitochondrial and cholinergic function in memory-sensitive mouse brain regions

Dr. Debapriya Garabadu,

Department of Pharmacology, Central University of Punjab, Bathinda.

Mitochondrial dysfunction is considered as one of the cardinal feature of Alzheimer's disease (AD) in addition to reduction in cholinergic activity and memory impairment. Adenosinergic 2b (A2b) receptor plays significant role in several physiological processes including oligodendrogenesis in mammalian brain. However, there is lack of information on the role of A2b receptor in the pathophysiology of amyloid beta (Aβ) aggregation. Therefore, the effect of Aβ 42 on the level of expression of A2b receptor was investigated in discrete memory-sensitive mouse brain regions. Aβ 42 was injected intracerebroventricularly to healthy male mouse to induce AD-like behavioral manifestations on Day-1 (D-1) of the experimental protocol. The animals were subjected to the Morris water maze (MWM) test on D-14 to D-18. On D-18, the animals were subjected to Y-maze test after 30 min lag to the MWM paradigm. Aβ 42 significantly attenuated the spatial working memory in MWM and Y-maze tests.In addition, Aβ 42 significantly increased cholinergic dysfunction in terms of decrease in the activity of ChAT and ACh level and increase in the AChE activity in the hippocampus, pre-frontal cortex and amygdala of AD-like animals. Further, there was a significant increase in the extent of apoptosis in the selected mouse brain regions. Moreover, Aβ 42 caused a substantial reduction in the mitochondrial function, integrity and bioenergetics in all the mouse brain regions. Furthermore, there was a significant decrease in the level of expression of A2b receptors in the selected brain regions of the rodents. Hence, it can be assumed that drugs facilitating A2b receptor activity could be considered as potential therapeutic option in the management of AD.

The critical role of Arc/Arg3.1 in the object recognition memory

Dr. Akash Gautam,
Centre for Neural and Cognitive Sciences, University of Hyderabad.

Background: The activity-regulated cytoskeletal (*Arc)* gene, also known as Arg3.1, is an immediate-early gene and known to be involved in all the forms of synaptic plasticity, i.e., long-term potentiation (LTP), long-term depression (LTD), and homeostatic plasticity. Expression, localization, and stability of the Arc transcript is highly regulated in response to an increase in synaptic activity in a range of behavioral and paradigms learning.

Objective: Many studies in the last five years have shown that the presence of Arc mRNA primes mGluR-dependent LTD in previously activated synapses upon re-exposure to the same environment. These studies suggest that the memory could be affected by the availability of Arc at the re-exposure time. Therefore, to confirm this, we investigated the changes in the temporal order memory and object recognition memory after the re-exposure to an environment in male mice.

Methodology: The object recognition memory, a type of visual-spatial memory, is commonly assessed using the object recognition test (ORT) in rodents. The ORTapparatus consists of an open-field maze and a few objects in the maze's desired locations. When rodents are exposed to a novel and a familiar object, they tend to spend a larger timeexploring the novel one. Thus, the object recognition memory is analyzed by measuringthe percentage of object exploration time. The ORT can also test short-term or long-term memoryby changing the retention interval, i.e., the duration between the test and familiarization phases. We studied Arc's involvement in these changes by inhibiting Arc protein expression via stereotaxic infusions of Arc antisense oligodeoxynucleotides in the hippocampus of mice.

Results: We found that both temporal order and object recognition memories are dependent on the inter-familiarization phase interval. Strikingly, we also found that Arc accelerated the memory decay of an object when mice were re-exposed to the environment without that object.

SYMPOSIUM

DIFFERENT SHADES OF HUNTINGTON'S DISEASE

ORGANISED BY:

PRAGYA KOMAL, ASSISTANT PROFESSOR, BITS-PILANI, HYDERABAD

SPEAKERS:

1. **Dr.Puneet Kumar**, Central University of Punjab, Bathinda
   Title: Chemicals induced animal models: insight into the pathogenesis of Huntington's disease

2. **Dr.PragyaKomal**, BITS-PILANI, Hyderabad
   Title: Vitamin D intake enhances Vitamin D receptor expression in the striatum and rescues memory and motor dysfunction in mouse model Huntington's disease

3. **Dr. Ana Christina Rego**, University of Coimbre, Portugal
   Title: Strategies of rescuing mitochondrial dysfunction in Huntington's disease

4. **Dr. David Stellwagen**, McGill University, Canada
   Title: Tumour necrosis factor-alpha alters the function of striatal synapses in YAC128 mouse model of Huntington's disease

Chemicals induced animal models: insight into the pathogenesis of Huntington's disease

Dr. Puneet Bansal, Associate Professor,

Department of Pharmacology, School of Health Sciences, Central University of Punjab, Bathinda

Huntington's disease (HD) is a hyperkinetic, autosomal neurodegenerative disease characterized by chorea, gait abnormalities, resting tremors,and developed due to abnormal repeat of Cytosine Adenine Guanine (CAG)trinucleotide in the huntingtin (Htt)gene. Besides this, oxidative stress, excitotoxicity, mitochondrial dysfunction, and neuroinflammation play an important role in HD's pathogenesis. Despitemultiple experimental efforts, no treatment is available yet to completely halt or delay the disease progression. Hence, pathophysiological understanding of the mechanism involved in disease progression is the key to develop potent therapeutic intervention. Animal models are the most reliable tool to understand the disease's pathophysiological features and allow rigorous hypothesis testing. The animal model is ideal if it mimics all the pathophysiological features of the disease; excitotoxicity, mitochondrial dysfunction, and oxidative stressare the pathological features of HD. Chemical models offer more authentic and highly reliable results with the least mortality rate. Chemical models mimic human HD by closely reflecting most of the pathophysiological features, such as 3- nitropropionic acid-induced mitochondrial dysfunction, quinolinic acid induced excitotoxicity, etc., show good predictive validity. But every model has its advantages and disadvantages based on the pathological features that the model mimics. So, the selection of an accurate model gives the best results for any therapeutic intervention. Here we are going to discuss the chemical induces models of HD along with important factors for selection.

Vitamin D intake enhances Vitamin D receptor expression in the striatum and rescues memory and motor dysfunction in mouse model Huntington's disease.

Dr. Pragya Komal, Assistant Professor,

BITS-Pilani, Hyderabad, India

A coordinated neuronal network between cortex and the basal ganglia is required for normal motor function, which gets severely impaired in Huntington's disease (HD). In particular, the selective loss of medium spiny neurons in the striatum is considered as a prime brain region responsible for movement disability observed in HD. In our study we show that Vitamin D3 (Cholecalciferol) intake significantly rescued striatal functions like motor activity, locomotion and spatial memory in 3-nitropropionic acid induced (3-NP) mouse model of Huntington's disease.A significant enhancement in the expression of key neurotrophic factors like brain-derived neurotrophic factor (BDNF) and nerve-growth factor (NGF) together with increased Vitamin D receptor (VDR) mRNA expression was observed from the striatal brain tissue extracted on 30th day between HD animals and Vitamin D supplemented HD animals. Altogether, our finding suggests that VD mediated downstream neuroprotective pathway possibly involves a cross-talk between VDR and neurotrophic family of receptors.

Strategies of rescuing mitochondrial dysfunction in Huntington's disease

Dr. Ana Cristina Rego, Professor

University of Coimbra (CNC-UC), Portugal

Huntington's disease (HD) is a motor neurodegenerative disorder caused by an abnormal expansion of polyglutamines in the huntingtin protein (HTT), primarily affecting the striatum and later the cortex. Several pathological mechanisms have been described in HD, including organelle dysfunction such as mitochondria, leading to energy depletion and cell death. Mitochondria also participate in intracellular calcium homeostasis and cell survival by maintaining a close interaction with the endoplasmic reticulum (ER) and by keeping a dynamic structure, adapting into fusion and fission processes and the transport along neurites. Thus, modulating the levels and activity of pro-survival mitochondrial proteins such as sirtuin 3 and activating proteins involved in ER-mitochondria interaction can constitute beneficial strategies in HD. Being a member of class III lysine deacetylases, mitochondrial sirtuin 3 is a major regulator of organelle acetylome. Here we show that sirtuin 3 is neuroprotective in HD by enhancing mitochondrial function and balanced dynamics, favoring mitochondrial elongation and improving mitochondrial neurite transport. Furthermore, because there is a lack of neuroprotective strategies that benefit HD patients, we tested the effect of pridopidine, a selective agonist of sigma-1 receptor (S1R) that is currently being used in phase III clinical trial for HD. S1R is a chaperone protein localized in mitochondria-associated ER membranes, which activation enhances mitochondria-ER tethering and improves mitochondrial function, elongation and motility in human and mouse HD models. Data show that ameliorating mitochondrial activity is beneficial in cell and animal models, favoring this as a relevant neuroprotective strategy in HD.

Tumour necrosis factor-αlpha alters the function of striatal synapses in YAC128 mouse model of Huntington's disease

Dr. David Stellwagen, Professor,

McGill University, Canada

Huntington's disease (HD) is an incurable neurodegenerative disease caused by an autosomal dominant mutation in the huntingtin gene, resulting from a variable expansion of a CAG repeat encoding polyglutamine. Despite ubiquitous expression of the mutant huntingtin protein (mHTT), neurodegenerationfirst occurs in the striatum, accompanied by an elevation in inflammatory cytokines. Using the pre-symptomatic YAC128 HD model mouse, we have observed an increase in excitatory synaptic strength specifically on direct pathway medium spiny neurons, accompanied by a decrease in inhibitory synaptic strength. Both of these changes are dependent on the pro-inflammatory cytokine tumor necrosis factor alpha (TNF) signaling through the TNFR1 receptor. The increase in excitability may potentiate excitotoxicity during the progress of HD.

SYMPOSIUM

MYELOID-LYMPHOID ACTIVITY TO UNDERSTAND BRAIN INJURY

ORGANISED BY: Dr. KUMAR VAIBHAV, DEPARTMENT OF NEUROSURGERY, MEDICAL COLLEGE OF GEORGIA, AUGUSTA UNIVERSITY, USA

SPEAKERS:

1. **Prof. Krishnan M Dhandapani**, Augusta Unievrsity, USA
   Title: Immunometabolicdysregulation initiates progressive neurodegeneration after brain injury

2. **Dr.TauheedIshrat**, University of Tennessee, Memphis, USA
   Title: TXNIP: a Potential Therapeutic Target for Brain Aging and Alzheimer's Disease

3. **Prof. BabakBaban**, Augusta University, USA
   Title: Innate Lymphoid Cells (ILCs) and Brain Injury

4. **Dr.PallaviShrivastava,**Universidad Católica de Santa María, Arequipa, Peru
   Title: Mystery of Fate of Microglia: Progenitor to Adult microglia priming in CNS disorders

Immunometabolic dysregulation initiates progressive neurodegeneration after brain injury

Prof. Krishnan M Dhandapani,

Dept. of Neurosurgery, Medical College of Georgia, Augusta University, USA

Epidemiological studies suggest a single severe traumatic brain injury (TBI) initiates progressive neurodegeneration and produces poor long-term outcomes via poorly defined molecular and cellular mechanisms. Chronic immune activation correlates with white matter loss and neurological deterioration, yet, causative mechanisms linking these processes require elucidation. In this study, we tested the hypothesis that acute infiltration of pro-inflammatory macrophages initiates the generation of autoreactive T-cells, which in turn, mediate progressive white matter loss after TBI. Genomic profiling of brain tissue after murine controlled cortical impact revealed upregulation of genes associated with myeloid cell activation, antigen presentation, and epigenetic regulation whereas genes associated with axon/dendrite structure and neural connectivity were downregulated. Myelin-laden macrophages were observed within the cerebrospinal fluid of severe TBI patients while CD45hi, MHC-II+ macrophages were identified as the major antigen presenting cells (APCs) within the central nervous system after TBI. APCs stimulated with myelin fragments ex vivo or isolated from the peri-contusional cortex after TBI increased T-helper (TH) cell proliferation and enhanced pro-inflammatory TH1 and TH17 polarization. Myeloid-selective activation of the metabolic regulator, 5'-adenosine monophosphate-activated protein kinase (AMPK), suppressed the generation of myelin auto-reactive effector T-cells, restored the PD-L1/PD-1 immune checkpoint, and reduced chronic white matter loss after TBI. Together, our studies identify that acute immunometabolic dysfunction drives the myeloid-lymphoid transition after TBI, suggesting targeted intervention during the early stage of injury may proactively limit progressive neurodegeneration after brain injury.

TXNIP: a Potential Therapeutic Target for Brain Aging and Alzheimer's Disease

Dr. Tauheed Ishrat, Associate Professor,

Department of Anatomy & Neurobiology, University of Tennessee, USA

Aging is the greatest risk factor for dementia and Alzheimer's disease (AD). Recent findings indicate that thioredoxin interacting protein (TXNIP), an inducible protein involved in oxidative stress and aging, is essential for NOD-like receptor pyrin domain containing-3 (NLRP3)-inflammasome activation. The NLRP3-inflammasome essentially connects "inflammaging" to senile cognitive decline. According to our preclinical studies, cerebral TXNIP was significantly upregulated in aged animals, associated with the NLRP3-inflammasome over-activity in both sexes, and closely linked to klotho depletion in males. TXNIP knock-out reversed age-related NLRP3-hyperactivity and enhanced thioredoxin (TRX) levels in aged brains. Further, pharmacological TXNIP inhibition replicated the TXNIP/NLRP3-inflammasome downregulation in aged animals. These alterations concurred with substantial improvements in both cognitive and sensorimotor abilities. Moreover, our immunostaining shows a significant increase of TXNIP/NLRP3-inflammasome activity in transgenic 5XFAD mice and AD human postmortem hippocampal specimens, supportive of potential mechanistic links between TXNIP and AD. Together, these findings unravel new information about upstream pathways in age-associated neuroinflammation.

Innate Lymphoid Cells (ILCs) and Brain Injury

Prof. Babak Baban,

Dept. of Oral Biology and Diagnostic Sciences, Augusta University, Augusta, GA, USA

Since their discovery about a decade ago, innate lymphoid cells (ILCs), which are part of the innate immune system, have been studied intensively. Due to their unique phenotype ILCs are able to respond quickly to a variety of stimuli in their immediate surroundings. Although, in the last years, the phenotype and role of the ILC subsets in different organs have been intensively investigated, however, very little is known about the presence of ILCs in the central nervous system (CNS) and specifically their potential role in brain injuries. We and others have shown evidence for their presence in the brain and their status in steady state and during neuroinflammation. Their role and potential function as neuroprotective, gatekeeper and regulatory agents will be discussed.

Mystery of Fate of Microglia: Progenitor to Adult microglia priming in CNS disorders

Dr. Pallavi Shrivastava, Research Investigator,

Department of Molecular and Biochemical Pharmacology, Universidad Católica de Santa María, Arequipa, Peru

Microglia are immune resident cells in CNS, that responds rapidly to pathological conditions and also contribute to synaptic pruning and homeostasis in the healthy brains. The origin of Microglia in brain remains obscure. There are some theories that postulate the myeloid progenitors origin of microglia recruited in CNS in early prenatal period. The others propose the resident microglia are independent of myeloid lineage and functionally different from myeloid progenitor cells. In a neuroinflammatory event, microglia responds to injury and self-proliferates in CNS developing gliosis. The BBB disruption may cause circulating monocytes invade the CNS parenchyma where they further differentiate into macrophages or inflammatory dendritic cells. It is difficult to distinguish between microglial populations from myeloid cells phenotypically but few functional characteristics features of microglia make them distinct form others. Here, we will discuss the ontogeny of microglia with current means to distinguish between these populations, and recent advances in functional characterization of microglia from myeloid cells.

MOLECULAR ASPECTS OF BRAIN TUMOURS AND NEURO-INFECTIONS

SPEAKERS:

1. **Dr.Rajpal Singh Kashyap**, CIIMS, Nagpur
   Title: IL 10 importance in Neuro-infections

2. **Dr. Y.B.V.K. Chandrasekhar**, KIIMS, Hyderabad
   Title: Role of Fluorescent dyes in Neurosurgery practice at a tertiary care centre

3. **Dr. M. Janaki**, Kurnool Medical College
   Title: Neuro-infections

4. **Dr.Nandakumar DN**, NIMHANS, Bengaluru
   Title: Advances in role of glutamate receptors and their crosstalk in growth and redox status of glioblastoma

5. **Dr.Vanisree**, Madras University, Chennai
   Title: Possible biomass contributors in glioma

6. **Dr.TruptiTrivedi**, GCRI, Ahmedabad
   Title: Dissecting Molecular Profiling for Management of Glioblastoma Patients

IL 10 importance in Neuroinfections

Dr. Rajpal Singh Kashyap,

Central India Institute of Medical Sciences, Nagpur

The prevalence of Neuroinfections is very high worldwide, especially in developing and under developed countries. Inflammation and cytokines pattern produced by immune cells play an important role in prognosis and treatment of Neuroinfections. In our previous studies of Tuberculous meningitis and stroke, we have shown the elevation of pro-inflammatory cytokines in these conditions at the time of admission or prior to treatment. However with the treatment we have shown the suppression of pro-inflammatory cytokines and interestingly elevated levels of anti-inflammatory cytokines, especially IL-10 have been observed. IL-10 is an anti-inflammatory cytokine and is known to be the main down regulator of the deleterious effect of pro-inflammatory cytokines. It is well established that IL-10 has immuno-modulatory activity in both physiological and pathological processes. In the present paper we will discuss the importance of IL-10 in Neuroinfections and neurological disorders; this could help us to understand the mechanism of IL-10 during these clinical conditions and also to design IL-10as a new molecule for tracking inflammation.

Role of Fluorescent dyes in Neurosurgery practice at a Tertiary care centre

Dr. Y.B.V.K. Chandrasekhar, Dr. ManasPanigrahi

Department of Neurosurgery, Krishna Institute of Medical Sciences (KIMS), Secunderabad.

Different types of Fluorescent Dyes are used in Neurosurgical proceduresFluorescein sodium **(FL)**, a fluorophore that has been well known in ophthalmic surgery for almost five decades, has been increasingly used and researched in neuro-oncologic surgery since the late **1990s**.

Materials and Methods:

Fluorescein sodium **(FL)**,Indocyanine green (**ICG)** and Aminolevulenic Acid (**ALA)** are routinely used in neurosurgical procedures.This study was performed at KIMS HOSPITALS from September 2017 to Nov 2020. Ethics committee approval has been obtained.

Results:

We routinely use Fluorescein sodium **(FL)** in most of the Brain tumor patients. It has to be given at the time of induction of Anesthesia. By the time the craniotomy is performed the tumor takes up the Fluorescein sodium **(FL)** as the blood brain barrier is breached in these cases. If required during the neurosurgical procedure

we can change the optic filter in the microscope and Maximum safe resection can be performed. Indocyanine green **(ICG)** is used in vascular neurosurgery to delineate vascular anatomy after Aneurysmal clipping

Conclusion:

Fluorescent dyes are very useful in Neurosurgical procedures and will help in achieving a better surgical out come.

Advances in role of glutamate receptors and their crosstalk in growth and redox status of glioblastoma

Dr.Nandakumar DN, Professor

Department of Neurochemistry, NIMHANS, Bengaluru.

Glioblastoma is the most aggressive and deadliest primary brain tumor. The overall survival rate is 18 months. Glioblastoma create tumour microenvironment and secrete factors which through intracellular signaling contribute to tumor growth. We focused on understanding excitotoxic glutamate milieu in the growthand redox status of glioblastoma and downstream signaling. Further we investigated cross-talk between NMDARs with AMPARs. We conclude that the activation of subtypes of glutamate receptors mediate growth of glioblastoma by increased proliferation and invasion through enhances activity of MMP-2 and its expression, helps in the maintenance of reduced state of glioma cells through increased GSH level and GR activity and provide protection within glioma cells against intracellular oxidants.

Dissecting Molecular Profiling for Management of GlioblastomaPatients

Dr. Trupti Trivedi,

Department of Cancer Biology, Gujarat Cancer & Research Institute, Ahmedabad, Gujarat, India.

Worldwide, gliomas are the most common malignant primary brain tumors of central nervous system (CNS). They are diverse group of tumors and are essentially incurable with grim prognosis, particularly grade IV glioma tumors. Glioblastoma multiform (GBM, WHO grade IV) is the most frequent biologically aggressive tumors of the adult brains, accounting for approximately >50% of glioma. Patients with GBM have universally poor prognosis due to strong treatment resistance and inevitable recurrence. Also, the recent 2016 WHO classification of CNS, has subdivided GBM into IDH mutant and IDH wild types tumors because IDH mutations are stable markers to classify gliomas in progression and prognosis. However, tremendous heterogeneity in clinical outcome has been noted within IDH mutant and wild type glioma tumors, indicating that further molecular distinguish based on IDH mutation status is still needed to improve clinical outcome. The current study we sought to build a high-efficiency prediction molecular profiling from the IDH mutant and IDH wild type of GBM tumors which could also be useful as targeted therapy.We studied panel of nine gene expression(SERPINE1, CD44, ATF3, THBS1, VEGFA, FABP5, FOSL2, TAGLN2, TGFBI) profiling using real-time RT-PCR from glioma patients. The incidence of expression of genes was noted in low grade glioma (LGG) and high grade glioma (HGG) tumors and distinguished their expressions between IDH wild and mutant type of tumors. We found significant up-regulation of CD44 ($p=0.012$), TGFβ ($p=0.015$), ATF3 ($p=0.0020$) in HGG tumors compared to LGG.

Further, patients with HGG with IDH wild type tumors and showed up-regulation of either TGF (p=0.016), VEGF (p=0.002), AFT3 (p=0.001) or CD44 (p=0.003) gene expression, the incidence of relapse was noted significantly high in patients treated with only surgery than surgery followed by radiotherapy and or radioand chemotherapy. None of the marker showed such significant difference for HGG with IDH mutant tumors. In Multivariate Cox proportional hazard model for relapse-free survival (RFS),upregulation of CD44 gene emerged as independent significant risk predictor for reduced relapsed for patients with HGG IDH wild type tumors, (HR=0.016, p=0.005). We found independent risk predictors for patients having low and high grade of tumors with respect to IDH mutational status using Multivariate Cox proportional hazard model. Thus, overall our study elucidated molecular panel based on IDH mutationalstatus of GBM tumors for better patient management and might be useful for personalized treatment strategies.

THERAPEUTIC APPROACHES OR INTERVENTIONS FOR RECOVERY AND NEURO-REGENERATION

SPEAKERS:

1. **Dr.SumanaChakravarty,** IICT, Hyderabad

   Title: Sex difference in zebrafish brain proteome profile indicates the critical role of H3K9me3 in recovery from acute hypoxia

2. **Prof. M. Ramanathan,** PSJ College of Pharmacy, Coimbatore
   Title: TribulusTerrestris Extract in the treatment of Neuropathic pain-preclinical studies

3. **Dr.Sudip Paul,** NEHU, Shillong
   Title: Efficacy of gaming therapy for oral motor and cranial nerve disorders

4. **Dr. Ravish,** NIMHANS, Bengaluru
   Title: Molecular Signature of the Immune Response to Yoga Therapy in Stress- related Chronic Disease Conditions: An Insight

5. **Prof. RashmiAmbasta,** Delhi University, Delhi
   Title: Therapeutic role of bone marrow derived mononuclear cells in diabetic neuropathy

6. **Dr. Shanti N. Dessai,** Goa University, Goa
   Title: Frontiers and Tools to Study Developmental Neurogenesis

7. **Dr.Omkumar RV,** RGCB, Kerala
   Title: Multi-target directed drugs for neurological disorders

Sex difference in zebrafish brain proteome profile indicates the critical role of H3K9me3 in recovery from acute hypoxia

Dr. Sumana Chakravarty,

Applied Biology, CSIR-Indian Institute of Chemical Technology, Hyderabad

Insight into the molecular basis of sex differences in neural response to acute hypoxic insult has reflective implications for the successful prevention and treatment of ischemic stroke. Global hypoxic-ischemic induced neural damage has been studied recently under the well-controlled, non-invasive, reproducible conditions using zebrafish model. Moreover, our earlier report on sex difference in global acute hypoxia induced neural damage and recovery in zebrafish prompted us for comprehensive study on the mechanisms underlying the recovery. Our approach for studying quantitative changes in brain proteome upon hypoxia insult following recovery was undertaken using iTRAQ-based LC-MS/MS approach. revealed that Core expression analysis by Ingenuity Pathway analysis (IPA) showed a distinct sex difference in the disease function heat map. On validation, translational upregulation of H3K9me3 in male led us to elucidate the mechanism of recovery by confirming transcriptional targets through ChIP-qPCR. The upregulation of H3K9me3 level in male at 4 hr post-hypoxia appears to affect the early neurogenic markers nestin, klf4 and sox2, which might explain the late recovery in male, compared to female. Acute hypoxia-induced sex-specific comparison of brain proteome led us to reveal many differentially expressed proteins, which can be taken further for the development of novel targets for better therapeutic strategy.

Standardized *Tribulusterrestris* extract in the treatment of Neuropathic pain- Preclinical studies

Dr. M. Ramanathan, Professor of Pharmacology,

PSG College of Pharmacy, Coimbatore.

Neuropathic pain is one the conditions where the nerve damage leads to hyperalgesic response. The major pathological reason includes diabetes, constriction injury, nerve degeneration; loss of myelin sheath. Chronic constriction injury (CCI) model is used in preclinical testing to evaluate drug's efficacy in controlling nerve injury related neuropathic pain. In CCI model both C and A fibers will induce and conduct pain perception. Further the pain is attributed to inflammation and immune stimulus. In our earlier studies we have reported neuropathic pain control of *Tribulusterrestris* along with regulation of inflammatory mediators in diabetic condition. In the present research work we have evaluated the analgesic and anti-inflammatory activity of standardized *Tribulusterrestris* extract (TTE) inCCI model. The analgesic response was measured in mechanical hyperalgesic and chemical induced models. Inflammatory mediators were measured through ELISA. TTE was administered (50 and 100mg/kg) once daily until the study period through oral route. Pregabalin (10mg/kg) was used as reference drug. The results have shown that TTE exhibited hyperalgesic response in Randall Selitto and von Frey filament tests in CCI rats. These behavioral data has been supported with improved sciatic nerve conduction velocity and sciatic functional index analysis. TTE significantly attenuated the elevated IL-1β, IL-6 and TNF-α level and restored the tissue morphology in the sciatic nerve caused due to nerve injury. It can be concluded that, TTE exhibited analgesic response in CCI model it is attributed due to neurogenesis and prevention of inflammatory mediator release.

Efficacy of Gaming Therapy for Oral Motor and cranial nerve disorders

Dr. Sudip Paul,

Department of Biomedical Engineering, North-Eastern Hill University, Shillong

Cranial nerve dysfunction is one of the major causes of oral motor disorder leading to non-speech oral disorder and speech disability. Motor and sensory deficits are caused due to various reasons that can be either signal transmission and reception issues or due to a lack of muscle strength to perform the required action. It can restrict our daily living and day to day activities. All these factors degrade our quality of living. Gaming therapy is an effective and attractive way to bring the disabled into astandard way of living to survive comfortably.

Gaming therapy is becoming popular nowadays because of various reasons like it reduces the burden on clinics and speech language pathologists and is always ready to use as many times a person wants to practice. Overall, these therapeutic practice changes are good and help strengthen oral musculature and bring everyday speech-language skills among oral motor disabled children.

This technique reduces many hurdles, whatever is faced by professionals while providing conventional therapy to a child. This innovative technique is attractive and eye-catching, along with greater efficacy and impact. Some therapeutic activities have shown much better performance than the current techniques followed by the speech-language pathologist.

Molecular Signature of the Immune Response to Yoga Therapy in Stress-related Chronic Disease Conditions: An Insight

Dr. Ravish,

NIMHANS, Bengaluru

The world Health Organization defines health as complete well- being in terms of physical, mental and social, and not merely the absence of disease. To attain this, individual should adapt and self- mange the social, physical and emotional challenges of life. Exposure to chronic stress due to urbanization, work stress, nuclear family, pollution, unhealthy food habits, lifestyle, accidental death in the family, and natural calamities are the triggering factors, leading to hormonal imbalance and inflammatio in the tissue. The relationship between stress and illness is complex; all chronic illnesses such as cardiovascular disease and asthma have their root in chronic stress attributed by inflammation.Inrecent times, yoga therapy has emerged as an important complementary alternative medicine for many human diseases. Yoga therapy has a positive impact on mind and body; it acts by incorporating appropriate breathing techniques and mindfulness to attain conscious direction of our awareness of the present moment by meditation, which helps achieve harmony between the body and mind. Studies have also demonstrated the important regulatory effects of yoga therapy on brain structure and functions. Despite these advances, the cellular and molecular mechanisms by which yoga therapy renders its beneficial effects are inadequately known. A growing body of evidence suggests that yoga therapy has immunomodulatory effects. However, the precise mechanistic basis has not been addressed empirically. In this review, we have attempted to highlight the effect of yoga therapy on immune system functioning with an aim to identify important immunological signatures that index the effect of yoga therapy. Toward this, we have summarized the available scientific evidence showing positive impacts of yoga therapy. Finally,we have emphasized the efficacy of yoga in improving physical and mental well- being. Yoga has been a part of Indian culture and tradition for long; now, the time has come to scientifically validate this and implement this as an alternative treatment method for stress- related chronicdisease

Therapeutic role of bone marrow derived mononuclear cells in diabetic neuropathy

Prof. Rashmi K. Ambasta,

Department of Biotechnology,

Delhi Technological University, Delhi

Diabetes is a complicated disease, leading to several organ damage including pancreas, kidney, heart muscle and brain. Therapies of diabetes using bone marrow mononuclear cell is an attractive way to treat diabetes.The aim of this work is to treat organ damage in diabetes including brain by transplanting bone marrow mononuclear cells in mice and identify protein markers for diabetes therapy.

The diabetic mice were generated by streptozotocin injection and later organ damage was studied histopathologically and markers was studied by immunofluorescence, Western blot and bioinformaticanalysis.The diabetic mice demonstrate organ damage at the level of pancreas, kidney, heart muscle and brain which was recovered by bone marrow transplantation. The markers playing critical role in organ damage and regeneration includes insulin, PECAM, VEGF, Tie1, CDK. The regeneration ability of organ damage in diabetic mice was improved further by curcumin administration. Several other biomolecules were compared bioinformatically to identify the common markers targeted in diabetes.

Therefore, it may be concluded that diabetes organ damage including brain was recovered by bone marrow transplantation. Several common and distinct protein markers were identified for therapeutic purpose by natural molecule administration as well.

Frontiers and Tools to Study Developmental Neurogenesis

Dr. Shanti N. Dessai, Assistant Professor,

Department of Zoology, Goa University, Goa

Developmental Neurogenesis involves generation of neurons from early embryonic development until early postnatal stages, with only a few neurogenic zones that remain active in the adult representing adult neurogenesis. Early embryonic neurogenesis is evidenced by events such as proliferation, differentiation, migration, and spatial arrangement of progenitor cells that directs architecture of developing nervous system. These events involve intrinsic determinant as well as extrinsic signals that influence progenitor cells maintaining temporal and spatial boundaries during developmental neurogenesis. In this review an attempts is being made to put forth some of the recent understandings and methodological tools for studying novel insights of signaling that occur during developmental neurogenesis. An attempt is made to focus on some of the important molecules involved in signaling pathway crosstalks of developmental neurogenesis along with various upcoming methodological tools with *in vitro* models to carryout frontier research in the field of developmental neurogenesis to recreate essential insights and opportunities with its applications in biomedical and biotechnological practice.

SYMPOSIUM

BILINGUALISM AND COGNITION: RECENT DEVELOPMENTS

ORGANISED BY: RAMESH KUMAR,

CENTER FOR NEURAL AND COGNITIVE SCIENCES, University of Hyderabad, Hyderabad.

SPEAKERS:

1. **SuvarnaAlladi,** NIMHANS, Bengaluru
   Title: Bilingualism and dementia: Implications for the concept of cognitive resilience

2. **BidishaSom,** Indian Institute of Technology, Guwahati
   Title: Investigating complexity in 'the bilingual experience' and its role in adaptive control

3. **Veeky Baths,** BITS, Goa Campus
   Title: Alzheimer's Detection Using Speech Analysis

4. **Ramesh Kumar Mishra,** University of Hyderabad
   Title: Bilingual language control and interaction in the social world

5. **Niels O. Schiller,** Leiden University Centre for Linguistics(LUCL) and Leiden Institute for brain and cognition (LIBC), Netherlands
   Title: What grammatical characteristics of words may tell us about our mind and cognition: Cross-linguistic evidence on the selection of lexico-syntactic features

Bilingualism and dementia: Implications for the concept of cognitive resilience

Suvarna Alladi, NIMHANS, Bangalore, India

Studies have shown that bilingualism affects attentional and cognitive control across all ages. In older ages, this results in enhancing cognitive resilience and delaying onset of dementia. However, factors like socio-economic status, fluid intelligence, education and immigrant status are known to affect the association between bilingualism and cognitive mechanisms. Our previous research has shown that bilingualism is related to cognitive reserve capacity/ resilience independent of literacy, education and immigration. However, the mechanisms underlying this have not been explored in the Indian context. Cognitive reserve is related to lifelong experiences, that could begin in early life. Here we present data showing the relationship between executive functions, cognitive control and bilingualism in relation to bilingual education among children in India using behavioral data. Their attentional and executive control mechanisms were explored and how various socio-demographic factors would affect the results was studied. At the other end of the spectrum, behavioral and structural MRI data were collected from elderly population with and without dementia, in an attempt to study cortical thickness as a marker of neuroplasticity. In the talk, we discuss the findings with respect to how bilingual speakers influence the organizing of neural, cognitive and linguistic systems across different ages and disease states, along with challenges in addressing the relationship between bilingualism and dementia, especially in the Indian context.

Investigating complexity in 'the bilingual experience' and its role in adaptive control

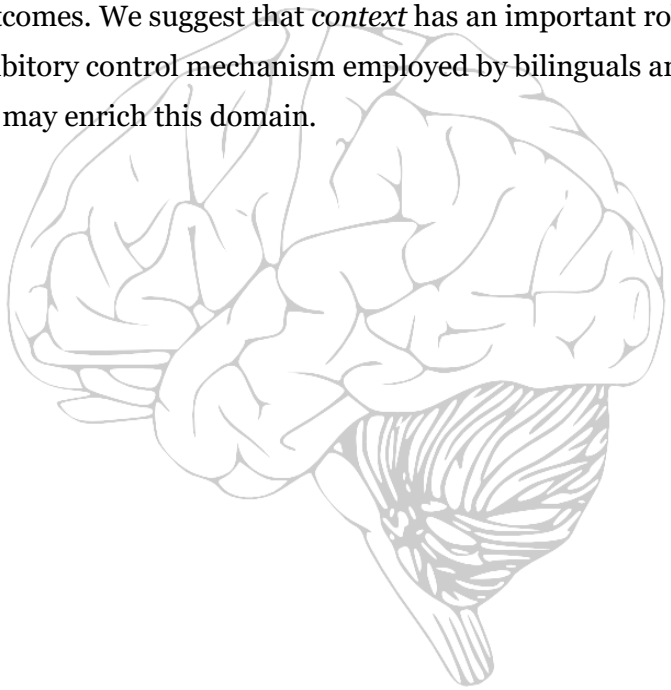
Bidisha Som,

Indian Institute of Technology, Guwahati

Bilingual language processing research, for many years now, has focused on the bilingual advantage. The result of these investigations has shown that the said advantage is not found in all participants and in all task conditions. As a result of this, the bilingual language use and the background of the communities have become important points to investigate. In this light, countries with complex social structure offer an opportunity to look at finer nuances of that 'bilingual experience'. India's north east, with 220 ethnic groups and languages, provide such a set up; here socio-cultural and linguistic diffusion has been going on between the various languages and groups. However, these groups have also resisted 'assimilation' and maintained distinct identities through centuries of coexistence. In a word, the social relation between the tribes is complicated. The present a study looks at the bilingual experience question through two experiments.

We investigated two indigenous groups of bilinguals [from the state of Nagaland]: Ao-Sangtam (Ao as L1 and Sangtam as L2) and SangtamAo (Sangtam as L1 and Ao as L2) in this backdrop of complex cultural set up in order to see the effect of language-use context on control behavior. . We report the findings of two studies: (1) a primed translation recognition task aimed at checking the effect of salient culture specific cues on language comprehension in both switch and non-switch conditions and (2) a Flanker task aimed at finding if they also exhibit a domain-general higher inhibitory control mechanism. We hypothesized that due to the context of language use in these communities, [which is rather demanding given the strict identity factors, the delicate power balance among the tribes and so on] they will show higher adaptive control with respect to ignoring the goal-irrelevant cues, in both the linguistic and non-linguistic tasks.

The results point to different outcomes with respect to the tasks; neither of the groups show any effect of the cues on performance in the linguistic task, however, the Flanker task does not show similar control in either of the groups. The first task closely imitated real life scenario of the two communities whereas Flanker was relatively unknown and abstract and this could be the reason for difference in outcomes. We suggest that *context* has an important role to play in shaping the attentional and inhibitory control mechanism employed by bilinguals and more work on non-WEIRD population may enrich this domain.



Alzheimer's Detection Using Speech Analysis

Veeky Baths,
Birla Institute of Technology & Sciences, Goa campus, India

Alzheimer's disease is a neurodegenerative disease that affects nearly 50 million individuals across the globe (1 million new cases per year in India) and is one of the leading causes of deaths. The usual onset of this disease is around 65 years old. Since many symptoms observed in early stages of Alzheimer's disease can also be attributed to normal ageing, it is difficult to distinguish amongst the two. Since a cure does not exist for this disability, one of the principal goals of Alzheimer's disease care is early diagnosis in order to promote optimal management.

Although memory problems are prevalent in Alzheimer's disease, patients also exhibit decaying effects in language and speech, typically starting with semantics and later affecting phonology and syntax. Current methods do not provide robust tools to capture the true nature of language deficits in spontaneous speech. Early detection of Alzheimer's Dementia from spontaneous speech overcomes the limitations of earlier approaches as it is less time consuming, can be done at home, and is relatively inexpensive. In this work, we extracted data from Dementia Bank's Pitt Corpusto train and compare classifiers for detecting Alzheimer's at an early stage. Some of the features we used are filled/silent pauses, syntactic complexity, semantic diversity, grammatical ratios, repetition and retracing of words, structural aspects of expressive language, etc.

We trained multiple classifiers for both binary classification as well as multi-class classification to see whether common disabilities like mild cognitive impairment, memory impairments, vascular impairments etc. affected speech factors as much as Probable cases of AD versus a Control group. We arrived at the following results:

Neural Network classifier gives the best accuracy in Binary classification (92.05 %), while the XGB classifier gives the best accuracy for all groups (74.4 %). A notable observation from the results is that MCI was very frequently being classified as Probable AD, which is suggestive of the fact that MCI cannot be reasonably distinguished from Alzheimer's disease using only speech data.

Bilingual language control and interaction in the social world

Ramesh Kumar Mishra
University of Hyderabad, India

Bilingualism is a social and interactive phenomena. How language control is shaped by the day-to-day experiences of a bilingual is beginning to be taken seriously by researchers worldwide. This topic is especially relevant in a country like India where bi- and multi-lingualism is prevalent and language experiences of different people vary widely across communities, cities and socio-cultural contexts. It is also now well-known that language control overlaps with domain-general executive control systems. As a result, the type of people a bilingual interacts with not only influences language processing, but is also expected to modulate executive control mechanisms. I will present data from my lab where we have found that a bilingual's language control mechanisms are shaped by the type and language proficiency of interlocutors they interact with. Our data shows effects of an interactional context on both language production and comprehension. In another set of studies, we also show that performance on an executive control task is modulated by the mere presence of a bilingual or monolingual interlocutor. These results provide powerful evidence for the role of interactional context on bilingual cognition. Such studies have particular relevance in the times of Covid-19 as the interactional context for most people worldwide has drastically changed in the last few months. The implications of such social changes on language processing and general cognition will also be discussed.

What grammatical characteristics of words may tell us about our mind and cognition: Cross-linguistic evidence on the selection of lexico-syntactic features

Niels O. Schiller
Leiden University Centre for Linguistics (LUCL) & Leiden Institute for Brain and Cognition (LIBC), The Netherlands

In this talk, I will first give an overview of the language production process and especially *grammatical encoding*. Then, I will present examples of studies on the *gender congruency effect* in noun phrase production. I will provide experimental evidence from different languages to demonstrate how theory-driven research has contributed to new insights regarding the discussion about the mechanisms and architecture in lexical access.

I also plan to present data from Konso, an understudied Cushitic language, native to parts of Ethiopia. Cushitic noun morphology exhibits an interesting interaction between gender and number morphology. Moreover, I will present data from Mandarin Chinese demonstrating that another category of grammatical features, i.e. classifiers, seem to be processed similarly to grammatical gender. These examples demonstrate the importance of field-based and cross-linguistic psycholinguistic data acquisition to inform theories of language processing.

SYMPOSIUM

C20s IN THE BRAIN-EICOSANOIDS IN NEURONAL HEALTH AND DISEASE

ORGANISED BY: RAVI SHANKAR AKUNDI, SOUTH ASIAN UNIVERSITY, NEW DELHI, INDIA

SPEAKERS:

1. **Dr.RitushreeKukreti**, CSIR-IGIB, Delhi
   Title: Cyclooxygenase-2 (COX-2) in Epilepsy: Potential mechanisms and new therapeutic strategies

2. **Ravi Shankar Akundi**, South Asian University, New Delhi
   Title: Purinergic Modulation of Prostaglandin E2 release in activated immune cells

3. **Dr.Undurthi Das**, UND Life Sciences 2221 NW 5th St, Battle Ground, WA98604, USA
   Title: Inflammation resolution deficiency in some neurological disorders and its clinical and therapeutic implications

4. **Dr. Eduardo CandelarioJalil**, University of Florida, USA
   Title: Role of Cyclooxygenase-2 in Neurovascular Injury following Ischemic Stroke

Cyclooxygenase-2 (COX-2) in Epilepsy: Potential Mechanisms and New Therapeutic Strategies

Dr. Ritushree Kukreti, Senior Principal Scientist
CSIR – Institute of Genomics & Integrative Biology (IGIB)
Delhi, India

Epilepsy, a common multifactorial neurological disease, affects about 69 million peopleworldwide constituting nearly 1% of the world population. About 40-45% of the patientswithepilepsy (PWE) do not respond to first antiepileptic drug (AED) monotherapy and nearly 30%suffer from medically intractable form i.e. refractory epilepsy. We aim to identify peripheralblood gene expression based predictive markers associated with variable response to AEDtherapy in patients with idiopathic epilepsy. We performed whole genome-expression (IlluminaHuman HT-12 Expression Beadchip) array on blood samples of "Drug-free" patients,"Responders" and "Non-responders" and analyzed the data using Bioconductor package in R.The patients those were categorized into "Drug-free" who had never been on any AED therapyor had not been on treatment since the past 6 months, "Responders" who remained seizure freeon AED therapy during the one year of study duration and "Non-responders" whoexperienced atleast 3 seizures on AED therapy during the one year of studyduration. PTGS2 which encodes the enzyme cyclooxygenase-2, COX-2 was significantlydownregulated in Valproate Responders and is believed to regulate the activity of P-glycoprotein(P-gp), a multidrug efflux transporter over-expressed at the blood-brain barrier (BBB) in drug-resistant epilepsy, via EP1 receptor signaling. Based on this, we hypothesizedthat PTGS2 downregulation by Valproate may reduce P-gp activity resulting in enhanced drugdelivery to brain in responders, hence leading to better efficacy.

These microarray results arecurrently being functionally validated in BBB in vitro model system, hCMEC/D3. Mountingevidences from preclinical and clinical studies suggested inflammation to play a crucial role inepilepsy pathophysiology and therefore, can be a potential therapeutic target for epilepsymanagement. Induced expression of key inflammatory mediators in brain and blood-brain barriermay alter neuronal function and excitability leading to increased seizure susceptibility. One ofthese is the enzyme cyclooxygenase-2 (COX-2) which synthesizes the proinflammatorymediators, prostaglandins and is considered to be a potential therapeutic target for controllingseizures in epilepsy. However, the effectiveness of COX-2 inhibitors depends on variousparameters such as their therapeutic dose, time of administration, treatment duration, andselectivity. Thus, the potential clinical use of COX-2 inhibitors as a future strategy for epilepsytreatment needs to be extensively investigated.

Purinergic Modulation of Prostaglandin E_2 Release in Activated Immune Cells

Dr. Ravi Shankar Akundi, Senior Assistant Professor
Faculty of Life Sciences and Biotechnology
South Asian University, New Delhi, India.

An important mediator of inflammation is prostaglandin E_2 (PGE_2), whose levels are determined by the activity of the enzyme cyclooxygenase (COX). Of the two isoforms of the enzyme, COX-2 has been shown to be induced in a variety of immune cells during inflammation. Although general COX inhibitors, belonging to the class of nonsteroidal anti-inflammatory drugs (NSAIDs), or specific COX-2 inhibitors, called coxibs, are useful in the control of acute inflammation, adverse reactions were seen when used chronically in the treatment of rheumatoid arthritis or neurodegenerative diseases. Extracellular ATP (eATP) has been reported as a damage-associated molecular pattern signal. In this report, we show that eATP synergistically increases the levels of COX-2 enzyme and PGE_2 in LPS-activated macrophages, monocytes, and microglia. Activation of macrophages also occurred when cultured in media obtained from dying neurons that contained higher levels of ATP. We show that eATP increases the levels of COX-2 protein which is sustained up to 36 h post-stimulation. This is in turn due to sustained levels of phosphorylated, or activated, cyclin-dependent kinase 9 (CDK9) and p38 mitogen-activated protein kinase (MAPK) in ATP-treated cells compared to LPS-stimulated cells. The eATP-dependent increase in COX-2/PGE_2 levels in LPS-activated cells could be abolished using antagonists for purinergic P2X7 and P2Y6 receptors. Similarly, the increase in COX-2/PGE_2 levels in the peritoneum of LPS-treated mice could be significantly abolished in mice that were pre-injected with the non-specific P2 receptor antagonist, suramin. P2 receptor antagonists, therefore, should be explored in our search for an ideal anti-inflammatory candidate.

Inflammation Resolution Deficiency in Some Neurological Disorders and it'sClinical and Therapeutic Implications

Dr. Undurthi Das, MD, DSc, FAMS, FRSC

UND Life Sciences2221 NW 5th St, Battle Ground, WA 98604, USA

The inflammatory process seen in multiple sclerosis and other inflammatory conditions of CNSare due to excess production of pro-inflammatory cytokines interleukin-1 (IL-1), IL-6, tumornecrosis factor-α (TNF-α), interferons (IFNs), macrophage migration inhibitory factor (MIF),HMGB1 (high mobility group B1) and possibly, a reduction in anti-inflammatory cytokines IL-10,IL-4, and transforming growth factor-β (TGF-β) that leads to increased secretion of reactiveoxygen species (ROS) including nitric oxide resulting in neuronal damage. It is suggested thatfailure of production of adequate amounts of resolution inducing molecules lipoxins, resolvins,protectins and maresins that suppress inflammation, ROS production, enhance wound healingand have neuroprotective properties results in inappropriate inflammation, delay inhealing/repair process and so neuronal damage continues as seen in multiple sclerosis. Hence,methods designed to enhance the production and/or administration of lipoxins, resolvinsandprotectins may form a new approach in the prevention and treatment of multiple sclerosis andother similar autoimmune diseases.

Role of Cyclooxygenase-2 in Neurovascular Injury following Ischemic Stroke

Dr. Eduardo Candelario-Jalil, Associate Professor,
Department of Neuroscience, McKnight Brain Institute, University of Florida College of Medicine,USA

Cyclooxygenase-2 (COX-2) is rapidly induced in response to ischemic stroke and significantly contributes to neuroinflammation and neuronal cell death. A dramatic increase in COX-2-derived prostaglandin E_2 (PGE_2) parallels the substantial increase in stroke-mediated blood-brain barrier (BBB) disruption and vasogenic edema. Breakdown of the BBB is a seriousconsequence of ischemic stroke, and is mainly mediated by matrix metalloproteinases (MMPs).We have found that COX-2, as well as the PGE_2receptor, EP1, play a crucial role in BBB damageand neuronal cell death in ischemic stroke by increasing the production of matrixmetalloproteinase-9 (MMP-9), a protease that degrades structural components of the BBBincluding tight junction proteins (TJPs) and extracellular matrix proteins. Genetic deletion orpharmacological inhibition of either COX-2 or the prostanoid receptor EP1 results in asignificant protection against stroke-induced neurovascular injury. Moreover, we show thatCOX-2 blockade significantly reduces the infiltration of MMP-9-laden neutrophils into theischemic brain. Our data suggest that targeting the COX-2/PGE_2/EP1 pathway is a promisingstrategy to ameliorate BBB damage and confer neuroprotection in ischemic stroke.

The tumor suppressor *MTUS1*/ATIP1 modulates gliomagenesis: association with epigenetics and DNA repair

Abstract

Background: Glioblastoma (GBM) is highly aggressive brain tumor. The resistance mechanisms in GBM present an array of challenges to understand the biological aspects and in screening the novel therapeutic interventions. We investigated the role of tumor suppressor gene (TSG) *MTUS1*/ATIP1 in glioma.

Methods: Clinical specimen, cells and stem cells of glioma were analysed for ATIP1 expression both at transcriptional and translational level. In order to analyse the role of hyper-methylation in *MTUS1* regulation, bisulfite sequencing (BSS) and decitabine treatment were used. The effect of Temozolomide (TMZ) and tumor irradiation on ATIP1 expression and its influence on survival were examined in both *in vitro* and *in vivo*. The impact of ATIP1 in irradiation-induced DNA repair was examined using phospho-γH2A.X foci.

Results: The present study reveals *MTUS1*/ATIP1 was significantly downregulated in high-grade glioma (HGG), GBM cells and glioma stem cells (GSC). BSS and decitabine treatment revealed the role of hyper-methylation in the downregulation of ATIP1. In GBM cells, overexpression of ATIP1 significantly inhibited proliferation, migration, invasion and clonogenic survival. In glioma bearing mice, elevated ATIP1 expression prolonged the overall and median survival. TMZ treatment recovered ATIP1 expression both *in vitro* and *in vivo*. Surprisingly, ATIP1 overexpression resulted in an increased repair of irradiation-induced DNA-damage and protects GBM cells from irradiation-induced cell death resulting in radioresistance.

Conclusion: Our findings indicate in glioma *MTUS1*/ATIP1 serves as a tumor suppressor regulating cell motility, proliferation and DNA repair and its downregulation is involved in the gliomagenesis and progression of this tumor. Additionally, it can be considered that in HGG higher expression of ATIP1 might interfere with the tumor irradiation therapy.

Key Words

Glioma, GSC, *MTUS1*/ATIP1, recurrent glioma, decitabine, hypermethylation, radioresistance

Brahmi (*Bacopa monnieri*): An ayurvedic herb against the Parkinson's disease

Abhishek Kumar, S. Gopika and Ahsas Goyal

Division of Pharmacology, Institute of Pharmaceutical Research, GLA University, Mathura, Uttar Pradesh, India

Abstract

Ayurveda is an ancient and traditionally used medical science concerned with the naturally originated medicinal plant products for the treatment of various neurodegenerative diseases. According to Ayurveda, three major elements controlled the human body, *viz* "Vata", "Pitta", and "Kapha" and the defects in these elements will disturb the entire human body's functions. Imbalanced "Vata" would cause neurodegenerative disorders and thus the prescribed herbal formulation for patients with the aim to stabilize the body's component "Vata". Parkinson is a chronic and gradually progressive neurodegenerative disorder caused due to the loss of dopamine-releasing neurons in the region of substantia nigra pars compacta (SNPC) characterized by the motor symptoms such as tremor, bradykinesia, akinesia, and postural instability. Proteinopathies, mitochondrial dysfunction induced dopaminergic neuronal deterioration and gene mutation are the hallmarks of Parkinson's disease. Bacoside A, Bacoside B, Bacosaponins, *etc;* are the bioactive component of Brahmi belonging to various chemical families. The neuroprotective role of Brahmi including reduction of neuronal oxidative stress, dopaminergic neuronal degeneration, mitochondrial dysfunction, aggregation inhibition of α-synuclein and improvement of cognitive and learning behavior. Researchers administered 10 mg /kg aqueous bacoside A gavage daily found that BM significantly increased brain levels of glutathione, vitamin C, vitamin E, and vitamin A in rats exposed to cigarette smoke in rats. Brahmi having potent antioxidant property as well as neuroprotective effects against PD that helps to reduce the oxidative stress, neuroinflammation, and also enhances dopamine level. The overall studies clearly proves that Brahmi is beneficial neuroprotective herbal medicine for the treatment of Parkinson's disease.

Vinpocetine facilitates the anti-amnesic activity of estrogen-receptor alpha agonist in bilateral ovariectomy-challenged animals

Ahsas Goyal[1], Debapriya Garabadu[1,2]

[1]Division of Pharmacology, Institute of Pharmaceutical Research, GLA University, Mathura, Uttar Pradesh, India.

[1,2]Department of Pharmacology, Central University of Panjab, Bathinda, Panjab, India.

ABSTRACTThe fluctuation in plasma estrogen level influences the cognitive function in females. The specific estrogen receptor alpha (ERα) agonist, (4,4′,4″-(4-propyl-[1 H] pyrazole-1,3,5-triyl) tris phenol (PPT), is reported to exhibit therapeutic activity similar to that of estrogen replacement therapy. However, the former can also exert cyclic adenosine monophosphate (cAMP)-dependent carcinogenic activity in the uterus of the ovariectomized animals. Moreover, there is no report of cGMP on ERα-mediated phosphorylation of Akt in the experimental condition. Vinpocetine increases the rate of formation of cGMP than cAMP in several tissues. Hence, the present study evaluated the neuroprotective effect of vinpocetine with or without PPT against ovariectomy-induced dementia in experimental rodents. The condition of estrogen insufficiency was induced in female rats through bilateral ovariectomy on day-1 (D-1) of the experimental schedule. Vinpocetine (20 mg/kg) and PPT attenuated ovariectomy-induced cognitive deficits in behavioral tests and increase in body weight in the rodents. Vinpocetine and PPT increased the cholinergic function and the ratio of cGMP/cAMP in the hippocampus, prefrontal cortex and amygdala of the ovariectomized animals. Further, ovariectomy-induced decrease in the extent of phosphorylation of ERα in all brain regions was attenuated with the monotherapy of either vinpocetine or PPT. Interestingly, the combination of vinpocetine and PPT exhibited better effectiveness than their monotherapy. However, vinpocetine attenuated the PPT-induced increased level of phosphorylated Akt in discrete brain regions and weight of uterus of these rodents. Hence, the combination could be considered as a better alternative candidate with minimal side effects in the management of estrogen insufficiency-induced disorders.

Role of Phytoestrogens in Parkinson's Disease

Aanchal Verma & Ahsas Goyal

Institute of Pharmaceutical Research, GLA University 17-Km. stone, NH-2 Mathura-Delhi Highway, P.O. Chaumuhan, Mathura-281406 (U.P.), India.

ABSTRACT

Parkinson's disease (PD) is a neurodegenerative disorder characterized by progressive damage of mesencephalic dopaminergic (DA) neurons of the substantia nigra (SN) and the striatal projections. Recent studies suggest that estrogen and estrogen-like chemicals have beneficial effects on neurodegenerative diseases, particularly Parkinson's Disease (PD). Studies on animals demonstrate that estrogens influence dopamine's synthesis, release and metabolism. In vivo studies have also shown the significant beneficial effects of estrogen, in shielding the brain from neurodegenerative processes like PD. Also, the expression and function of dopamine receptors can also be modified by estrogens. Phytoestrogens are compounds derived from plants that are present in a large spectrum of foods, most specifically soy. Soy infant formula now constitutes up to a third of the US market, and soy protein is now added to many processed foods. Phytoestrogens are non-steroidal compounds that share structural as well as functional similarities with 17β-estradiol and can be used as a supportive treatment to strengthen cognitive impairment in PD. Phytoestrogens are present in numerous dietary supplements and widely marketed as a natural alternative to estrogen replacement therapy. Despite of the beneficial effects of phytoestrogens, their effect on human health may depend on age, health status, and even the presence or absence of specific gut microflora. In addition to their antioxidant properties, soy products or phytoestrogens also have the ability to exhibit neuroprotective activity in patients with Parkinson's Disease via interaction with estrogen receptors α and β, with a higher affinity for ERβ. Phytoestrogens offer a valuable model for fully exploring the biological effects of endocrine disruptors in general. However, observational studies and randomised controlled trials in humans have resulted in inconclusive findings within this domain. This review will consider the evidence in animal models and human epidemiological data as to whether developmental exposure to various classes of phytoestrogens, adversely or beneficially impact the neurobehavioral programming in PD.

Keywords: Phytoestrogens, Parkinson's Disease, Estrogen, Dopamine & Neuroprotection

Effect of Succimer on Cognitive and Motor Behavioral Deficits Induced by Arsenic Neurotoxicity in Swiss Albino mice.

Bhaskar Nagilla, Sunitha Gaddam, Pratap Reddy Karnati*

Neurobiology lab, Department of Zoology, University College of Science, Osmania University, Hyderabad – 500 007. Telangana, I N D I A.

Abstract

The present study was designed to investigate the effect Succimer on post natal male mice (21 day) that were exposed to sodium arsenate (5ppm Na3AsO4) in drinking water. Swiss Ablino male mice were divided into three groups in a randomized trial; with control group consisting of mice that received normal drinking water; while group experimental control and experimental treated received 5ppm Na3AsO4 in drinking water and group experimental treated were subsequently administered with Dimercaptosuccinic acid (Succimer) (50mg/kg body wt.,) orally daily from day one. On 21st day of experimentation cognitive tests (Spatial learning) like Morris water maze, Novel Object recognition (NOR) test and depression-like behavior test (forced swimming test) and behavioral test such as Randall pain test, Roto rod test and Hot plate test was conducted. These basic activities of learning was compared with complex analysis of Intellicages an automated system that was designed for continuous recording of Home cage behavior in social groups and spatial learning and reversal spatial learning was done. On 40th day histopathology of cortex and hippocampus was done. Morris water maze and NOR test revealed learning disturbances in Arsenic toxic mice, revealed pre-disposition of depression like behavior. Motor function deficits were revealed by Roto Rod test. All these test shown experimental rats treated with Succimer and Mechanical and thermal nociception was also neutralized. Intellicages analysis of behavior was more sensitive in detecting alterations in memory and learning paradigms, which also supported the traditional results of Morris water maze in proving the protective effects of Succimer on Arsenic toxicity. Even histological analysis of Hippocampus and Cerebral Cortex showed less number neurons degenerated in experimental mice treated with Succimer. This study provides novel evidence that the mice in growth phase exposure to Arsenic can affect cognitive functions and also motivation-driven behaviors that can be corrected by Succimer treatment.

Key words: Dimercaptosuccinic acid, Arsenic neurotoxicity, Behavior, Intellicages, Cognition.

Chlorogenic Acid confers Neuroprotection in Ischemic Stroke

Gaurav Kumar

School of Biosciences & Biomedical Engineering, Galgotias University, Greater Noida, Uttar Pradesh, India
Email: Gaurav.rs.bme14@iitbhu.ac.in

Abstract

Chlorogenic acid (CGA, 5-O-caffeoylquinic acid) is a major polyphenolic component of *Coffea canephora, Coffea arabica L.*, and Mate (*Ilex paraguariensis A. StHil.*). Evidence suggests that CGA has neuroprotective, neurotrophic, anti-oxidative, and anti-inflammatory activities. The ischemic cascade is initiated in the hypoperfused region of the brain that leads to neuronal cell death. Identification of multitarget inhibitor against prominent molecular mediators of ischemic cascade might be a suitable strategy to combat cerebral ischemic stroke. The present study is designed to evaluate the neuroprotective efficacy of chlorogenic acid (CGA) in the global cerebral ischemic rat model. The effective dose of CGA was evaluated on the basis of reduction in cerebral infarction area percentage, Evans blue extravasation, and restoration of brain water content. The level of glutamate, calcium, and nitrate in different regions of the brain, as well as cerebrospinal fluid (CSF), was evaluated. The level of calcium and nitrate was compared with ifenprodil—an antagonist of N-methyl-D-aspartate receptor (NMDAR) and 7-nitroindazole—an inhibitor of neuronal nitric oxide synthase (nNOS) respectively. Further, molecular docking was performed to compare the inhibition potential of CGA against NMDAR and nNOS with their inhibitors. Dose optimization results revealed that intranasal administration of CGA (10 mg/kg b.w.) significantly reduced the cerebral infarction area, Evans blue extravasation and restored the brain water content compared with ischemia group. It also significantly reduced the calcium, nitrate, and glutamate levels compared with ischemia group in the cortex, hippocampus cerebellum, and CSF. In molecular docking study, CGA displayed similar binding interaction as that of Ifenprodil and 7-nitroindazole with NMDAR and nNOS respectively. The current findings suggest that the treatment with CGA confers neuroprotection in global ischemic insult by inhibiting and downregulating the different molecular markers of cerebral ischemia.

Keywords: Chlorogenic acid, Ischemic stroke, Neuroprotection, cerebral infarction

Determination of Etiology and Epidemiology of Viral Central Nervous System Infections by Quantitative Real-Time Polymerase Chain Reaction in Central India Population

Ragini I. Tiwari, Shradha S. Bhullar, Nitin H. Chandak, Neeraj N. Baheti, Hatim F. Daginawala, Lokendra R. Singh, Rajpal S. Kashyap

Abstract:

Introduction: Viral infections of the central nervous system (CNS) are the most common cause of hospital admission in worldwide and remain a challenging disease for diagnosis and treatment. The most common infectious agents associated with viral CNS infections are cytomegalovirus (CMV), Epstein-Barr virus (EBV), varicella zoster virus (VZV), Japanese encephalitis virus (JEV), dengue virus (DENV), West Nile virus (WNV), and Chandipura virus (CHPV). The aim of the present work was to find the etiology of CNS viral infection in the Central India population by comparing real-time polymerase chain reaction (PCR) method [one-step and two-step reverse transcriptase (RT-PCR)] in cerebrospinal fluid (CSF) and blood samples of CNS viral infections patients.

Materials and Methods: One-step and two-step real-time PCR assays were evaluated in CSF and parallel blood samples from patients with viral CNS infections for detection of DNA and RNA viruses. A comparative analysis was also done between gDNA, gRNA, cDNA, and plasmid-based real-time PCR methods for an efficient quantitation of viral particles in clinical samples for determination of viral etiology.

Result: On evaluation of 150 CSF and 50 parallel blood samples from suspected cases of viral CNS infections, a viral etiology was confirmed in 21(14%) cases, including 3% for EBV, 1% of CMV, and 5% for VZV and JEV. The one-step RT-PCR has a higher detection limit for detection and quantitation of viral RNA in comparison to two-step RT-PCR.

Conclusion: Our result reveals that VZV and JEV are the most usual cases of CNS viral infection in hospitalized patients in the Central India population and one-step RT-PCR shows higher viral load detection limits for quantitation of viral genome and more sensitivity in comparison to two-step RT-PCR.

Escitalopram-induced amelioration of cognitive deficits and neurotropic factors in an animal model of depression

Shilpa BM[*] and Shankaranarayana Rao BS[#]
*School of Basic and Applied Sciences, Dayananda Sagar University, Kumarswamy Layout, Bengaluru, Karnataka, 560111
#Department of Neurophysiology, National Institute of Mental Health and Neuro Sciences, Bengaluru, Karnataka, 560029

Abstract

Major depressive disorder (MDD) is one of the main psychiatric disorders affecting 21% of world population. Chronic stress, which induce functional impairments and morphological changes in the hippocampus, frontal cortex and amygdala, plays a vital role in pathogenesis of MDD. Currently, there are no efficient pharmacotherapy options for chronic stress-induced learning and memory impairments, neuronal damage and molecular changes. Escitalopram, a selective serotonin reuptake inhibitor used clinically to treat MDD. In the current study, adult male Wistar rats were subjected to chronic immobilisation stress (CIS). Depressive-like behaviours were assayed by sucrose preference test, test used to anhedonia in animals and forced swim test for the behavioural despair. Stress-induced anxiety-like phenotype was assessed by open field test and elevated plus maze. Alternation in the cognitive deficits due to stress was calculated by reference and working memory components, measured using a partially baited 8-arms radial maze. 40µm thick anterio-posterior coronal sections were stained and quantified for volumes of dentate gyrus, hippocampus and basolateral amygdala using the Stereoinvestigator software. Western blotting was carried out to quantify expression of GFAP, BDNF and VEGF in the hippocampus, frontal cortex and amygdalar complex. Exposure to CIS resulted in behavioural depression, decreased the number of open arm entries of the elevated plus-maze and reduced exploratory behaviour in the open field test, compromised the spatial learning and memory with dentate gyrus, hippocampal atrophy and amygdalar hypertrophy. Also, the molecular markers BDNF, VEGF and GFAP were reduced. Interestingly, escitalopram treatment ameliorated all these deficits either completely or partially in a dose-dependent manner. Our data suggest that escitalopram significantly protected CIS-induced learning and memory deficits, behavioural depression and anxiety. Antidepressant also normalizes neurotropic factors and glial pathology in depressed animals. Current study illustrates an experimental evidence for the clinical application of escitalopram in treating depression and associated cognitive deficits.

Evaluation of neuroprotective activity of American ginseng against Chronic Unpredictable Mild Stress challenged animals

Arushi Srivastava[1,2] and Dr. Debapriya Garabadu[1,3]

[1]Institute of Pharmaceutical Research, GLA University, Mathura; [2]D.S. College of Pharmacy, Aligarh, U.P; [3]Department of Pharmacology, Central University of Punjab, Bathinda

Abstract

Stress is a bodily condition wherein the homeostasis of the body is disturbed. The varying level of stress leads to depression. The effect of herb American Ginseng as an adjuvant in the management of stress is considered here in the study. However, experimental evidence is yet to be established. Therefore, the anti-stress, anti-depressant activities of American ginseng (200 mg/kg) were evaluated. Moreover, the cannabinoid pathway (CB-2 receptor) was checked for its role in the management of depression. The CB-2 Receptor antagonist AM-630 was considered here to validate the pathway along with American ginseng in the mice which were exposed to Chronic Unpredictable Mild Stress (CUMS) model of depression for 14 days straight. Fourteen-day treatment of American ginseng significantly attenuated the CUMS-induced anxiety in open field, hole-board, elevated plus maze tests, and compulsion in the marble-burying test. American ginseng significantly reversed the CUMS-induced decrease and increase in the levels of serotonin (5-HT) and its metabolite (5-hydroxyindole acetic acid) in the prefrontal cortex, and attenuated the CUMS induced increase in the levels of inflammatory markers such as interleukin-6 and tumor necrosis factor-α in the prefrontal cortex and normalized the plasma corticosterone level. The CB-2 Receptor pathway showed its potentiating role in managing stress in the different behavioural and biochemical estimations as observed when the CB-2 receptor antagonist was used. Thus, it can be speculated that American ginseng could be a better option in the treatment of stress.

Keyword: Stress, Depression, American ginseng, Chronic Unpredictable Mild Stress, Cannabinoid Receptor-2.

"Exploration of the effects of selective calpain inhibitor A6185 in the mitigation of Alzheimer's disease like cognitive deficits induced by β-amyloid(25-35) in mice"

Darshpreet Kaur[1]*, Amarjot Kaur Grewal[1], Thakur Gurjeet Singh[2]

Chitkara College of Pharmacy, Chitkara University, Rajpura, Distt. Patiala 140412, Punjab, India

Abstract

Calpains are cysteine proteinases that selectively cleave proteins in response to calcium signals. Exacerbated activation of calpain has been implicated as a major component in the signalling cascade that leads to β-amyloid (Aβ) production and tau hyperphosphorylation in Alzheimer's disease (AD). In this study, we tested the cognitive, biochemical and histopathological effects of selective calpain inhibitor A6185 in Aβ25-35 treated Swiss albino mice. Aβ (5 µL, injected intracerebroventricular (i.c.v), on both sides of the brain), was used to induce dementia in separate groups of Swiss mice. Morris water maze (MWM) and step-down test were performed to assess learning and memory of the animals. A battery of biochemical and histopathological studies were also performed. Extent of oxidative stress was measured by estimating the levels of brain reduced glutathione (GSH), thiobarbituric acid reactive species (TBARS), catalase and brain acetylcholinesterase (AChE) activity. Aβ produced a marked decline in MWM and step-down test performance of the animals, refecting impairment of learning and memory. Aβ treated mice exhibited a marked accentuation of AChE activity and TBARS, along with a fall in GSH and catalase levels. Further, the stained micrographs of Aβ-treated mice indicated pathological changes, severe neurophilic infiltration and amyloid deposition. A6185 i.p. administration for 11 days significantly attenuated Aβ-induced memory deficits, biochemical and histopathological alterations. Therefore, the findings demonstrate potential of calpain inhibitor A6185 in memory dysfunctions which may probably be attributed to its anti-cholinesterase and anti-oxidative effects.

Keywords: calpains, amyloid-beta, reduced glutathione, brain acetylcholinesterase, catalase, neurophilic infiltration