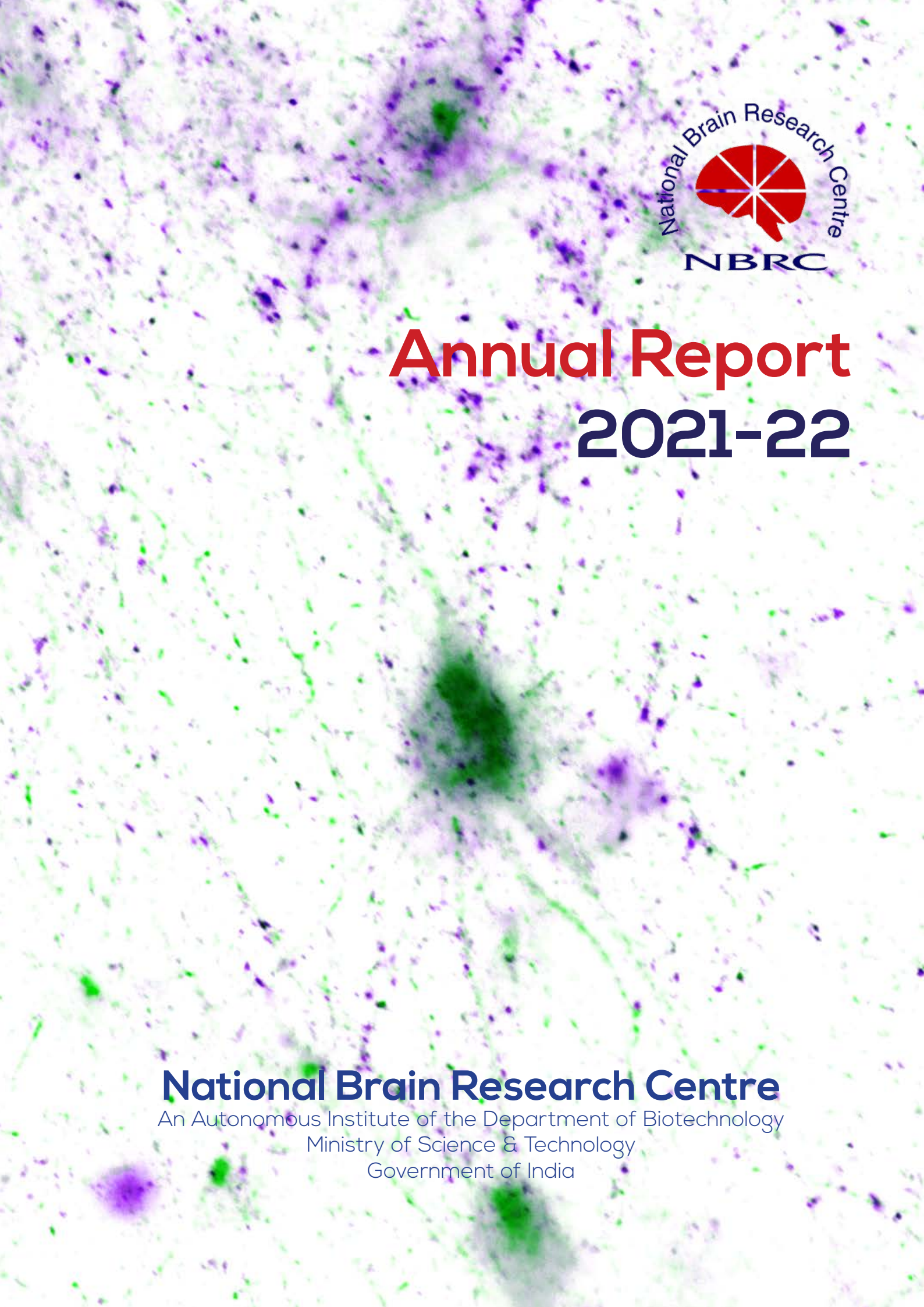

Annual Report 2021-22

National Brain Research Centre

An Autonomous Institute of the Department of Biotechnology
Ministry of Science & Technology
Government of India

Annual Report
2021-22

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CONTENTS

Mandate & Objectives

MANDATE

- Pursue basic research to understand brain function in health and disease
- Generate trained human resources with the capability to carry out inter-disciplinary research in neuroscience
- Promote neuroscience in India through networking among institutions across the country

VISION

The vision we have for NBRC is that it would not only grow into a world-class institute for brain research but also create a vibrant active neuroscience community by catalyzing the overall growth of this discipline in India. The desirable outcome of this initiative is the generation of skilled manpower in neuroscience research who would help India achieve an international leadership in this frontier area of science. This initiative would help Indian neuroscientists to participate in global research efforts as equal partners. The knowledge base generated from these efforts would help diagnostic tools and therapeutic strategies for treatment of brain-related disorders. A unique role for NBRC is that it will act as a node with linkages to other centers carrying out neuroscience research in the country, acting in effect as the “hub of the wheel” rather than the wheel itself.

From The Director's Desk

The brain is a well-organized architecture performing complex tasks seamlessly and silently. Understanding the brain's development, protective mechanisms from oxidative stress, neuroinflammation, and other external factors (COVID-19, etc.) are the frontier area of neuroscientific research across the globe and also an avenue for novel therapeutic development. The mandate of National Brain Research Centre (NBRC) is to understand brain function in health and disease, to generate trained human resources, and lead the nation in brain-related research activities. In continued efforts over the last two decades, NBRC has been established as an exclusive multidisciplinary centre for cutting-edge brain research under one roof. Scientists and researchers from various disciplines are engaged in fast-track mode to understand the causal molecular processes of neurological diseases that can offer possible solutions and eventually help society through bench-to-bedside approach.

NBRC successfully offers Master's and Doctoral programs in neuroscience. It is of great satisfaction that in December 2021, the National Assessment and Accreditation Council (NAAC) through its robust review process recognized NBRC as NAAC-accredited deemed-to-be-university. As of today, NBRC has achieved another milestone by awarding Ph.D. degrees to more than 100 students. Both our M. Sc and Ph.D graduates are great ambassadors of NBRC, spread across every continent, and many of them serve various national institutes or work as project lead in top biotechnology firms in India and abroad. The project staff (senior R&D engineer, neuropsychologists, etc.) are well placed after the completion of their respective projects. A state-of-the-art 3T MRI center was inaugurated by the Honorable Minister of Science and Technology, Dr. Jitender Singh in the presence of Prof. Rajesh S Gokhale (Secretary, Department of Biotechnology). This 3T MRI scanner has unique multi-nuclear MR spectroscopy as well as combined EEG-fMRI capabilities.

The research work carried out by our scientists is published in prestigious journals with high citations. Some of the research highlights of scientists are briefly mentioned.

Dr. Anindya and his laboratory has established the polymodal PVD neuron in *C. elegans* as a model for dendrite regeneration and found that dendrite regeneration is independent of the major signalling pathways controlling axon regeneration. They also identified that the RAC GTPase CED-10 is required for the initiation of dendrite regrowth after physical breakage of the dendrites.

Dr. Soumya and co-workers have demonstrated for the first time that δ-ORs are expressed in the pallium, basal ganglia, cerebellum, and hippocampus of a commonly studied species of songbirds, that is, zebra finches. These receptors are strongly expressed by components of the vocal motor pathway, whereas lower levels were present

in components of the pathway important for context-depended singing in male zebra finches. They concluded that δ-ORs may also be involved in vocalization, vocal learning, and context-dependent singing in male zebra finches.

Dr. Mayanglambam Dhruba Singh and co-workers are working on human neurodevelopmental and neurodegenerative disorders using the Drosophila model system. They are interested in finding the molecular target of human neurodegenerative disorders such as Huntington's disease, spinocerebellar ataxia, and Alzheimer's disease.

Prof. Pankaj Seth and co-workers focus on understanding the cellular and molecular mechanisms of virus-induced neurodegeneration. The research findings from his laboratory identified how viruses like HIV-1 and Zika cause damage to neurons and human neural stem cells, respectively. The laboratory is also exploring the molecular mechanisms that lead to neuronal damage in COVID-19 cases to better understand the scientific basis of brain fog and neurological symptoms reported in long COVID-19 patients.

Dr. Anirban Basu and co-workers have developed an experimental mouse model of acute flaccid paralysis, which essentially demonstrates how the non-canonical RIG-I pathway induces apoptosis upon infection in motor neurons. They also found that upon infection, host cells remain resistant to the antiviral effects of IFNs and encounter apoptosis following the understudied IFN-independent pathways.

Dr. Ellora Sen and co-workers have found changes in mitochondrial dynamics and alterations in redox homeostasis by YAP1 influences their sensitivity to ROS stressors. They report the existence of auto-regulatory dynamic rewiring between metabolite lactate (L)–inflammatory cytokine IL-1B (I) – Circadian CLOCK (C) (LIC) in glioma and several malignancies of distinct genetic origins. Based on the correlation between the components of LIC circuitry with anti-cancer drug sensitivity and patient survival, they suggest the possibility of designing rational therapeutics aimed at targeting the LIC circuitry.

In the Neuroimaging and Neurospectroscopy laboratory (NINS), we use multimodal neuroimaging techniques to investigate how a healthy aged person converts into Alzheimer's and or Parkinson's disease patients. Our research aims to identify early diagnostic markers for AD and PD, and we have identified an imbalance of prooxidant (heavy metal deposition) and antioxidants using non-invasive imaging modalities, including MR spectroscopy. Our clinical research of early diagnostic biomarkers is currently moving toward the first clinical trial for enhancing the cognitive profile in mild cognitive impairment patients, to be conducted at NBRC in collaboration with AIIMS, New Delhi, as approved by the Drug Controller General of India. A patent has also been granted by the US Patent and Trademark Office for the NINS-developed brain signal processing platform (KALPANA). All neuroimaging data is now part of the SWADESH database and data analytics program.

NBRC offers medical services to citizens and those from surrounding districts, from the neurological outpatient department services at Civil Hospital, Gurgaon. Patients with epilepsy visit the campus for medical check-ups using the magnetoencephalography facility in collaboration with AIIMS, New Delhi. NBRC conducts awareness programs for senior citizens residing at old age homes regarding mental health and neurodegenerative diseases in collaboration with HelpAge India.

The Green Canopy club in NBRC has continued its efforts to increase tree plantation in NBRC. Recently launched cafeteria Kalpataru is a well-liked gathering place for faculty and students. The Science Sethu webinar series was conducted as part of DBT's star college outreach initiative and was appreciated by the students. NBRC has established a science museum in a secondary school at Nuh district, Haryana.

On the 75th Independence Day, NBRC conducted flag hoisting ceremony on 15th Aug 2022. I sincerely thank the Department of Biotechnology for its continued generous funding support. Thanks to all NBRC staff members for being a great research resource. Members of all the various committees of NBRC and scientific colleagues who served on various committees, thesis examiners as well as collaborators of NBRC are highly appreciated. I anticipate continued support from everyone to help NBRC to be an active contributor to the global human brain simulator initiative.

Prof. Pravat Kumar Mandal
Director-in-Charge,
National Brain Research Centre
&
Honorary Professor
Florey Institute of Neuroscience and Mental Health, Melbourne, Australia

Scientific Reports

Anindya Ghosh Roy

Development and repair of neural circuit in *C. elegans*

Research Associate/ Post-doctoral Fellows

Swagata Dey (India Alliance Early career fellow)

PhD Students

Harjot Kaur,
Sibaram Behera,
Sunanda Sharma,
Pallavi Singh,
Dhyey Vyas

MSc Students

Dyutika Banerjee

Project Assitants

Kavi Nila,
Mydhiy Vasudevan,
Sruthy Ravivarma
(SERB grant)

Technical Assistant

Sumit mahapatra

Background

The goal of our research team is to understand how neurons and neuronal circuits develop and maintain normal function and regenerate

We are using a variety of approaches to study the development and function of neural circuits in vivo, including genetics, genomics, sub-cellular imaging, laser neurosurgery and optogenetics. Since *C. elegans* is transparent and has a simple nervous system, we can manipulate and observe individual neurons in intact, living animals.

We are interested in understanding how neurons are polarized during the initial stages of development, how neural circuits respond to injury in adulthood; and how molecular mechanisms such as cytoskeleton dynamics, RNA based mechanisms, and intracellular signalling affect these processes. One major focus is axon regeneration.

1) Regulation of neuronal microtubule cytoskeleton:

Neuronal polarization is defined by the formation of axons with parallel arrays of plus-end-out and dendrites with the non-uniform orientation of microtubules (MTs). In *C. elegans*, Posterior Lateral Microtubule (PLM) neuron is bipolar with its two processes growing along the anterior-posterior axis under the guidance of Wnt signaling. We found that loss of Kinesin-13 family microtubule depolymerizing enzyme KLP-7 causes hyper-stabilization of neuronal microtubules leading to ectopic extension of axon-like processes from PLM cell body (Puri et al 2021, JCB).

To find out novel regulators of microtubule cytoskeleton in neuron, we have screened and identified mutants those suppress the neuronal phenotype of *klp-7* mutant. Mutants affecting many of the microtubule stabilizing factors involving plus or minus end binding proteins, and centrosomal proteins did not suppress *klp-7(0)*. However, the drug Colchicine that destabilizes MTs suppressed the same. Some of the identified genes code for proteins encoding RNA binding protein, beta tubulin, and

adaptor for vesicular transport, kinesin.One of the genes we identified is *muscleblind-1/mbl-1* that encodes for the polypyrimidine tract binding protein. Muscleblind family proteins are known to control RNA splicing. We found that MBL-1 is necessary and sufficient for axon growth of PLM and ALM neuron. Loss of *mbl-1* destabilizes the microtubules and affects axonal transport in PLM neuron leading to short axon phenotype (Figure-1) and improper synapse formation. MBL-1 tagged with GFP is present both in nucleus and axon. Our data showed that *mbl-1* is genetically epistatic to *mec-7* (β tubulin) and *mec-12* (α tubulin) for axon growth. The immunoprecipitation of MBL-1 pulls down the *mec-7*, *mec-12*, and *sad-1* mRNAs. Additionally, the mbl-1 mutants show a reduction in the level and stability of mec-7 and *mec-12* transcripts. Independently, *mbl-1* is epistatic to *sad-1* for synapse formation. Our work elucidated a previously unknown link between RNA binding protein and cytoskeletal machinery for the development and maintenance of the nervous system (Puri et al 2022, doi: https://doi.org/10.1101/2022.09.07.506915).

Fig-1: Muscleblind-1/MBL-1 is required for neurite growth and Maintenance

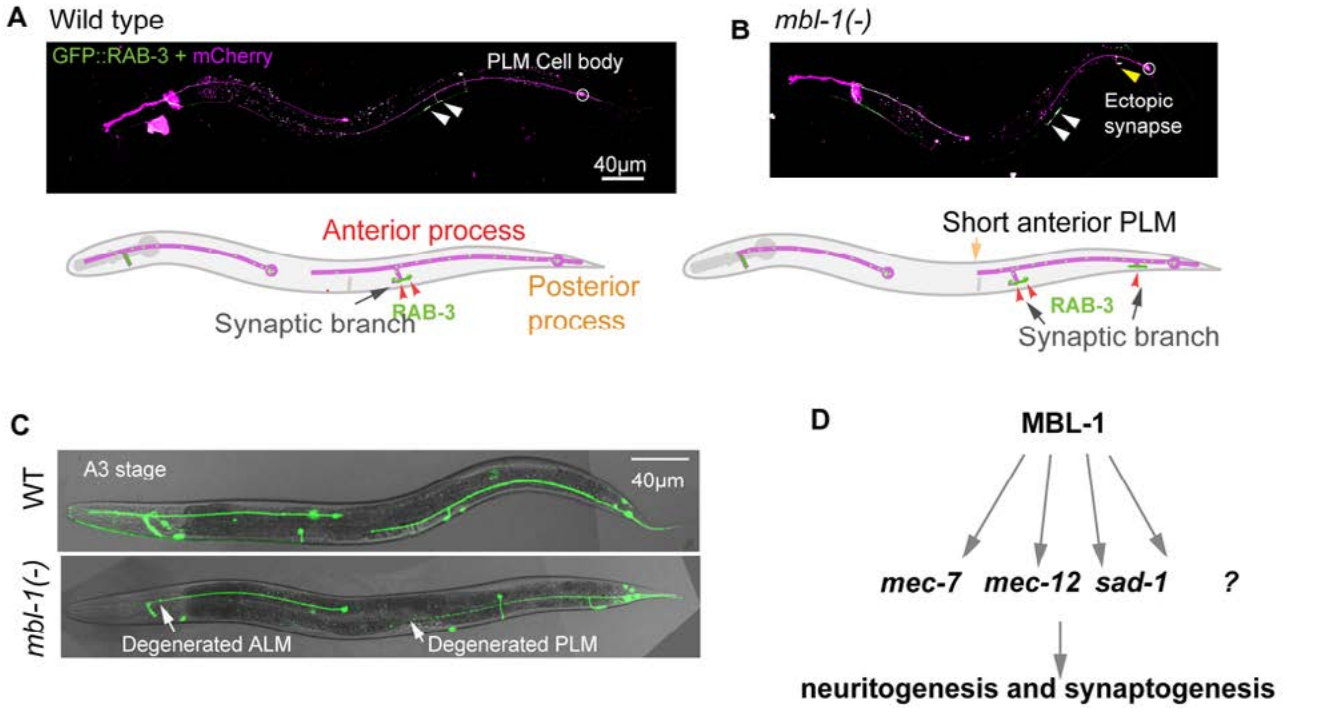


Figure 1: Role of mbl-1 in axon growth and synapse formation.

(A-B) Confocal images of ALM and PLM neurons in WT, and *mbl-1(-)background. In mbl-1(-), short anterior process of ALM and PLM is marked in orange arrow. The presence of ectopic synapse in mbl-1(-) is marked in the red arrow. (C) mbl-1(-) mutant shows early onset of degeneration. (D) Model explaining the function on MBL-1 in regulating tubulin mRNAs.*

2) Neuronal Regeneration

During the lifetime of an individual, routine activities may cause injury to neuronal circuits which affect the quality of life or in severe cases can be fatal. Despite a comprehensive understanding of the mechanisms underlying the development of the nervous system, the pathways that repair damage after injury remain poorly understood. This is very important from the point of therapeutics as adult nervous system is extremely refractile to repair after accidental damage. Our past work has helped develop *C. elegans* mechanosensory neuron as a model for axon regeneration studies. The conserved Dual Leucine Zipper Kinase (DLK-1) pathway is essential for axon regrowth. Consequent to these discoveries, several efforts have been made using model systems such as worm, fly, and fish to understand the neuron-intrinsic mechanisms of axon regrowth. However, mechanistic aspects of functional recovery during axon regeneration was unclear. In our lab at the National Brain Research Centre, we have established a neurosurgery protocol with 2-photon lasers. We further found that the axotomy of Posterior touch neuron PLM leads to a dramatic loss of posterior touch sensation. Using this experimental paradigm, we have shown the regeneration potential declines both at anatomical and functional level as the worms age. Furthermore, we screened for known axon regeneration pathways that might improve functional recovery in older age.

i) *let-7* miRNA functional recovery: We found that during the regeneration phase, the fusion between the proximal and distal fragments of an injured axon leads to a rapid functional recovery (Basu et al 2017, PNAS). We also discovered that let-7 miRNA inhibits functional restoration via the fusogen molecule, EFF-1 (Basu et al 2017, PNAS, Fig 1).

ii) Insulin Signalling regulates functional rewiring of injured axon: We have seen that the injured axons which do not show a fusion-like phenomenon also correlated to the functional recovery in later stages. Particularly, the axons which reach the original target area and accumulate presynaptic proteins in the ventral nerve cord are likely to give functional recovery. Ventral targeting of the regrowing axon and functional restoration decline with age. We found that loss of Insulin signalling

Fig-2: Pathways controling axon regeneration

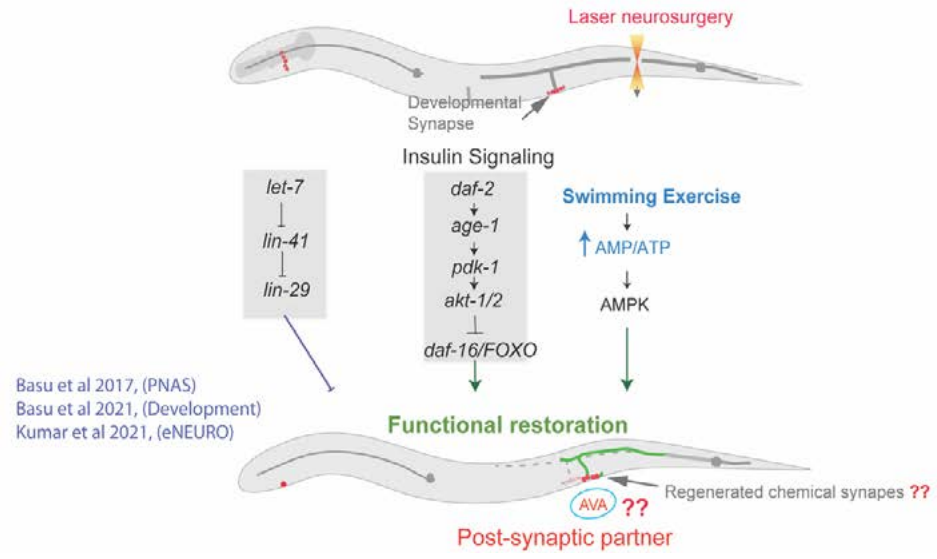


Figure 2: The illustration shows how manipulation of either let-7 miRNA, Insulin signalling (IIs) or AMP Kinase promotes axon regeneration in adulthood.

(IIS) receptor, DAF-2 promotes ventral targeting in a DAF-16 dependent manner, irrespective of age. We further showed that coordinated activities of DAF-16 in both neurons and muscles, promote ventral targeting. In response to axotomy, DAF-16 upregulates the expression and localization of the Netrin receptor UNC-40 in the growth cone of the proximal stump (Basu et al 2021, Development, Fig 1).

iii) Finally, we have recently shown that axon regeneration can be enhanced by physical exercise (Kumar et al 2021, eNEURO). Using the swim-exercise model we showed that swimming exercise, following axonal injury, improves functional restoration through the regeneration of the injured axon. Moreover, we found that the activity of the metabolic energy sensor AMP activated kinase (AMPK) is crucial both in neuron and muscle for seeing the beneficial effect of the swim-session (Kumar et al 2021, eNEURO, Fig 1).

Although the regrowing PLM axon can reach the anatomical location where the original target neuron is located, it is not clear whether it establishes a chemical synapse with its post-synaptic partner neuron AVA. It is also not clear how Insulin signalling, and *let-7* miRNA pathway regulate functional recovery in adulthood. A high throughput screening platform for overcoming age related barriers in functional recovery might allow us to uncover new molecular approaches to treat nervous system injury.

Study of Dendrite Regeneration using PVD neuron as Model

The information-receiving units of a neuron, dendrites are equally vulnerable to physical insults. However, less is known about dendrite regeneration (y Cajal, 1991, Thompson-Peer et al., 2016). To understand the mechanisms of dendrite regeneration, we used PVD neurons, which have branched dendrites. The PVD neurons are responsible for harsh touch sensation. After the primary dendrite was severed near the cell body, we observed that the regrowth started from the injured tip and continued following a similar trajectory with complex branching patterns. To test whether the dendrite regeneration shares the mechanism with that of an axon, we tested the major signalling hubs such as DLK-1, cAMP, let-7 miRNA, Akt-1, Phosphatidylserine (PS) exposure that control axon regeneration. We found that neither initiation of regrowth nor branching is affected by the axon injury pathways. Surprisingly, we found that a small GTPase CED-10 (RAC) and and upstream

Fig-3: CED-10 RAC GTPase regulates dendrite regeneration

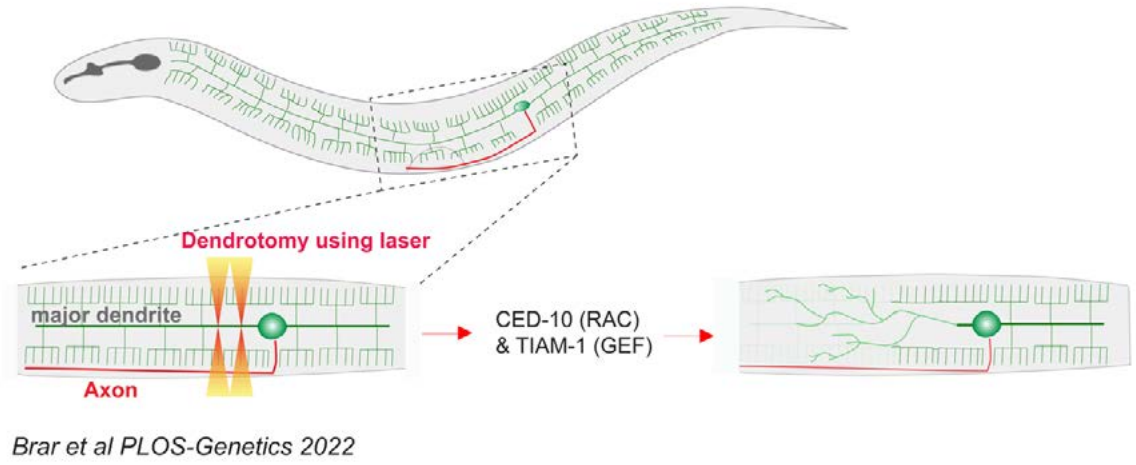


Figure 3: The illustration shows how CED-10 RAC GTPase controls dendrite regeneration in PVD neuron.

GEF TIAM-1 is essential for dendrite regeneration. Our work provides a framework for understanding the cellular mechanism of dendrite regeneration using PVD neuron (Brar et al 2022, PLOS-Genetics).

Publications

1. Brar, H.K; Dey, S; Bhardwaj, S; Pande, D; Singh, P; Dey, S; and Ghosh-Roy, A. Dendrite regeneration in C. elegans is controlled by the RAC GTPase CED-10 and the RhoGEF TIAM-1. (PLOS-Genetics), March, 2022, https://doi.org/10.1371/journal.pgen.1010127

2. Dey, S; and Ghosh-Roy, A. In vivo Assessment of Microtubule Dynamics and Orientation in Caenorhabditis elegans Neurons (J Vis Exp), 2021 Nov 20;(177). https://doi.org/10.3791/62744.

3. Kulkarni, SS; Sabharwal, V; Sheoran, S; Basu, S; Matsumoto, K; Hisamoto, N; Ghosh-Roy, A and Koushika, SP. (2019) UNC-16/JIP3 negatively regulates actin dynamics dependent on DLK-1 and microtubule dynamics independent of DLK-1 in regenerating neurons. (Genetics), https://doi.org/10.1093/genetics/iyab139

4. Basu, A; Dey, S; Behra, S, Bhardwaj, S; Dey, S; and Ghosh-Roy, A. (2021), Regulation of UNC-40/DCC and UNC-6/Netrin by DAF-16 promotes functional rewiring of the injured axon. (Development), 148(11) (2021):dev198044. doi: https://doi.org/10.1242/dev.198044

5. Kumar, S; Basu, S; Behera, S; Dey, S; and Ghosh-Roy, A. Swimming exercise promotes post-injury axon regeneration and functional restoration through AMPK (eNEURO), 0414-20.2021. DOI: https://doi.org/10.1523/ENEURO.0414-20.2021

6. 6) Puri, D; Ponniah, K; Biswas, K; Basu, A; Dey, S; Lundquist, E.A; and Ghosh-Roy, A (2021), Wnt Signaling Establishes the Microtubule Polarity in Neuron Through Regulation of Kinesin-13. (Journal of Cell Biology) 220(9):e202005080. https://doi.org/10.1083/jcb.202005080 Epub 2021 Jun 17

Presentations

1. Anindya Ghosh Roy : 25th Feb 2022, IN-EMBO webinar series. Title of the lecture: "*C. elegans* as a model for nerve regeneration study"

2. Anindya Ghosh Roy : Brain Awareness Week, March 14 to 20 at DBT-InStem, organized by InStem, Bangalore, Title of seminar: "Study of neuronal regeneration using *C. elegans*"

Funding

1. NSERB (CRG/2019/00294): 2020-2023

2. NBRC Core

Collaborators

- Sandhya Koushika, TIFR, Mumbai, India
- Sourav Banerjee, NBRC, India
- Smarajit Polley, Bose Institute, Kolkata
- Kavita Babu, IISER-Mohali

Degrees Awarded

- Atrayee Basu (PhD degree)
- Dharmendra Puri (PhD degree)
- Debapriya Roy (MSc degree)

Anirban Basu

Molecular approaches to understand the pathophysiology and pharmacology of infection and inflammatory disorders of Central Nervous System

PhD Students

Surojit Chakrabarty

Meenakshi Bhaskar

Shivangi Sharma

Stuti Mohapatra

Indira S Priya

Research Associate

Atreye Majumdar

Technician C

Kanhaiya Lal Kumawat

Technician B

Manish Dogra

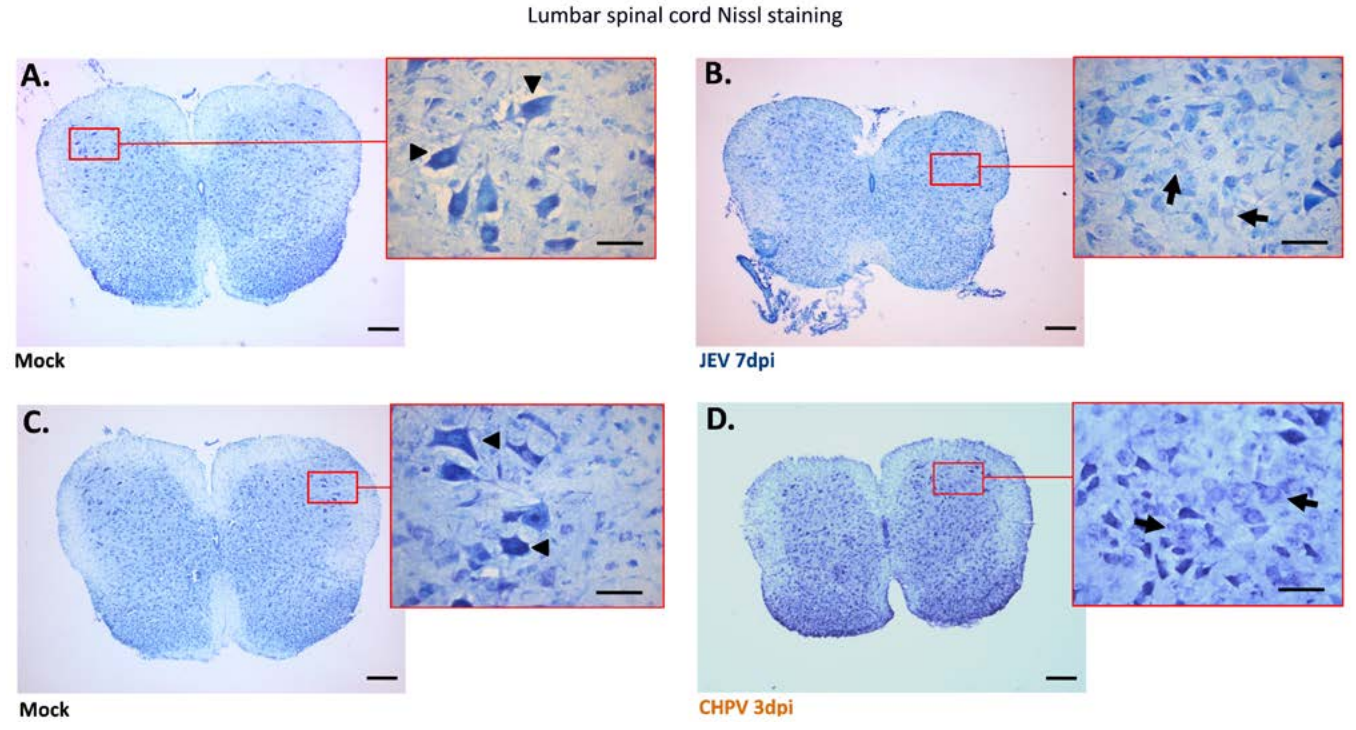
Japanese Encephalitis Virus (JEV) entry into the host is followed by viral replication in the periphery which in turn is accompanied by activation of innate and adaptive arms of immune system. In case of adults, immune system is normally capable of eliminating virus from the circulation thus preventing it from invading central nervous system (CNS). Whereas in children and geriatric patients, owing to weaker immune response against JEV, the latter gains entry into CNS thus initiating a vicious cycle of inflammatory reactions which ultimately lead to neuronal death and subsequent glial cell activation. This virus-induced encephalitis is considered as most critical factor resulting in patient mortality in case of JEV infections. Virus replication inside host cell is a complex process involving various steps like viral entry, unpacking of viral genomes, genome replication, virus packaging and egress. Each of the aforementioned processes involve activity of a plethora of molecules which acting in concert result in the successful completion of intracellular life cycle of virus. Our lab has been working on deciphering the molecular details of various steps of viral life cycle thus contributing significantly to the field of host-virus interactions.

Poliomyelitis-like illness is a common manifestation associated with neurotropic virus infections. Functional loss and death of motor neurons in spinal cord often led to reduced muscle tone and paralysis, which subsequently result in clinical symptoms like movement disorders, cognitive impairment and long-term neurological sequelae among survivors. Despite several reports on molecular basis of encephalopathy, the pathogenesis of flaccid paralysis upon viral infection remained largely unknown.

Neurotropic viral-infections are increasingly common cause of immediate or delayed neuropsychiatric sequelae, cognitive impairment, and movement disorders or in severe cases death. Given the highest reported Disability-Adjusted Life Years (DALYs) and mortality rate worldwide, a better understanding of molecular mechanisms for underlying clinical manifestations like Acute Flaccid Paralysis (AFP), will help in development of more effective tools for therapeutic solutions.

In a recently published work, we have elucidated the mechanism responsible for limb paralysis by studying clinical isolates of JEV and Chandipura virus (CHPV) causing clinical-AFP (Acute flaccid paralysis) in vast region of south-east Asia including Indian subcontinent. Experimental model for studying virus-induced AFP was generated by intra-peritoneal injection of 10-day old BALB/c mice. Pups were subjected to a series of behavioural tests to assess gait, neurodegeneration and locomotory behaviour. Progressive decline in motor performance of infected animals was found when compared with control animals. Paralysis was correlated with death of motor neurons (MN) by studying various cell death-assays both in *in vivo* and *in vitro* settings. Furthermore, this study demonstrates that upon infection, extrinsic apoptotic pathway gets activated in MNs in a RIG-I-dependent fashion via activation of transcription factor IRF-3 and IRF-7. Once activated, this pathway leads to interferon-independent apoptosis of MNs. Both gene-silencing experiments using specific RIG-I-siRNA and in-vivo morpholino abrogated cellular apoptosis, thus validating important role of pattern recognition receptor (PRR) RIG-I in MN death.

Surprisingly with our *in vivo*-model, we made contrasting observations where CNS ablation of RIG-I significantly enhanced resistance to infection, clearly visible by reduced expression of viral-proteins and apoptotic markers rather than increased susceptibility to infection as reported previously. Our results provide one clear explanation as to how transient silencing of RIG-I in motor neuron NSC34 cells attenuated apoptosis by suppressing pIRF3/7 signaling effectively by blocking p-IRF3-induced IFN-independent genes (likely ISG54, ISG56) and not any other IFN-dependent pathways (Interferon-β production and IFNAR signaling).



Pathology of lumbar motor neurons (MNs) following JEV and CHPV infection in mice. 10 day old BALB/c pups were either mock infected with PBS or inoculated intraperitoneally with $3X10^4$ PFU of JEV or $1X10^4$ PFU of CHPV in 25µl volume. Animals were examined daily and sacrificed at day7 pi JEV and day3 pi CHPV, when pups displayed complete hindlimb paralysis with difficult or no movement at all. Thin sections of 20µm thickness prepared from both mock-infected and virus-infected lumbar cord tissue, were examined using Nissl stain. A and C) Coronal lumbar-cord sections of respective age-matched control animal (Mock-infected) with red-outlined boxes representing enlarged image of anterior horn SC (spinal cord) with healthy MNs indicated by black arrowheads. B and D) Representative image of infected lumbar-cord sections upon JEV and CHPV infection with magnified area displaying dying MNs pointed by black arrows in respective image panels. Scale bar denotes 50µm and 200µm, Oil magnification. Data are representative of minimum three independent experiments performed.

Hence from our experimental observations, we have demonstrated that host innate antiviral response might play a critical role in deterioration of motor functioning and pathogenesis of flaccid paralysis upon neurotropic virus infections.

Publications

1. M Bhaskar, S Mukherjee, and A Basu (2021) Involvement of RIG-I Pathway in Neurotropic Virus-Induced Acute Flaccid Paralysis and Subsequent Spinal Motor Neuron Death. *mBio* 12(6):e0271221. (*Recommended article by Faculty opinions*)
2. D Vedagiri , D Gupta , A Mishra , G Krishna, M Bhaskar , V Sah , A Basu , D Nayak , M Veettil , K H Harshan (2021) Retinoic Acid Inducible Gene-I like Receptors Activate Snail to Limit RNA Viral Infections. *Journal of Virology* 3;95(21): e0121621.
3. S Sehrawat, R Khasa, A Deb, S Prajapat, S Mallick, A Basu, M Surjit, M Kalia, and S Vrati (2021) Valosin-containing protein/p97 plays critical roles in the Japanese encephalitis virus life cycle, *Journal of Virology* 95 :11 e02336-20

Presentations

1. A Basu Primary Cell Culture model: An excellent tool to study the effects of Viral Infection of CNS; 6th International Brain Research School, Suleyman Demirel University, Isparta, Turkey, 21-27 June 2021. (*on line mode*)
2. A Basu Innate Immunity in the central nervous system: Redefining the relationship between "Immune system" and "Nervous system" School of Life science, JNU, 31st July 2021. (*on line mode*)
3. A Basu Drug repositioning/repurposing: Promising strategy to develop therapy against viral infections; Annual Meeting of the Indian Academy of Sciences 12-14th November 2021. (*on line mode*)
4. A Basu Biosecurity: Developing a healthy Immune system. Ted^{X}XIMUniversity, 13th of February, 2022. (*on line mode*)
5. A Basu Molecular basis of virus-induced acute flaccid paralysis; Correlation with motor neuron dysfunction; INDO-US Symposium on Molecular Virology, IIT-Mandi; 15-17th February, 2022. (*on line mode*)
6. A Basu Modulation of Neural Stem/Progenitor Cells fate following Japanese Encephalitis Virus infection 6th International Anatomical Sciences and Cell Biology Conference, National University of Singapore, Singapore, 21-23 February 2022. (*on line mode*)

Funding

1. MicroRNA mediated regulation of neural stem/progenitor cell fate in neurotropic flaviviral infection (DBT), starting from 29/12/2017 for three. (got one year no cost extension) (BT/PR22341/MED/122/55/2016)] (completed)
2. Understanding the therapeutic role of adult stem cell derived exosome in combating virus induced neurodegenerative disease (DBT), Starting from 20/03/2018 for three years. (got one year no cost extenstion) (BT/PR15984/MED/31/325/2015) (completed)
3. Deciphering Antiviral Properties of Statins against Japanese Encephalitis Virus Infections (DBT). Starting from 26/12/2018 for two years. (got one year no cost extension) BT/PR27796/MED/29/1301/2018 (completed).
4. Elucidating the role of long non coding RNAs (lncRNAs) in neuronal cell death during Japanese Encephalitis (JE), Starting from 26/12/2018 for three years. (BT/PR126590/MED/122/113/2017).

5. J C Bose Fellowship (SERB), Starting from November 2021 for five years. (JCB/2020/000037)

Collaborators

- Pankaj Seth, and Arpan Banerjee, NBRC
- Sudhanshu Vrati, Prasenjit Guchhait, Manjula Kalia, and Arup Banerjee RCB, NCR Biotech Cluster, Faridabad
- Vivek Sharma, Department of Biological Sciences, Birla Institute of Technology and Science Pilani, Hyderabad Campus, Hyderabad

Awards

1. J C Bose Fellowship (SERB), 2021-2026
2. Drs. Kunti & Om Prakash Oration Award (Basic Sciences)- (Indian Council for Medical Research)-2020. (Declaration of the *award in Dec 2021*)

Degree awarded

Ankit Shah (MSc in Neuroscience)

Arpan Banerjee

Neuro-cognitive network mechanisms using multimodal neuroimaging

Post-Doctoral Fellows
Dr Soibam Shyamchand Singh
Dr Zinkal Shah
Dr Priyanka Chakraborty
Dr Suman Saha

PhD Students
Neeraj Kumar
Priyanka Ghosh
Anagh Pathak
Ritu Moni Borah
Nisha Chetna Shashtry
Kirti Saluja
Pratika Siwatch
Shahswati Tripathi
Guncha Bhasin

Project Assistants
Varun Madan Mohan
Shubham Singhal

Cognitive Brain Lab (CBL) is engaged in basic and translational research using non-invasive neuroimaging tools EEG, MEG, TMS & fMRI. We have primarily two themes of research: 1) Exploring and innovating novel research designs and analysis tools for MEG/ EEG & fMRI recordings and 2) Studying mental health and investigating various functional brain networks related to speech perception and in particular multisensory integration following the approved objectives of this project. Here we outline the major project updates from the period April, 2020 - March, 2021. The overarching goal of these projects is to develop an understanding for the neurobiological mechanisms of multisensory integration and basic sensory function. The three projects on which we have focussed are related to determining efficient tools for cortical source localization from EEG/ MEG data, investigating the spatiotemporal representational space of neuronal entrainment to tonal rhythmic stimulus and exploring multiscale models of human resting state brain activity.

Project 1: Stability of sensorimotor network sculpts the dynamic repertoire of resting state over lifespan

Temporally stable patterns of neural coordination among distributed brain regions are crucial for survival. Recently, many studies highlight association between healthy aging and modifications in organization of functional brain networks, across various time-scales. Nonetheless, quantitative characterization of temporal stability of functional brain networks across healthy aging remains unexplored. This study introduces a data-driven unsupervised approach to capture high-dimensional dynamic functional connectivity (dFC) via low-dimensional patterns and subsequent estimation of temporal stability using quantitative metrics (Figure 1). Healthy aging related changes in temporal stability of dFC were characterized across resting-state, movie-viewing, and sensorimotor tasks (SMT) on a large (n = 645) healthy aging dataset (18–88 years). Prominent results reveal that (1) whole-brain temporal dynamics of dFC movie-watching task is closer to resting-state than to SMT with an overall trend of highest

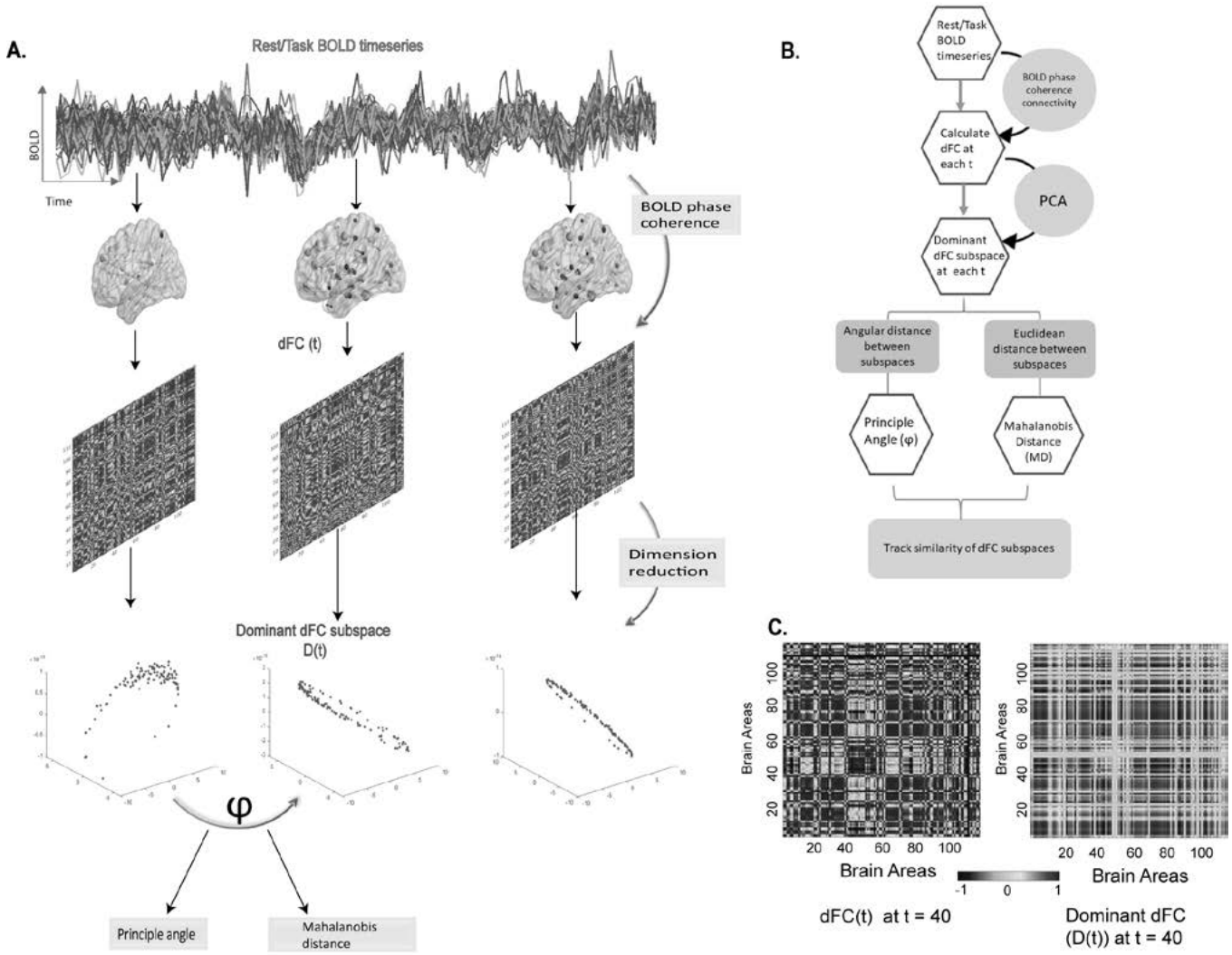


Figure 1: Brief overview of the unsupervised approach (A). The schematic diagram shows how the temporal stability of dynamic functional connectivity subspaces (dFC) are computed. Dominant dFC subspace, at each time point, is estimated using the first three principal components of dFC(t), that was computed using the measure of BOLD phase coherence. The similarity between dFC subspaces are calculated using Angular distance (principal angle) and Mahalanobis distance (Euclidean distance). If the dominant dFC subspaces are similar for extended timepoints, then they are considered to be stable. (B). A flowchart representation of the method (C). Matrix representation of dFC patterns (dFC(t)) and reduced Dominant dFC patterns (D(t)) at t=40.

temporal stability observed during SMT followed by movie-watching and resting-state, invariant across lifespan aging, (2) in both tasks conditions stability of neurocognitive networks in young adults is higher than older adults, and (3) temporal stability of whole brain resting-state follows a U-shaped curve along lifespan—a pattern shared by sensorimotor network stability indicating their deeper relationship. Overall, the results can be applied generally for studying cohorts of neurological disorders using neuroimaging tools.

Project 2: Spatiotemporal mapping of the neural markers of prediction error processing across multisensory and unisensory modalities

Prediction errors in the brain are indexed by two event-related potentials – MMN and P300, which are elicited upon violation of regularity in the occurrence of repetitive stimuli. While MMN reflects the brain's ability to perform automatic comparisons between consecutive stimuli and provides an electrophysiological index of sensory error detection, P300 is associated with cognitive processes such as update in working memory. Till date, there

has been extensive research on the roles of MMN and P300 individually, because of their potential to be used as clinical markers of consciousness and attention, respectively. However, the relationship between these two ERPs, specifically in terms of their underlying cortical generators, in context of prediction error propagation along the hierarchical brain across multiple modalities is an open question. Our objective in this article is two-fold. First, we reconfirm previous reports regarding the generators of MMN and P300 in sensor space through source-space analysis using an accurate individual subject level co-registration of MRI and EEG data collected from healthy humans. We demonstrate that in multisensory environments, MMN and P300 markers represent "modality-specific" and "modality-independent" information processing, respectively (Figure 2). Advancing an earlier understanding that multisensory contexts speed up early sensory processing, our study reveals that this temporal facilitation extends to even the later components of prediction error processing, using custom-designed experiments that allow comparisons across different modality combinations. Such knowledge can be of immense value in clinical research for determining the stages of various treatments in aging, schizophrenia and depression, and their efficacy on cognitive function.

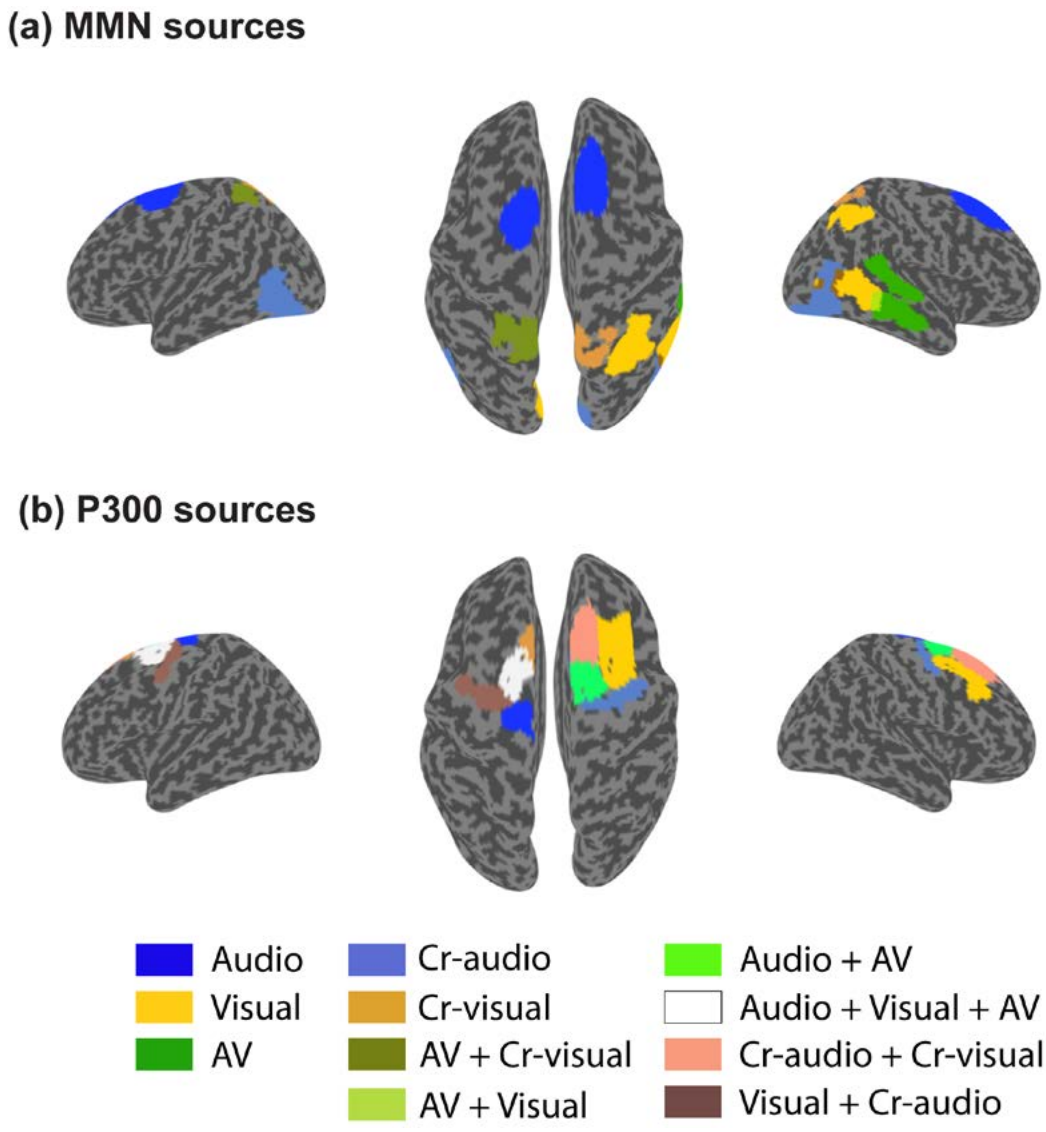


Figure 2: eLORETA source localization results using time locked analysis (at threshold level 95%) representing the underlying (a) MMN and (b) P300 sources for Audio, Visual,Audio-Visual, Cross-Visual and Cross-Audio modalities.

Publications

1. Sastry, N.C., Roy, D., & Banerjee, A. (2022): Stability of sensorimotor network sculpts the dynamic repertoire of resting state over lifespan. Cerebral Cortex, 1-22 https://doi.org/10.1093/cercor/bhac133

2. Thuwal, K, Banerjee, A. & Roy, D. (2021): Aperiodic and periodic components of ongoing oscillatory brain dynamics link distinct functional aspects of cognition across adult lifespan. eNeuro. 8 (5) ENEURO.0224-21.2021; DOI: https://doi.org/10.1523/ENEURO.0224-21.2021

3. Yazin, F., Das, M., Banerjee, A., & Roy, D. (2021) Contextual Prediction Errors Reorganize Episodic Memories in Time. Scientific Reports. 11(1). 12364. 1-17. https://www.nature.com/articles/s41598-021-90990-1

4. Naskar, A., Vattikonda, A., Deco, G., Roy, D., & Banerjee, A. (2021) Multiscale dynamic mean field model (MDMF) to relate resting-state brain dynamics with local cortical excitatory-inhibitory neurotransmitter homeostasis. Network Neuroscience 5 (3): 757–782 https://direct.mit.edu/netn/article/doi/10.1162/netn_a_00197/100794/Multi-scale-dynamic-mean-field-model-MDMF-relate.

5. Ghosh, P., Roy, D., & Banerjee, A. (2021) Psychophysical data to study the brain network mechanisms involved in reorienting attention to salient events during goal directed visual discrimination and search tasks. Data in Brief, 107020. https://www.sciencedirect.com/science/article/pii/S2352340921003048#!

Presentations

1. Dr. Arpan Banerjee: Brain, mind, and behavior: The ethereal triumvirate. Invited speaker for Brain Awareness week IISER Behrampore (March 2022)

2. Dr. Arpan Banerjee: Career in Sciences, DAV Model School, Durgapur. (Dec 2021)

3. Priyanka Ghosh: Distinct roles of MMN and P300 in processing prediction errors across modalities; *NeuroCog* , University of Louvain, Belgium

Recognition and Service

2022	Visiting Professor at Ashoka University (Spring semester), Taught Mind & Behavior
2021	Editorial Board Member, NeuroImage (Elsevier)
2021	Associate Editor, Frontiers in Computational Neuroscience
2021	Review Editor, Frontiers in Network Physiology & Frontiers in Brain Imaging Methods

Funding

- NBRC Core
- Department of Sports, Ministry of Youth Affairs & Sports (Feb 2019- Feb 2022) Early diagnosis and structural and functional decline of the brain and associated injuries in professional athletes playing contact sports.
- Department of Biotechnology, Ministry of Science & Technology. Flagship programme of NBRC: Comparative mapping of common mental disorders (CMD) over lifespan.

Collaborators

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- Ellora Sen NBRC
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Linking lifespan associated changes in brain dynamics and oscillations with cognitive functions using multimodal neuroimaging techniques

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Our Lab investigates the interaction among large-scale brain networks and dynamics during maturation or development of Cortex and healthy aging process. The methods and techniques employ to study attention, perception and different catergories of memory and executive functions involves multimodal neuroimaging (fMRI, EEG/MEG) and designing cognitive tasks to capture goal directed behavior. Moreover, using neuroimaging data acquired from Autistic and neurotypical controls we could disentangle the complexity associated with atypical developmental trajectory of executive functions and cognitive flexibility. Our key findings of linking core behavioural deficits such as repetitive and restrictive beahviour and speech, language processing disability as well as social responsiveness and neural flexibility of neurocognitive brain regions opened novel ways of understanding atypical neurodevelopment. We found several large-scale brain networks comprise of sensorimotor hand, face regions and higher order default mode, salience and central executive networks exhibited atypical neural flexibility going from children to adolescence to adulthood which provide us an opportunity to ask fundamental questions in Cognitive Neuroscience to uncover mechanisms and neural basis of sensory and higher order cognitive processing and Cognitive flexibility with age. A related but a slightly different concept lies within the area of synaptic plasticity and cortical development/maturation. Many of the neurocognitive theories of aging have argued that changes during aging process are either beneficial or detrimental. However, the field complete lacks a coherent account of how the dynamical changes in brain networks unfolds over multiple timescales EEG/MEG (fast time scale in the order of milliseconds to seconds) and fMRI (slow time scale in the order of multiples of seconds to minutes) due to topological reorganization and pruning in underlying stable structural scaffold which supports large number of major cognitive functions (perception, working memory, episodic memory, emotion processing, decision making etc.) throughout adult life span.

Atypical Brain Network dynamics, time-scale hierarchy, and core deficits in sensory and social cognition during Brain Development

One of the fundamental questions that our lab investigated by doing behavioural experiments, brain network mapping using fMRI, and quantifying brain network dynamics using Brain Electrical Signals using EEG is to examine the large-scale spatial and temporal interactions among brain networks and dynamics during abnormal maturation or development of the brain (autism spectrum disorder and ADHD). There are well documented stages from children to adolescence to adult lifespan which provide us an opportunity to ask fundamental questions in Cognitive and Computational Neuroscience to discover fundamental mechanisms and neural basis of atypical sensory and higher order cognitive processing and Cognitive flexibility in children, adolescence, and adults during typical and atypical development with age. One of the key dynamical processes that takes place in the brain is the interaction between core-periphery brain regions, which undergoes constant fluctuations associated with developmental time frames (see **Figure 1**). Core-periphery dynamical changes associated with macroscale brain network dynamics span multiple timescales and may lead to atypical behaviour and clinical symptoms. For example, recent evidence suggests that brain regions with shorter intrinsic timescales are located at the periphery of brain networks (e.g., sensorimotor hand, face areas) and are implicated in perception and movement. On the contrary, brain regions with longer timescales are core hub regions. These hubs are important for regulating interactions between the brain and the body during self-related cognition and emotion. In our recent work, we summarize a large body of converging evidence derived from time-resolved fMRI studies in autism to characterize atypical core-periphery brain dynamics and how they relate to core and contextual sensory and cognitive deficits exhibited by Autistic individuals.

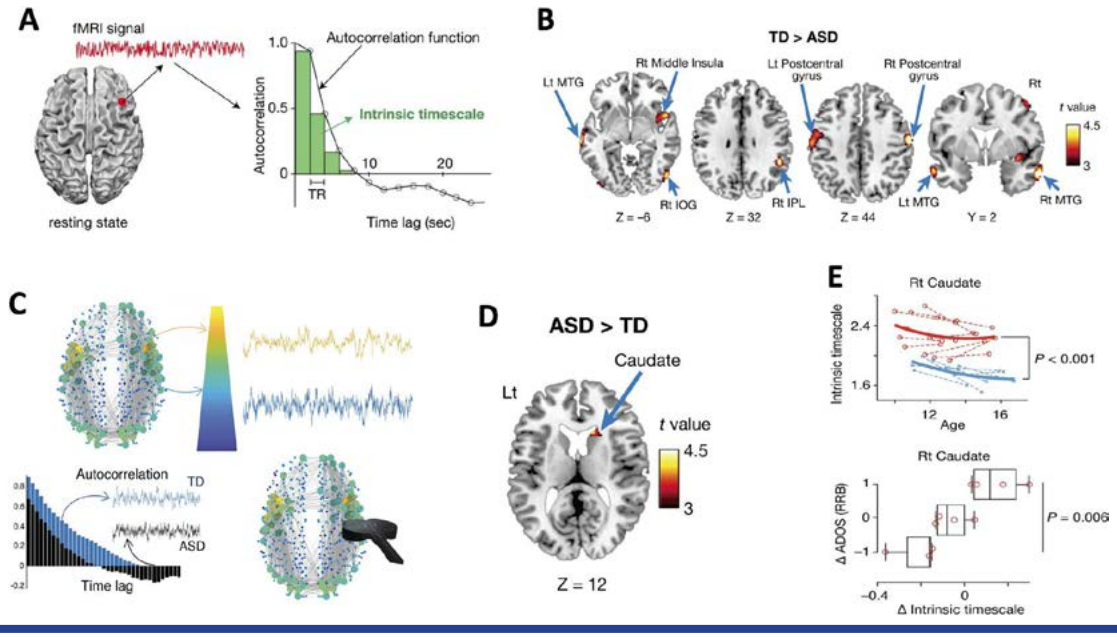

Figure 1. Atypical intrinsic neural timescale in autism. (A) Estimated neural timescale from fMRI BOLD signal, based on sum of autocorre- lation function. (B) Intrinsic neural timescales are plotted in bilateral middle insula, pre- and postcentral gyrus (exhibiting shorter timescales). (C) Brain core regions located at the top of the hierarchy are shown in large (yellow) circles and have longer timescales. Brain regions located at the periphery are represented by small (blue) circles and have shorter timescales. Individuals with autism spectrum disorders (ASD, black) have different intrinsic timescales (quantified by the autocorrelation function) compared with typically developing individuals (TD, blue). A schematic display that noninvasive brain stimulation (black coil) may be used to selectively modulate atypical brain regions to restore their intrinsic timescales. (D) Intrinsic neural timescales in the right caudate are longer in the ASD group compared with the TD group. (E) The intrinsic neural timescale in the right caudate is plotted as a function of age in TD (blue) and ASD (red) during adolescence and the correlation of intrinsic neural timescales with progression of RRB symptoms. Autocorrelation function, ACF; typically developing, TD; autism spectrum disorder, ASD.

Neural Substrates of Behavioral Variability in Autism: Predictions from Atypical Core-Periphery Dynamics

There are very few studies that have examined the relationship between age-related change in intrinsic functional connectivity and gender in ASD and TD. Many resting-state fMRI studies of autism have focused on characterizing intrinsic large-scale brain network organization in adolescent and adult males, barring a few studies that have given some consideration to both age and gender. A large majority of these studies found that ASD exhibits increased functional integration at the expense of decreased functional segregation. Based on our recent finding adolescents with ASD, there is a significant decrease in modularity, suggesting a less robust modular organization, and an increase in participation coefficient, suggesting more random integration and widely distributed connection edges. Modularity decreased nonlinearly in the ASD group with age, as evidenced by an increase and then a decrease over development. Age effects on modularity were localized to the somatosensory network. Furthermore, there is significant hypoconnectivity observed in the adolescent group, especially in the DMN, while children showed both hyper- and hypoconnectivity. Efficient functioning of specialized sensorimotor and cognitive networks relies on two complementary organizing principles: functional segregation (or differentiation), emphasizing the degree to which different regions or networks are specialized, and functional integration, referring to the communication between regions within a specialized network. The differential relationship between modularity and age seen in ASD was in a large part due to the peripheral networks (somato-sensorimotor and visual networks). This result from localization analysis suggests that the somatosensory network drives, at least in part, the increase in modularity across time seen in neurotypicals relative to those with ASD. Thus, differentiation and specification of regions related to the visual and somato-sensorimotor network appears to contribute greatly to functional connectivity changes across development. However, a network knockout approach was used to isolate the influence of specific functional networks, a simple leave-one-out process demonstrating that the somatosensory cortex had no effect on global efficiency models, which suggests that the differences in global efficiency between ASD and TD were not localized to the somatosensory cortex, but rather reflect a more global whole-brain phenomenon. Beyond revealing brain regions activated in response to specific task conditions, resting-state functional connectivity approaches permit analysis of how cognitive functions emerge from precise timing and concerted activity in the specialized large-scale brain network interactions. Dynamic functional connectivity (dFC) approaches further enable the study of moment-to-moment variability in neurotypical and autistic individuals, as documented by several of our recent studies. Furthermore, dFC variability is quantified by the standard deviation of time-varying dynamic functional connectivity. Hence, dFCVar tracks the changes in variability in dynamic functional connectivity between brain regions anchored in large-scale neurocognitive networks (see **Figure 2**). These measures are now frequently used to characterize atypical hyper- and hypofunctional connectivity variability in neurodevelopmental disorders.

Taken together, this work highlights the need for more targeted future research and investigation of the brain mechanisms at various stages of maturation in both male and female ASD to pinpoint subtypes of functional connectivity patterns across development linking adaptive behavior, cognitive flexibility, executive task processing, and manifestations of core and contextual deficits in ASD across the life span.

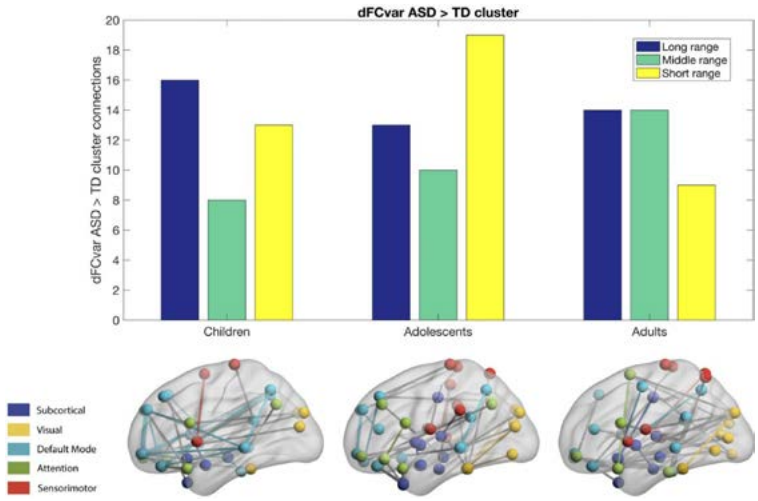

Figure 2. Hypervariant ASD connections estimated using dFCVar matrix. A large majority of connections in children are long-range, while the adults exhibit hypervariability in dFC in both middle- range and long-range connections. Adolescents are seen to have majority short-range connections exhibiting hypervariability.

Prediction Error and Memory Reactivation: How Incomplete Reminders Drive Reconsolidation with age

Another fundamental question that we have recently started investigating that is associated with healthy and pathological aging process is the relationship between episodic memory, prediction error and age associated alterations. Memories are labile and easily distorted. What contexts and conditions in daily life specifically allow acquired and encoded memories to be altered? Imagine that you see your favourite actor sitting in your chair while entering the office, much to your surprise. The memory of such an event would be harder to forget than other memories in the same office. Due to the low expectation of such events occurring within the given context, the substantial memory consolidation of this event displays the dependency of our day-to-day memories on the underlying context and predictive processes. Episodes or events being the canonical components of episodic memory are marked by a clear beginning and an end with temporal relations. As such, our memories are organized sequentially in contexts that evolve in time. However, whether and how unpredicted events can affect this temporal code of our experienced memories is something that surprisingly remains mostly unexplored. Converging evidence supports that prediction error, or surprise, as a key mechanism that renders memories malleable. A handful of reconsolidation studies have used incomplete reminders to elicit prediction error; retrieval cues that partially replicate an encoding experience or encoded memory trace to be distorted, updated, and strengthened. However, knowledge gap remains as to how encoded memory traces are updated and strengthen with aging? Our recent studies along key studies from other labs have recently begun to fully understand the underlying cognitive phenomenon providing demonstrative evidence that incomplete reminders in principle govern human memory updating, ranging from classical conditioning to naturalistic episodes. Through the proposed unifying theme of predictive coding, we argue that both animal and human reconsolidation research gain critical understanding by scrutinizing prediction error and incomplete reminders as key factors governing episodic memory consolidation and retrieval. These findings bear implications for pathological fear memories, false memories, misinformation, and their alterations during healthy aging process.

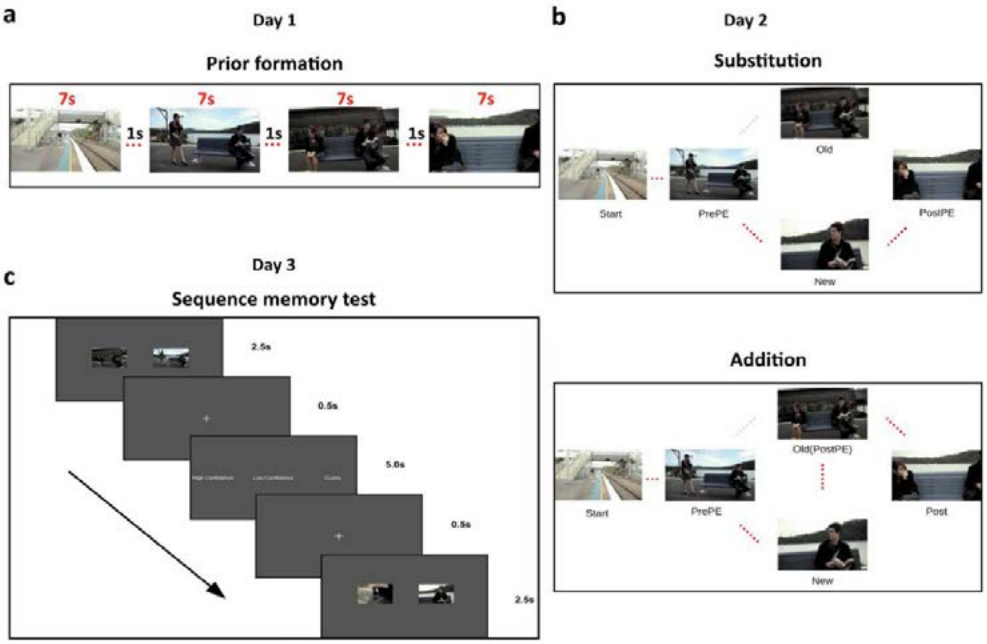

Figure 3. Experimental paradigm involving human episodic memory recall and role of contextual prediction error [14] studies have demonstrated that surprising and incomplete reminders influence many types of memory, from simple associations to naturalistic episodes. Participants watched two movies (divided into several different events having multiple segments) on Day1. On Day2, they saw the same movies in either two conditions— Substitution and Addition. Substitution had another contextually fitting segment substituting a prior encoded segment, while in Addition, the omitted segment is viewed again (after the prediction error). A sequence memory task of adjacent segments tested participants' temporal order memory for each event on Day3. **(a)** Example of an event seen on Day1. Each segment is 7 s with a 1 s blank screen in between (not shown). **(b)** Day2 conditions. Substitution (top) where participants were predicting a segment (Old) seen the previous day (faded red dots) while the actual segment (New) is a different one which fits with the context. Addition (bottom) which has the Old (predicted) segment re-experienced (hence reactivated) after the New segment induces the prediction error. Pre PE-Old temporal sequence memory is taken as Old sequence and Pre PE-New temporal sequence is taken as New sequence. **(c)** Schematic of Day3 Sequence memory test block. Each sequence was shown by displaying representative screenshots of those segments involved (in both normal and reverse order). Participants had to choose the correct order of the segments in the order they saw in the movie.

Prediction errors reorganize temporal episodic memories

A core property of episodic memory is the sequential arrangement of the events and how they occurred in their respective contexts. A context in its simplest form is described as an aspect of the episode that binds its constituent elements together, be it spatial, temporal, or conceptual. Daily life involves numerous instances where multiple different events share the same context. For example, the recent trends of online classes by school children at home involves encoding different kinds of memories (subjects) in the same context. The Temporal Context Model (TCM) of memory posits that such memories sharing the same temporal context are encoded separately, creating source confusion during memory recall. Memories of items shared in the same context have been observed to be weakened. An important line of work termed reconsolidation can also explain this. According to this, the older memories get updated due to a prediction error. This is demonstrated behaviourally by an asymmetric intrusion of memories in the same context during recall. However, a recent theory that builds on and unites many theoretical frameworks of memory proposes contextual binding as a unified mechanism with the hippocampus playing a central role in item and context binding. In addition to hippocampal associative learning mediating context representation, this theory also posits that forgetting occurs mainly due to contextual interference from shared memories. The hippocampus, interestingly, is also predictive in nature and is sensitive to prediction mismatches. These viewpoints set

up testable hypotheses on how interactions between these two properties affect episodic memories, particularly by incorporating the role of time in them.

In the present study, we test the hypothesis that the contextual prediction errors would fundamentally alter the memorized sequence of events. Specifically, sequences that did not match predictions in a context would be weakened. Concurrently, the newly encoded sequences that were seen instead would be strengthened. From the perspective of predictive coding surprising new information that violates expectations drives stronger learning. These newly formed sequences would be strengthened over older encoded sequential information to minimize future errors. Our key finding is that contextual prediction errors strengthen the newer memory sequences in time while weakening the order of previously encoded sequences, thereby reorganizing encoded temporal memories. This enhanced performance, reflected by faster reaction times, on subsequent modelling showed that it results from a lower decision threshold while remembering, signifying a more automatic response for the newer sequences. Critically, even the re-exposure of mispredicted segments in an event, later, did not exempt it from getting weakened while recalling. Collectively our findings reveal how prediction errors play a crucial role in determining how episodic memories are organized in time.

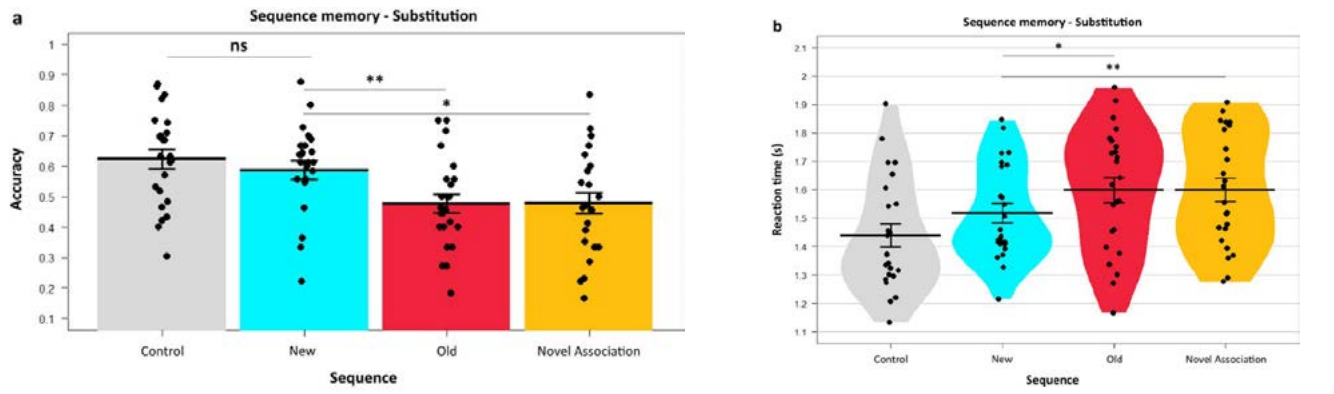

Figure 4. Effect of prediction errors on temporal order memory in substitution. In *Substitution*, New event is formed after a prediction error (surprise), when participants were expecting a previous sequence (Old). (**a**) Memory accuracy performance showing a significant difference between New and Old sequence for temporal order judgement. No significant difference in accuracy between New and Control sequences was observed. (**b**) Reaction time data reflecting the main result of accuracy between New and Old sequence. Dots represent participants' individual performance (n=24). Error bars denote SEM.

Multivariate Bayesian regression confirms the behavioural results

To better estimate and provide more substantial evidence to these findings, we deployed a multivariate hierarchical Bayesian model that contained both the Accuracy and Reaction time as the outcome variable. This model could capture the main effect of Addition and Substitution, and that of all four types of Stimuli, in addition to the interaction effect of each of these two predictors. Furthermore, both the population level variance and participant level variance are integrated into a single multidimensional model. The latter is achieved by allowing the coefficients to vary across the participants hierarchically. It is essential to point out that such a model helps capture the covariance among the response variables to estimate the standard error correctly. Since it comes from a single distribution, any exaggerated memory effects of specific sequences are automatically taken care of due to the partial-pooling effect. Simulated posterior predictive distributions (1000 draws) showed a good fit in reproducing the observed data distribution for accuracy and response times. One-sided Bayesian hypothesis testing performed here ('contrasts' in the

general linear model scheme) is the posterior probability under the hypothesis against its alternative. This posterior is analogous to a one-tailed *p*-value, except that it shows a 90% CI instead of the usual 95%. Consistent with the empirical results, the regression results support the main finding that New and Old sequences show differential effects in memory performance measures depending on the Condition in which they are experienced. One-sided Bayesian hypothesis testing revealed a high posterior probability for New sequence accuracy over Old in *Substitution* ($p=0.98$, Estimate = 0.11, 90% CI [0.03 0.19]) (Fig. 5a, top). This hypothesis importantly had much less posterior probability in *Addition* New vs. Old sequence accuracy ($p=0.85$, estimate = 0.05, 90% CI [−0.03 0.13]) (Fig. 5b, top). In concordance with the behavioural results, reaction times showed high posterior probabilities of the Old sequence having a longer response duration than the New sequence. This result was demonstrated in *Substitution* ($p=0.95$, estimate = −0.08, 90% CI [−0.16 0]) (Fig. 5a, bottom) as well as in *Addition* ($p=0.98$, estimate = −0.1, 90% CI [−0.17 −0.02]) (Fig. 5b, bottom).

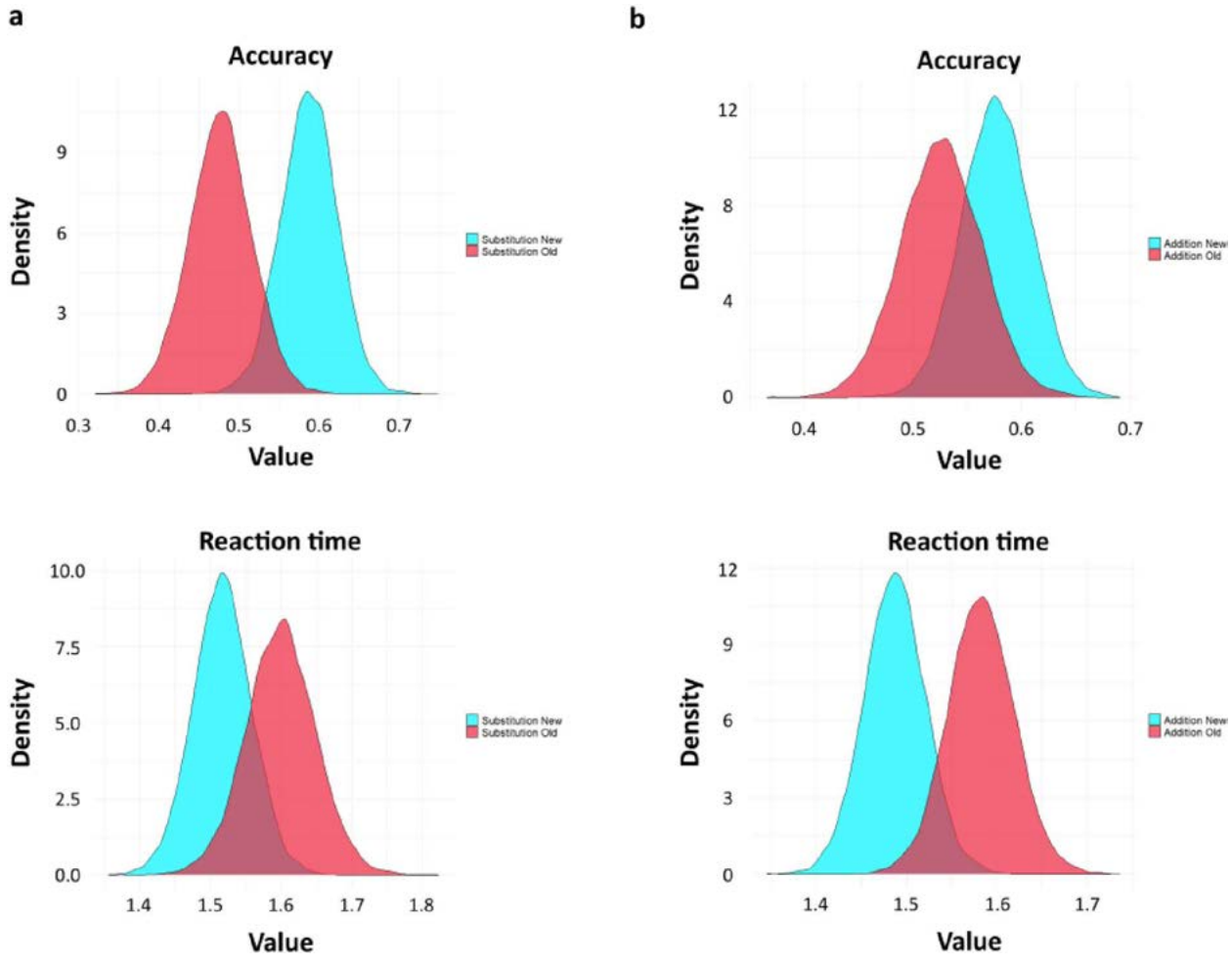

Figure 5. Posterior density estimates and Bayesian hypothesis testing. Posterior estimates of the main effects of temporal order memory. Bayesian hypothesis testing performed here is the posterior probability under the hypothesis against its alternative and is analogous to a one-tailed *p*-value. (**a**) Substitution. (Top) Posterior density estimates of the New and Old sequence showing high evidence of higher accuracy for the New sequence ($p=0.98$). (Bottom) Reaction times showing high evidence for New sequences being faster to recall than Old ($p=0.95$). (**b**) Addition. (Top) Much less evidence for the hypothesis that accuracy for the New sequence is more than the Old ($p=0.85$). (Bottom) Reaction times showing substantially more evidence for New sequences being faster to recall than Old ($p=0.98$).

Aperiodic and periodic components of ongoing oscillatory brain dynamics link distinct functional aspects of cognition across adult lifespan

In one more recent study, we have investigated spontaneous brain oscillations during healthy aging and their impact on memory, perceptual processing, and attentional control. MEG resting state and task data collected from young adults (18-35 years), middle young (36-50 years), Middle late (51-65 years) and elderly (66-88 years) across four critical stages of adult lifespan**.** This investigation was driven by a fundamental question of resilience and vulnerability of neurocognitive networks and cognition with age. Healthy ageing brain exhibits gradual deterioration of structure and yet surprisingly maintains reasonable cognition. These structural changes are often accompanied by the reorganization of functional brain networks. The field still lacks a coherent account of how the dynamical changes in the functional brain networks unfolds over multiple timescales EEG/MEG (fast time scale) and fMRI (slow time scale). Despite the topological reorganization and pruning in underlying stable structural scaffold that supports cognitive functions in multiple domains e.g., working memory and Attention, Language and speech processing, Episodic memory, Emotion processing, Executive Control and Decision making throughout adult life span. We tend to depart from conventional approach of age wise classification of trends with aging, rather, we track the variability in local and global network dynamics. Using neural noise hypothesis/ variability of brain signals employing a multimodal approach using both MEG and fMRI along with computational modelling we systematically address subject-wise variability and their relationship with cognition and memory across lifespan.

Visual Short Term Memory stimuli and task

In Cam-CAN, the design was adapted from Zhang and Luck 2008 study (see **Figure 6**). On each trial, participants were presented with one, two, three, or four colored discs (mimicking different memory load conditions) for 250 ms. Following that, a blank screen was presented for 900 ms to hold those colors in memory. One of the original locations was highlighted by a thick black border (acting as a probe for participants to remember the color at that location), and at the same time, a response color wheel was presented. Participants had as much time as required to report by touching or clicking, as accurately as possible the remembered hue of the highlighted disk. No feedback was given. After every trial, there was 830-ms fixation period. Participants complete two blocks of 112 trials, with memory load (1, 2, 3, or 4) counterbalanced and randomly intermixed. For each set size (memory load), four different measures were estimated by fitting the error distribution with a mixture model of von Mises and uniform distributions. In brief, as a model-free index of performance, the response error, the angular difference between the target color presented and the color reported, was calculated. This model-free index cannot be used to distinguish errors because of imprecise memory of an item, from errors because of reporting the wrong item, or guessing when an item is not kept in memory at all. To estimate these, Maximum likelihood estimation was used to decompose the data from each subject into three parameters that represent a mixture of a uniform distribution of errors and a von Mises distribution of errors. The von Mises distribution is the circular analog of the Gaussian distribution and was used because the tested color space was circular. The uniform distribution was represented by a single parameter, P_m, which is the probability that the probed item was present in memory at the time of the probe. K is calculated by multiplying the memory load by P_m. The von Mises distribution was represented by two parameters, its mean (μ) and its Standard Deviation (SD); μ reflects any systematic shift of the distribution away from the original color value. The "precision" of each item held in memory is reported as the reciprocal of the SD of the fitted von

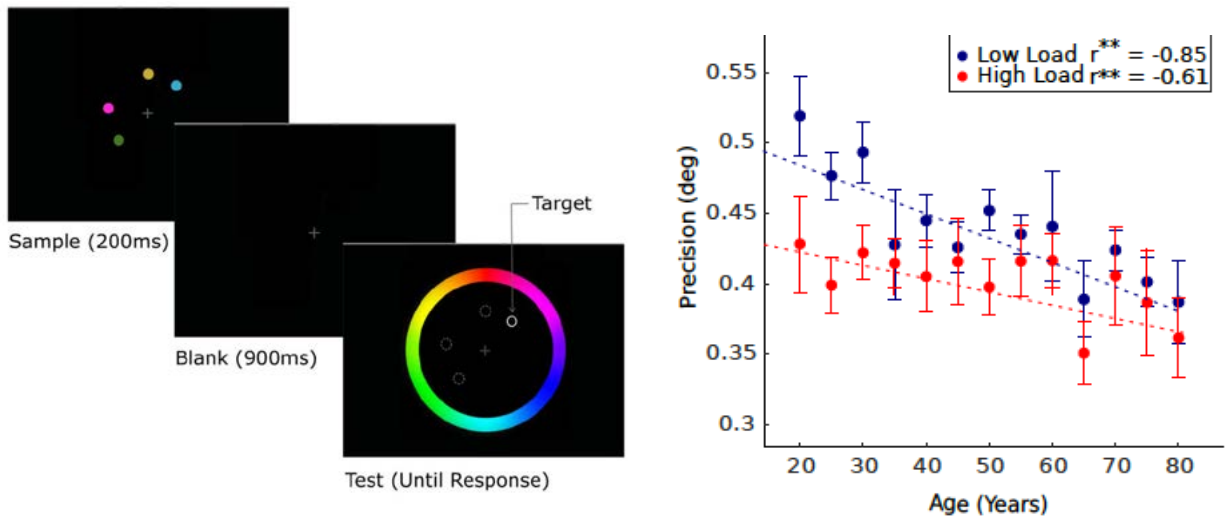

Figure 6. Experimental design of color recall Visual Short-Term working memory task and accuracy of memory recall in young and elderly group of participants.

Mises distribution. Subjects indicated their uncertainty in their choice of color by the length of time they touched the wheel: as they held their finger down, white confidence intervals spread out around the selected point indicating greater uncertainty about their selection. To assess metacognitive awareness, the angular width of the reported confidence intervals provided a trial-by-trial measure of subjective uncertainty. To summarize overall uncertainty for each individual and condition, the mean was taken across trials. Participants with smaller values thus reported more confidence in their responses.

Topographical Distribution of Frequency Band Ratios with age

Band Ratio (BR) measures have been argued to be a marker of various cognitive measures in healthy adults as well as in pathologic conditions which also gets affected by 1/ frequency (1/f) activity. We investigated how these global BRs change with age after effectively removing the background 1/f activity. We looked at θ/α, θ/β, and α/β BRs, where the ratio of all periodic features (PW, CF, BW) was analyzed for each frequency band. For all BR measures, we calculated correlations between the spectral features of each oscillation-band and age. Here, we showed the global change (averaged across all sensors) in the BR measures across the lifespan.

The age-associated nonlinear change was mostly observed in frontal and parietal sensors (see **Fig 7A**). For age categories, we found a significant difference between OA versus ME ($t_{(134)}$=2.38, p=0.018), OA versus ML ($t_{(134)}$= 3.19, p=0.0018), YA versus ME ($t_{(138)}$=3.30, p=0.0012), and YA versus ML ($t_{(138)}$=4.09, p=0.00007). For the CF ratio, we found α/β ratio to vary nonlinearly (quadratic) with age (β_1 = −0.0059138, R^2 = 0.61 p=0.005), whereby first decreases for middle age and subsequently an increase for older age participants suggesting an overall U-shaped response of α/β ratio through lifespan (see **Fig 7B**).

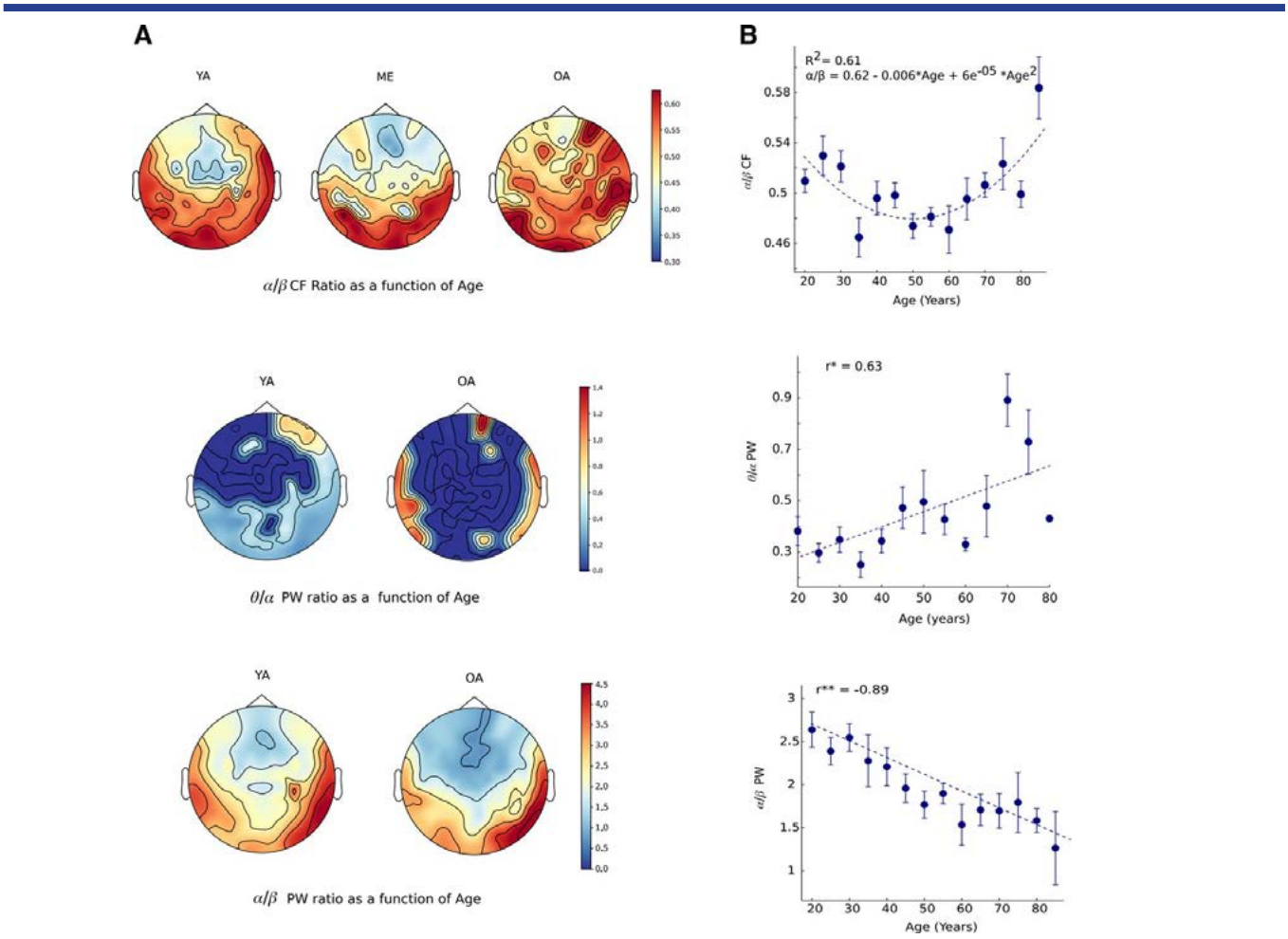

Figure 7. Spatial topography of BR measures as a function of age. (A), Spatial topography of α/β PF ratio (α/βα/β CF; top), α/β power ratio (α/β PW; center), and θ/α power ratio (bottom) for young (YA) and old adults (OA). (B), Regression fit model for each of the ratio measures keeping age as an explanatory variable. Error bar represents SEM. R2 represents goodness of fit, and r represents the correlation coefficient.

Predicted central frequency, power, band ratio and exponent relate to different aspects of cognition in the memory task

Using three different measures (aperiodic 1/f slope and offset, Peak Frequency, and Band Raito of power in various frequencies), we have systematically investigated the spontaneous temporal dynamics and dynamical changes during resting state associated with healthy adult lifespan. Subsequently, we have demonstrated how these measures potentially link distinct behavioral responses during short-term working memory processing. Many previous studies in aging literature have demonstrated that task-relevant oscillatory changes accurately demarcate task performance in various cognitive domains. As the resting-state serves as a baseline/control for the diverse task-related changes, it is crucial to characterize how specifically aging alters the normative brain network dynamics to impact cognition.

Significance and implications:

- Our study provides **MEG oscillatory and aperiodic markers** across the healthy adult lifespan.
- Shows how different frequency bands and their **spectral features mediate age-related changes, in multiple cognitive and metacognitive domains,** which not only provides us with a better understanding of the ageing process but

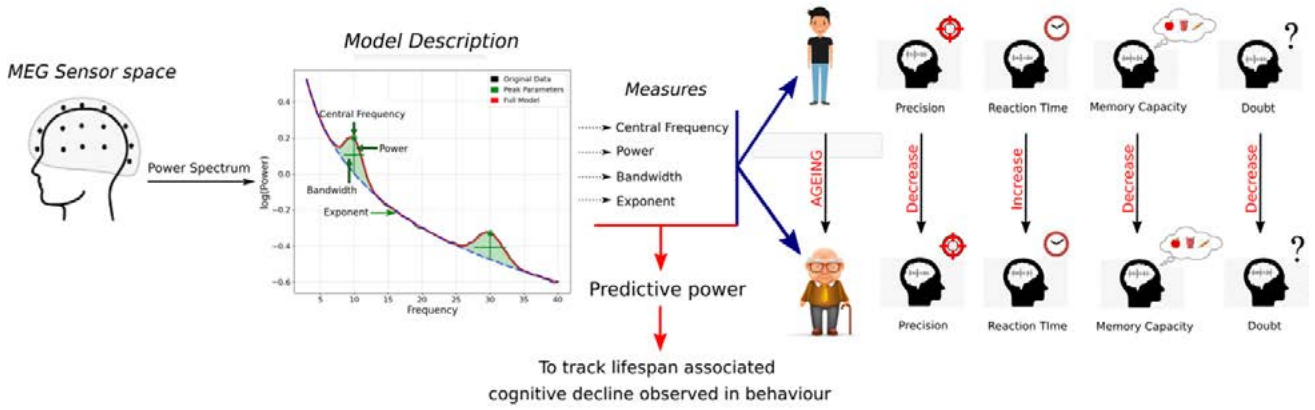

Figure 8. Schematics of how lifespan associated ongoing oscillatory periodic and aperiodic features of power spectrum links distinct aspects of cognition precision, reaction time, memory capacity and metacognitive awareness (self-doubt towards accuracy of response in behavioural task)

would also **help in better prevention of cognitive impairments.**

- All the measures proposed in this study together can track vast majority of **changes associated with healthy and atypical neurodevelopment** and healthy and pathological aging conditions under a variety of task settings which is important for **developing non-invasive biomarker in future clinical applications.**

Publications

1. Thuwal, Kusum, Arpan Banerjee, and Dipanjan Roy**.** "Aperiodic and periodic components of ongoing oscillatory brain dynamics link distinct functional aspects of cognition across adult lifespan." Eneuro 8, no. 5 (2021).

2. Yazin, Fahd, Moumita Das, Arpan Banerjee, and Dipanjan Roy. "Contextual prediction errors reorganize naturalistic episodic memories in time." *Scientific reports* 11, no. 1 (2021): 1-17.

3. Naskar, Amit, Anirudh Vattikonda, Gustavo Deco, Dipanjan Roy, and Arpan Banerjee. "Multiscale dynamic mean field (MDMF) model relates resting-state brain dynamics with local cortical excitatory–inhibitory neurotransmitter homeostasis." *Network Neuroscience* 5, no. 3 (2021): 757-782

4. Ghosh, Priyanka, Dipanjan Roy, and Arpan Banerjee. "Organization of directed functional connectivity among nodes of ventral attention network reveals the common network mechanisms underlying saliency processing across distinct spatial and spatio-temporal scales." *Neuroimage* 231 (2021): 117869.

5. Ghosh, Priyanka, Dipanjan Roy, and Arpan Banerjee. "Psychophysical data to study the brain network mechanisms involved in reorienting attention to salient events during goal-directed visual discrimination and search tasks." *Data in Brief* 36 (2021): 107020.

6. Roy, Dipanjan, and Lucina Q. Uddin. "Atypical core-periphery brain dynamics in autism." *Network Neuroscience* 5, no. 2 (2021): 295-321.

7. Das, Moumita, Vanshika Singh, Lucina Q. Uddin, Arpan Banerjee, and Dipanjan Roy. "Reconfiguration of directed functional connectivity among neurocognitive networks with aging: Considering the role of thalamo-cortical interactions." *Cerebral Cortex* 31, no. 4 (2021): 1970-1986.

Presentations

1. D. Roy Invited Speaker Psychology Departmental seminar series at Ashoka University "Lifespan associated change in coherent communication and behavior and cognitive processing" 03rd December 2021

2. D. Roy Invited Speaker Cognitive Science Colloquium series at IIT Delhi Cognitive Science Department 29th October 2021.

Funding

1. Role of Default Mode Network in Cognitive functions BT/RLF/Re-entry/07/2014 Department of Biotechnology (DBT) Ramalingaswami Re-entry fellowship 2016-2021

2. Oscillatory Network Dynamics in Perceptual Learning SR/CSRI/21/2016 Department of Science and Technology (DST) 2017-2021

3. BT/MED-III/NBRC/Flagship/Program 2019 Government of India Ministry of Science and Technology, Department of Biotechnology (DBT) for phase-I three years 2019-2022

4. NBRC Core fund and computational facility

Collaborators

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Ellora Sen

Metabolism-Inflammation cross-talk in Glioblastoma: Implications in tumor progression

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Background and significance

Cancer cells reprogram their metabolism for sustaining the increased bioenergetic and biosynthetic demands. Importantly, inflammation is an important contributing factor in cancer development, and a dynamic network of metabolic adaptations and inflammatory responses drives tumor progression. Glioblastoma multiforme (GBM) - the most malignant of brain cancers is largely refractory to current therapeutic regimens. Despite evidences indicating the close relatedness of metabolism and inflammation through sharing of common signaling molecules, the molecular link connecting these two crucial drivers of tumor progression remains largely elusive. We use multipronged approaches involving epigenetics, biochemistry, immunology and cell biology to provide mechanistic insight into the dynamic interaction between metabolic reprogramming and inflammation.

1. As desynchronized circadian rhythm in tumors is coincident with aberrant inflammation and dysregulated metabolism, their inter-relationship in cancer etiology was investigated. Our findings suggest that the metabolite Lactate (**L**), inflammatory cytokine ILIβ (**I**) and cellular circadian CLOCK **(C)** are linked together in a feed forward mode of regulation in glioma cells. This novel **LIC** (Lactate-Inflammation-Clock) regulatory network sustains the pro-tumorigenic factors and aid proliferation of cancer cells. The LIC circuit was not only observed in several cancer types, but significant correlation of LIC circuit with patient survival and anti-cancer drug sensitivity was noted. By demonstrating that cancer cells sustain proliferative signals through LIC feed-forward regulatory loop, this study suggests the importance of chronotherapy in cancers *(Gowda et al, Molecular Cellular Biology, 2021).*

2. Somatic mutations in the isocitrate dehydrogenase 1 (IDH1) gene in glioma have been associated with better prognosis than those harboring wild-type IDH1. Mutation in IDH1 (IDH1-MT), leading to the production of oncometabolite D-2-hydroxyglutarate (2-HG) from α-ketoglutarate, is associated

with better prognosis in glioma. Yes-associated protein 1 (YAP1) – an important regulator of tumor progression was found to be involved in altering mitochondrial dynamics, increasing ROS generation and extranuclear shuttling of TERT into mitochondria to affect redox homeostasis in IDH1-MT glioma. By showing a novel role of YAP1 in regulating mitochondrial dynamics, our study suggests that the altered mitochondrial function and redox status in IDH1 mutant gliomas have clinical relevance pertaining to their sensitivity to oxidative stress inducers. As IDH1-MT in glioma patients is a predictor of better responsiveness to drug treatments, integrating YAP1 inhibitors together with regulators of nuclear-mitochondrial TERT shuttle has important implications for determining the sensitivity of both IDH1 WT and IDH1 R132H cells to ROS stressors. *(Patrick S et al, Journal of Cell Science 2021 PMID: 34651186).*

3. We have highlighted the role of ATPase domain of chromatin remodeller BRG1 in regulating redox homeostasis and sensitivity to oxidative stressors in glioma cells. Created by BRG1 mutation vulnerability to elevated ROS levels can be therapeutically exploited, with ROS stressors as a promising therapeutic target for the treatment of BRG1-mutant cancers. *(Gowda P et.al., Neurochemistry International, 150:105189.*

4. Keeping the current COVID-19 pandemic in perspective, we investigated whether the cytopathic effects of viral proteins lead to exaggerated inflammatory responses, and identify molecules that could inhibit cytokine storm as well as viral replication. Our findings suggested the multi-pronged ability of anti-inflammatory Methotrexate to mitigate SARS-COV2 viral protein induced lung cell death and attenuate cytokine release. Collectively, these findings suggest that Methotrexate might constitute a viable therapeutic option in patients with SARS-CoV-2 infection. *(Gowda P et.al., Inflammation, 45(1):172-179 and Cytokine, 142: 155496).*

Publications

1. Patrick S, Gowda P, Lathoria K, Suri V, Sen E. (2021) Diminished YAP1 affects mitochondrial dynamics in IDH1 mutant glioma. *Journal of Cell Science, 134(22): jcs259188.*

2. Gowda P, Lathoria K, Sharma S, Patrick S, Umdor SB, Sen E (2021). Rewiring of lactate-IL-1β auto-regulatory loop with Clock-Bmal1: A feed-forward circuit in glioma. *Molecular and Cellular Biology, 41(9):e0044920.*

3. Gowda P, Lathoria K, Umdor SB, Sen E (2021). Brg1 mutation alters oxidative stress responses in glioblastoma. *Neurochemistry International, 150:105189.*

4. Gowda P, Patrick S, Joshi SD, Kumawat RK, Sen E (2021). Repurposing Methotrexate in dampening SARS-COV2-S1 mediated IL6 expression: Lessons learnt from lung cancer. *Inflammation, 45(1):172-179.*

Presentations

1. Ellora Sen: "Molecular Clock in Linking inflammation-metabolism axis in cancers". Amity University Manesar, 16th April 2021

2. Ellora Sen "Inflammation in diseases". National webinar on diversity in zoology - classical and modern. Dept. of Zoology, Mithibai College, Mumbai 28th July 2021

3. Ellora Sen "Influence of dysregulated metabolism on immune evasion and cellular circadian rhythm in glioma" Cell and Molecular Biology Seminar Series, IISER, Kalyani 14th August, 2021

4. Ellora Sen "Reprogramming the tumor microenvironment: Implication in cancer therapy". World Cancer Day, 4th Feb 2022, CNCI Kolkata

5. Ellora Sen "Epiphany of the Self: Identity with pure existent". Concept of Consciousness: Neuroscience & Indian Philosophical Perspective. Organized by Centre for consciousness studies NIMHAS & Indian Council of Philosophical Research (ICPR), September 2021.
6. Ellora Sen "Viewing Women Leadership in Science through the lens of Existential philosophy". International Conference on "Women's Leadership in Science and Technology" NIT, Durgapur, October 2021
7. Ellora Sen "Resurgence of Ayurveda: Sharing the learning." Vigyan Sarvatra Pujyate, Azadi ki Amrit Mahotsav, Kurukshetra Feb 28, 2022
8. Ellora Sen Women in Science: Dethroning the myth of Femininity. Women's day 2022, IITR Lucknow
9. Ellora Sen Existentialism and the future of Women Leadership in Science. Women's day 2022, NBRC

Funding

- Inflammation regulated metabolic reprogramming: Implications in tumor progression. Unit of excellence in cancer biology DBT. (#BT/MED/30/SP11016/2015)
- Early diagnosis of structural and functional decline in brain circuits stemming from traumatic brain injuries in professional athletes playing contact sports. Ministry of Youth Affairs and Sports. (K-15015/42/2018/SP-V, February 2019)

Collaborator

- Dr. Vaishali Suri. Professor, Neuropathology Dept. of Pathology, All India Institute of Medical Sciences, New Delhi

Awards

- Haryana Vigyan Ratna Award. Department of Science and Technology, Govt. of Haryana, 2021. Awarded in 2022
- SERB-POWER (Promoting Opportunities for Women in Exploratory Research) Fellowship, 2022

Degrees awarded (PhD)

Pruthvi Gowda (Thesis: Influence of dysregulated metabolism on genes associated with immune-evasion and cellular circadian rhythm in glioma)

Pankaj Seth

Novel Insights into Cellular and Molecular Mechanisms of HIV-1, Zika and SARS-CoV2 Virus Induced Neuropathogenesis

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Virus induced neuronal damage often leads to neurocognitive deficits or compromised brain functions. Several neurotropic viruses such as Human Immunodeficiency virus -1 (HIV-1), Zika virus (ZIKV) have been of interest to our laboratory as they cause neurological disorders in patients. HIV-1 induced neurocognitive and motor impairments are reported in HIV/AIDS survivors. The ZIKV infection of mothers in their first trimester of pregnancy often leads to birth of infants with abnormally small head size, or microcephaly. This results in irreversible impairment of neurological functions. More recently, the novel coronavirus SARS-CoV2, the causative agent of COVID-19 pandemic has also been associated with Brain Fog reported in Long COVID cases. Brain Fog is characterized with lack of concentration, headache, difficulty in focusing, memory recall and several other neuropsychiatric disorders. The prevalence of Brain Fog / NeuroCOVID has been reported to be around 30-40% of Long COVID patients, which is alarming. Collectively, the burden of virus induced neurological complications has long-term implications in survivors even after recovery from the infection. This has necessitated in-depth investigations into cellular and molecular mechanisms of virus induced neuronal damage. Our laboratory has carved a niche into this area and contributed immensely into understanding of the molecular basis and cellular mechanisms of HIV-1, Zika and more recently SARS-CoV2 induced neuronal damage.

The laboratory has also developed several *in vitro* models comprising human brain cells. We have overcome the challenges of finding alternative for animal models, specially where we study human specific viruses, such as HIV-1, and utilized primary cultures of human brain cells in an attempt to develop physiologically relevant experimental models that represent the disease, as close as possible. In that direction, the laboratory has developed a well characterized model of primary cells of human brain derived neural stem cells (hNSCs). From these hNSCs, we regularly differentiate human astrocytes, neurons and oligodendrocytes. Utilizing these cells, we developed a two cell model of human blood brain barrier (BBB) with primary cultures of human brain microvascular

endothelial cells (BMECs) and hNSCs derived human astrocytes. The integrity of the BBB was assessed by high Trans Endothelial Electrical Resistance (TEER), and inability of fluorescence dye across the barrier. We have employed the two-cell BBB model of human origin for studying the effects of ZIKV proteins induced alterations in tight junction proteins and identifying microRNAs (miRNA) that alter BBB integrity following exposure to ZIKV viral proteins. We have also employed these *in vitro* models to identify which pathways of neuronal damage are triggered by SARS-CoV2 viral proteins with an aim to understand the molecular and cellular mechanisms that may be contributing to Brain Fog.

Zika virus is an enveloped *Flavivirus* belonging to family *Flaviviridae.* Previously, our laboratory has demonstrated that the envelope (E) protein of the virus that is involved in interaction with host surface receptors for facilitating the viral entry, significantly impacts the stemness of the hNSCs through alterations in the miRNA circuitry and affects the Wnt, NOTCH and Pax3 pathways. Taking this work further, we have now demonstrated that ZIKV E- protein modulates the miR-204-5p/Wnt axis to impact the proliferation and causes immature neurogenesis that may contribute to the microcephaly seen in infants born to mothers infected with ZIKV. Our work with BBB has also provided novel findings that suggest that the ZIKV E protein is affecting the expression of tight junction proteins such as ZO-1, Claudin and Occludin, and hence altering the BBB integrity. This was studied in an *in vitro* contact-based co-culture of human BBB model using transwell apparatus. A downregulation of genes involved in endothelial homeostasis were also observed in our experiments, that may further contribute to the impairment of BBB functions.

To study the effect of other non-structural proteins (NS) on human brain cells, we are studying the effect of NS-4A and NS-4B by co-transfection of these proteins in hNSCs and human astrocytes. Our experiments so far have revealed novel mechanisms, including autophagy, that are influencing the self-renewal properties of hNSCs and resulting in activation of astrocytes. Similarly, in-depth studies with SARS-CoV2 proteins are in progress in human neurons and several viral proteins have been identified that are contributing to the neuronal damage through non-apoptotic pathways. The *in vitro* findings of the SARS-CoV2 proteins are being validated in post-mortem brain sections of COVID-19 cases. Detailed experiments are in progress.

Our studies with HIV-1, Zika and SARS-CoV2 suggest that while most viral proteins may lead to glial activation and subsequent neuronal damage, the molecular pathways are different. Insights into these pathways and identification of miRNAs that are driving virus induced degeneration will help attenuate astrocyte-mediated neuronal damage and hopefully reduce post-infection neurological complications.

Publications

1. AK Sarkar, K Debnath, H. Arora, P. Seth, NR. Jana and NR Jana (2022). Direct Cellular Delivery of Exogenous Genetic Material and Protein 2 via Colloidal Nano-Assemblies with Biopolymer. ACS Applied Material and Interfaces January 14(2): 3199-3206, 2022. doi.org/10.1021/acsami.1c22009

2. HS Pandey, R. Kapoor, Bindu, and P. Seth (2021). Coronin 1A facilitates calcium mobilization and promotes astrocyte reactivity in HIV-1 Neuropathogenesis. FASEB BioAdvances October 4: 254-272, 2021. doi: https://doi.org/10.1096/fba.2021-00109

3. *R.* Bhagat, P. Rajpara, G. Kaur, K. Gupta and P. Seth (2021). *Zika virus E protein dysregulate mir-204 WNT2 signalling in human fetal neural stem cells.* Brain Research Bulletin November 2021, 176: 93-102. 10.1016/j.brainresbull.2021.08.009.

4. CMS Singal, P. Jaiswal, A. Mehta, K. Saleem and P. Seth (2021). Role of EphrinA3 in HIV-1 neuropathogenesis. Am Society of Neurochemistry – Neuro 13: 1-15, 2021. doi: 10.1177/17590914211044359

5. R. Chaudhuri, H. Arora and P. Seth (2021). Mitochondrial calcium signaling in the brain and its modulation by neurotropic viruses. Mitochondrion April 8; 59: 8-16, 2021. doi:10.1016/j.mito.2021.03.010

6. R. Bhagat, G. Kaur and P. Seth (2021). *Molecular mechanisms of Zika Virus pathogenesis - an update.* Indian Journal of Medical Research Mar 154 (3): 433-445, 2021. doi: 10.4103/ijmr.IJMR_169_20

Presentations

1. Pankaj Seth Guest Faculty, *Use of human neural stem cells as model to study healthy and diseased brain,* at Course on Application of Animal Cell culture and its applications, organized by Marinda House, University of Delhi, India, March 24, 2022.

2. Pankaj Seth Invited Speaker, *Molecular insights into virus induced neurodegeneration*, at the 6th International Anatomical Sciences and Cell Biology Conference (IASCBC) meeting organized by National University of Singapore, Singapore Feb 23, 2022.

3. Pankaj Seth Session Speaker, *Using primary cultures of human brain stem cells for research - a "Made in India" initiative*, by Dr Pankaj Seth, National Brain Research Centre under the theme *Science, Technology and Innovation for Self Reliance/Atmanirbar Bharat*, organized during Science Showcase Mega Expo - *for Vigyan Sarvatra Pujyate,* Feb 22-28 2022.

4. Pankaj Seth Session Speaker, *Cell based systems developed in India for understanding brain disorders*, by Dr Pankaj Seth, National Brain Research Centre under the theme *Science, Technology and Innovation for Self Reliance/Atmanirbar Bharat* organized during Science Showcase Mega Expo - ***f****or Vigyan Sarvatra Pujyate,* Feb 22-28 2022.

5. Pankaj Seth Invited Speaker, *Virus induced neurodegeneration- what we know and what we need to know*, at the *Vigyan Sangam* lecture series under the Azaadi ka Amrit organized by Centre for Biomedical Research, Lucknow and Uttar Pradesh Academy of Sciences, on January 7, 2022.

6. Pankaj Seth Invited Speaker, *Molecular mechanisms for SARS-CoV-2 mediated neuronal death*, at the 39th Online Annual meeting of Indian Academy of Neurosciences, Organized by Indian Institute of Science Education and Research- Kolkata, India, December 16-19, 2021.

7. Pankaj Seth Grand round talk *Exploring the Virus and Brain connection: our journey from neuroAIDS to neuroCOVID,* at the University of Wisconsin, USA. December 1, 2021.

8. Pankaj Seth Invited Speaker, *Creating infrastructure for PD functional studies using neural stem cells.* During the Genetic Architecture of Parkinson's disease (GAP- India) meeting organized by the Luxembourg German Indian Alliance on Neurodegeneration and Therapeutics (LUX-GIANT) during Nov 26-27, 2021.

9. Pankaj Seth Invited Faculty, *The virus - brain connection: what I knew and what is new* at International Brain Research Organization - Asia Pacific Regional Committee (IBRO-APRC) Associate School is being organized by Amity University NOIDA, India September 30, 2021.

10. Pankaj Seth Invited Faculty, *What I knew and what is new – in virus induced neurodegeneration* at International Brain Research Organization- Asia Pacific Regional Committee (IBRO-APRC) Associate School organized by Department

of Zoology, Indira Gandhi National Tribal University (IGNTU), Amarkantak (MP), India September 21, 2021.

11. Pankaj Seth Invited Lecture, *Brain Fog – Post COVID Neurological Complication,* webinar at the Faculty Enrichment Programme, on *Cutting Edge Science in Cellular and Molecular Biomedicine* organized by Amity Institute of Molecular Medicine & Stem Cell Research (AIMMSCR) Amity University, NOIDA, India, July 28, 2021.

12. Pankaj Seth Invited Lecture, *Post COVID Neurological Complications* as Awareness webinar jointly organized by Association of Knowledge Workers and CSIR-Pensioners Association, July 17, 2021.

13. Pankaj Seth Valedictory Speaker, *Molecular basis of neurological complications in SARS-CoV-2 cases,* at Frontiers in Biomedical Research-2021 organized by Dr. BR Ambedkar Center of Biomedical Research and Delhi School of Public Health, University of Delhi, India, June 25, 2021.

14. Pankaj Seth Invited Speaker, *Neurotropic viruses – What we know and what we need to know*, Research Focus Talks, Kasturba Medical College, Manipal, India, June 11, 2021.

Funding

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Collaborators

- A. Basu, SK Sharma and S. Sinha, NBRC, Manesar, India.
- S. Sharma, and A. Singh, Civil Hospital, Gurgaon, India.
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- C. Sachidanandan, IGIB, New Delhi, India.
- S. Singh, BHU, Varanasi, India.
- S. Sen, AIIMS, New Delhi, India.
- C. Mukhopadhyay, Jawaharlal Nehru University, New Delhi, India.
- M. Sharma, University of Tubingen, Germany.
- R. Wadhwa, AIST, Japan.
- A. Nath, D. Wang, National Institutes of Health, Bethesda, USA.

Degrees Awarded (M.Sc.)

Pooja Kumari Gupta

Pravat Kumar Mandal

Early Diagnostic Biomarker for Alzheimer's Disease and possible prevention

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The NeuroImaging and NeuroSpectroscopy Laboratory (NINS) has discovered early diagnostic biomarker for Alzheimer's disease. The lab members also developed a multimodel quality checked data with necessary data data analytics pipeline called SWADESH.

Publications

1. Tripathi, M., Kaur, K., Ramanujam, B., Viswanathan, V., Bharti, K., Singh, G., Singh, V., Garg, A., Bal, C. S., Tripathi, M., Sharma, M. C., Pandey, R., Dash, D., Mandal, P., & Chandra, P. S. (2021) Diagnostic added value of interictal magnetic source imaging in presurgical evaluation of persons with epilepsy: A prospective blinded study. European journal of neurology, 28(9), 2940–2951. https://doi.org/10.1111/ene.14935

2. Samkaria, A., Punjabi, K., Sharma, S., Joon, S., Sandal, K., Dasgupta, T., Sharma, P., & Mandal, P. K. (2021). Brain Stress Mapping in COVID-19 Survivors Using MR Spectroscopy: New Avenue of Mental Health Status Monitoring. Journal of Alzheimer's disease: JAD, 83(2), 523–530. https://doi.org/10.3233/JAD-210287

3. Goel, A., Roy, S., Punjabi, K., Mishra, R., Tripathi, M., Shukla, D., & Mandal, P. K. (2021). PRATEEK: Integration of Multimodal Neuroimaging Data to Facilitate Advanced Brain Research. Journal of Alzheimer's disease: JAD, 83(1), 305–317. https://doi.org/10.3233/JAD-210440

4. Samkaria, A., & Mandal, P. K. (2021). Brain Imaging in COVID-19. ACS chemical neuroscience, 12(16), 2953–2955. https://doi.org/10.1021/acschemneuro.1c00467

5. Shukla, D., Mandal, P. K., Mishra, R., Punjabi, K., Dwivedi, D., Tripathi, M., & Badhautia, V. (2021). Hippocampal Glutathione Depletion and pH Increment in Alzheimer's Disease: An in vivo MRS Study. Journal of Alzheimer's disease: JAD, 84(3), 1139–1152. https://doi.org/10.3233/JAD-215032

6. Mandal, P. K., Samkaria, A., & Maroon, J. C. (2021). AD Hypotheses and Suggested Clinical Trials. ACS chemical neuroscience, 12(21), 3968–3971. https://doi.org/10.1021/acschemneuro.1c00627

7. Prasad, K., Dwivedi, S. N., Kant, S., Vibha, D., Pandit, A. K., Karthikeyan, G., Tripathi, M., Srivastava, A. K., Nehra, A., Vivekanandhan, S., Garg, A., Chutani, A. M., Verma, V., Kumar, S., Kumar, A., Gulati, K., Gulati, A., Makharia, G., Seth, T., Dhingra, K., Mandal, P. K., Mishra, N. K., Ikram, A., Tiemeier, H. (2022). Cohort Profile: The LoCARPoN-a population-based prospective cohort study in middle-aged and older adults in India. International journal of epidemiology, 51(1), 29–30m. https://doi.org/10.1093/ije/dyab078

8. Mandal, P. K., & Perry, G. (2022). SWADESH: A Comprehensive Platform for Multimodal Data and Analytics for Advanced Research in Alzheimer's Disease and Other Brain Disorders. Journal of Alzheimer's disease: JAD, 85(1), 1–5. https://doi.org/10.3233/JAD-215354

9. Craven, A., Bhattacharyya, P., Clarke, W., Dydak, U., Edden, R., Ersland, L., Mandal, P., Mikkelsen, M., Murdoch, J., Near, J., Rideaux, R., Shukla, D., Wang, M., Wilson, M., Zöllner, H. J., Hugdahl, K., Oeltzschner, G. (2022). Comparison of seven modelling algorithms for GABA-edited 1 H-MRS. NMR in Biomedicine, 35.

10. Handa, P., Samkaria, A., Sharma, S., Arora, Y., & Mandal, P. K. (2022). Comprehensive Account of Sodium Imaging and Spectroscopy for Brain Research. ACS chemical neuroscience, 13(7), 859–875. https://doi.org/10.1021/acschemneuro.2c00027

Presentation

1. Pravat Kumar Mandal: Diagnostic Biomarker for Alzheimer's Disease, Science Setu, Govt. Raj College, Jargan, West Bengal, September 2021.

Funding

1. Artificial Intelligence for early prediction of Alzheimer's disease, MEITY (Govt. of India), Grant 4(5)/201-ITEA (2019-2023).

Collaborators

1. Prof. Manjari Tripathi, M.D., All India Institute of Medical Sciences (AIIMS), New Delhi, India

2. Prof. Ashley Bush, M.D., Florey Institute of Neuroscience and Mental Health, Australia

3. Prof. Peter Barkar, Ph.D., The Johns Hopkins Hospital, United States

4. Prof. Joseph C. Maroon, M.D., Medical School, University of Pittsburg, United States

Ranjit Kumar Giri

Regional and cell specific expression of CPEB1, 2, 3 and 4 in mouse brain.

Research Associate
Dimpi Gandhi

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Lab Attendant
Lalit Bidla

Cytoplasmic polyadenylation element binding proteins (CPEBs) are family of mRNA binding proteins initially identified due to their role in regulating polyadenylation of target RNA in *Xenopus* oocytes. They play a major role in the regulation of cell cycle and maturation. In recent years, Cytoplasmic Polyadenylation element binding protein (CPEB) has gained attention for its role in memory formation. Four CPEB paralogs have been identified in mouse brain. CPEB under translational stimulus facilitate poly(A) elongation by Gld2 poly(A) polymerase and translational activation. Under basal condition, CPEB binds to cytoplasmic polyadenylation element (CPE) of several poly(A) tail containing mRNA and protect the mRNA from degradation and keep these mRNA in dormant or repressed state. Under translational stimulus, CPEBs undergo either phosphorylation or degradation which dissociates poly(A)-specific ribonuclease and facilitate poly(A) elongation by Gld2 poly(A) polymerase from the same shortened and dormant transcripts. Since CPEBs are regulators of cell cycle and cell senescence related transcripts, their participation in cancer seems highly conceivable. Similarly, the association of CPEBs in memory suggest its immense role in neuronal cell development and maintenance. Therefore, their participation in the pathologies of the nervous system seems reasonable. In order to understand the role of CPEBs in any brain disease like Alzheimer's or prion diseases, it is important to find their expression in brain. However, the expression of CPEBs in different structure and different cells of brain are not well characterized. Therefore, in this study, we wanted to investigate systematically the expression of CPEB1, 2, 3 and 4 in different regions and cell types of mouse brain.

Normal C57BL/6 mice brains were used to study the basal level of CPEBs at regional and cell specific level using dual immunofluorohistochemistry. Frozen mouse brains were sagittally sectioned at 14µm thickness using Leica cryotome. All CPEBs were counter stained with cell specific marker such as neurofilament heavy fragment (NFH; a standard marker for mature neurons), glial fibrillar acidic protein (GFAP), a common

marker for astrocytes and 2',3'-Cyclic-nucleotide 3'-phosphodiesterase (CNPase), a common marker for oligodendrocytes. It is important to mention here that these three cells are the cells of neural origin. Full brain images were acquired using 20X objective lens of a fully motorized Nikon inverted microscope controlled by MetaMorph software employing same image acquisition settings. Images were displayed with equal display settings.

Region Specific Expression of CPEBs in mouse brain

CPEB1 is expressed in most part of the brain except white matter areas. It is expressed maximum in hippocampal region followed by cerebellum. CPEB1 expression is more or less similar in cortex, subicullum, enterhinal cortex, putamen, thalamus and hypothalamus areas of the brain (Figure 1, upper panel, right). Expression pattern of CPEB2 follows similar pattern to that of CPEB1. However, cells in frontal cortex express more CPEB2 than CPEB1. CPEB2 expression is also minimal in corpus collosum and in the tracts of putamen, cerebellum, mid and hindbrain (Figure 1, lower panel, left). Although CPEB3 expression follow similar pattern to that of CPEB1 and CPEB2, but is also expressed in midbrain and hindbrain region. In addition it's expression is more than other CPEBs (Figure 1, lower panel, middle). Finally, CPEB4 is least expressed in most part of the brain than other CPEBs. It is expressed mostly in hippocampus and very weakly in cortex, subicullum, thalamus, amygdala, hypothalamus and cerebellum areas of mouse brain (Figure 1, lower panel, right).

Cell specific expression of CPEBs in mouse brain

Different types of neurons, astrocytes and oligodendrocytes are of brain origin and derived from neuroepithelial cells. Cells of non-neural origin were not studied in this study. Neurons, astrocytes and oligodendrocytes are detected using antibody against heavy fragment of neurofilament (NFH), GFAP and CNPase respectively. Top row of figure 2 demonstrates expression of CPEB1 in neuron (left), astrocytes (middle) and oligodendrocytes (right). CPEB1 is expressed more in neurons than astrocytes and oligodendrocytes. CPEB2 is expressed mainly in neurons (Figure 2, 2nd row, left). It is expressed in most of the cortical neurons and CA3 neurons of hippocampus. It is also expressed more in purkinje cells of cerebellum with marginal expression in cells of granular and molecular layer. However, neurofilament positives tracts are devoid of CPEB2 expression. Unlike neurons, most of the astrocytes and oligodendrocytes are weakly positive for CPEB2 expression(Figure 2, 2nd row, middle and right). NFH expressing

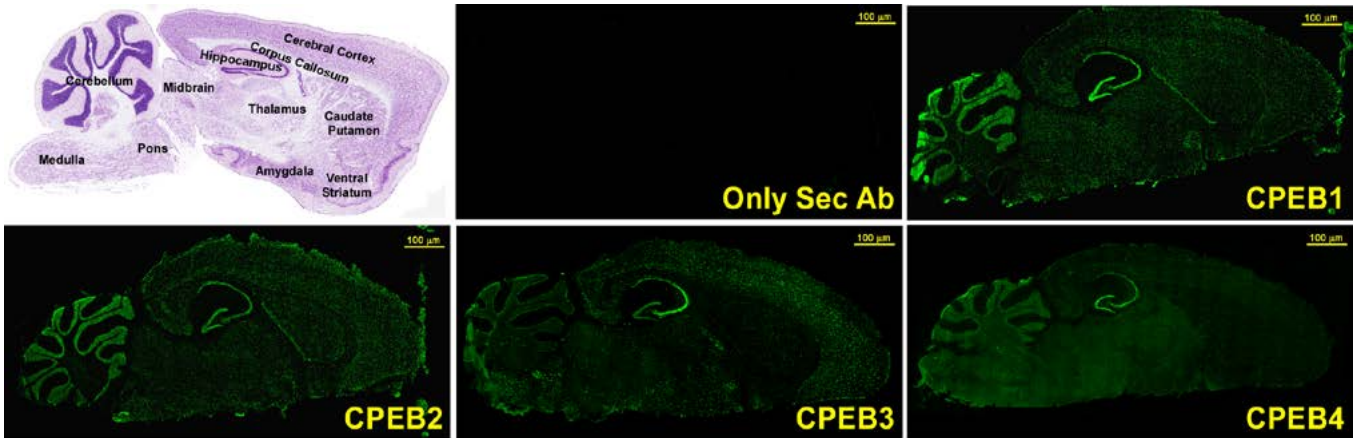

Figure 1: Regional variation in expression of CPEB1, CPEB2, CPEB3 and CPEB4 in mouse brain. Upper-left image depicts graphical representation of different regions of mouse brain. Upper middle image is obtained from a brain section without any primary antibody but with secondary antibody and detection reagents similar to CPEBs, in this case it is CPEB1.

neurons are always positive for CPEB3. However, NFH positive tracts are negative for CPEB3. Intense dual staining of NFH and CPEB3 is observed in hilus, CA3, and purkinje cells of cerebellum (Figure 2, 3rd row, left). GFAP positive astrocytes are weakly positive for CPEB3. A similar pattern is also observed for CNPase positive oligodendrocytes (Figure 2, 3rd row, middle and right column respectively). Maximum CPEB4 expression is seen in the neurons of hilus and CA3 region of hippocampus followed by purkinje cells of cerebellum. NFH positive neurons of midbrain and hindbrain region are also positive for CPEB4 expression (Figure 2, 4th row, left). GFAP positive astrocytes are negative for CPEB4 (Figure 2, 4th row, middle) but CNPase positive oligodendrocytes are weakly positive for CPEB4 (Figure 2, 4th row, right).

Collectively, the results from the above study confirm the expression of CPEBs in mouse brain and neurons of cortex, hippocampus, subiculum, thalamus and purkinje cells of cerebellum. CPEBs expression is weak in astrocytes and oligodendrocytes. The techniques developed and expression maps of CPEBs in mouse brain obtained in present study will support our future research on prion and Alzheimer's disease.

Funding

This work is funded by NBRC Core to RKG.

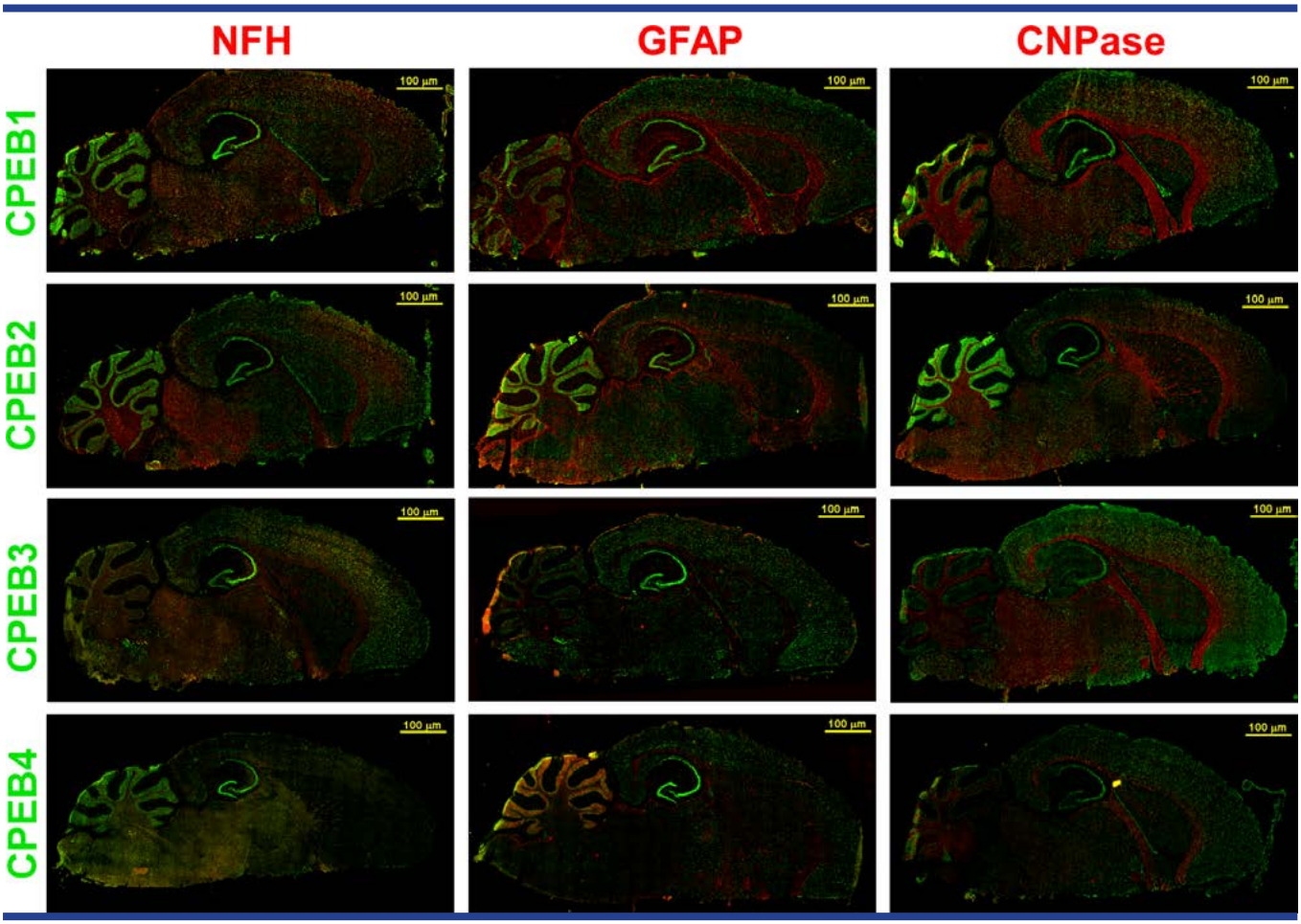

Figure 2: Dual staining of CPEBs with Neurons (NFH positive), astrocytes (GFAP positive) and oligodendrocytes (CNPase positive) in mouse brain.

Shiv Kumar Sharma

Processes relevant for Memory Formation and Memory Impairment

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My laboratory aims to understand the mechanisms that are involved in memory formation, and the processes that are involved in memory impairment in Alzheimer's disease. This dementia condition is the most common form of dementia among the elderly population. Seminal aspects of research in both the projects are described below.

Mechanisms of memory formation: Memory plays crucial roles in the life of every individual. We use the information that we learned in the past for our proper day-to-day functioning. The learned information that is retained in the form of memory helps us make plans for the future. Considering these aspects, scientists are devoting significant efforts aimed at understanding the processes that go into making memories. My laboratory has been using a multidisciplinary approach wherein we combine molecular, electrophysiological and behavioural esperiments to gain comprehensive understanding of memory formation. In the molecular analysis, we examine changes in important signalling molecules. In the electrophysiological aspect, we study long-term potentiation. Long-term potentiation is a kind of synaptic plasticity that is considered to be the synaptic basis of memory formation. In the behavioural approach, we examine memory in the behaving animals using tasks that help us evaluate memory.

Studies from my laboratory as well as the laboratories of other scientists have shown that modifications in proteins including phosphorylation and acetylation play critical roles in long-term potentiation as well as memory. Another modification of proteins is sulfation which critically regulates protein function. We have been trying to understand whether this modification of proteins has a role in synaptic plasticity and memory. Our results show that sulfation plays critical roles in long-term potentiation as well as memory. The findings of this aspect of our research have now been published.

Research on Alzheimer's disease: Alzheimer's disease accounts for majority of the dementia cases in the elderly population. Pathologically, it is characterized by the presence of amyloid

plaques, which are found extracellulary, and neurofibrillary tangles, which are present intracellularly. A small peptide, amyloid beta, a major component of the plaques, is considered to be the primary causative agent in this condition, The neurofibrillary tangles consist of hyperphosphorylated tau proteins. Impairment in neuronal signalling, synaptic plasticity and eventually cell death is observed in Alzheimer's disease. Previously we have studied the effects of compounds on oxidative stress, inflammatory markers and neuronal cell death induced by amyloid beta. We continue to examine the effect of herbal compounds on processes related to Alzheimer's disease. Our recent results suggest that the herbal compound under study may provide beneficial effects in Alzheimer's disease.

Publications

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Funding

Department of Biiotechnology and NBRC Core funds.

Soumya Iyengar

Delta Opioid Receptor Expression in the Zebra Finch Brain

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The endogenous opioid system consists of the opioid ligands endorphin, enkephalin and dynorphin and the receptors that they preferentially bind to, that is, the μ, δ and κ- subtypes. Opioid receptors (ORs) are inhibitory in nature and belong to the Gi/Go-coupled superfamily of receptors. Whereas μ-ORs are most well-studied and are known to be important for analgesia, recent studies have demonstrated that the δ- and κ-ORs also play a role in this function. Besides being involved in the pain pathways, it is well-known that the endogenous opioid system is evolutionarily conserved across reptiles, birds and mammals and modulates varied brain functions such as learning, memory, cognition and reward. To date, most of the behavioral and anatomical studies in songbirds have mainly focused on μ-ORs. Earlier studies in our lab have demonstrated that these receptors are widely distributed in the brains of adult male zebra finches (an Australian species of songbirds, widely used in the lab). Furthermore, these receptors expressed by nuclei of the song control system which is important for vocalization (the vocal motor pathway or VMP) as well as in a connected neural circuit which is important for song learning during development and contextual singing during adulthood (the anterior forebrain pathway or AFP).

Recent studies have shown that besides modulating pain, δ-ORs are involved in learning and memory. Furthermore, activation of these receptors leads to antidepressant-like effects in rats. However, the expression patterns of δ-ORs in zebra finches has not been studied in detail. We therefore used a specific riboprobe against the δ-OR mRNA to perform fluorescence in situ hybridization on sections from the brain of adult male zebra finches. Quantitative analysis of the expression of δ-ORs was then performed by measuring the intensity of fluorescent label in individual neurons across different parts of the brain.

Our results demonstrated that δ-OR mRNA was expressed in different parts of the pallium, basal ganglia, cerebellum and the hippocampus. Amongst the song control nuclei of the AFP, the expression of δ-OR mRNA was moderate in LMAN (lateral magnocellular nucleus of the anterior nidopallium; **Figure 1A**

and **1C**) and low in the MSt (medial striatum), Area X and DLM (dorsolateral nucleus of the medial thalamus; **Figure 1A**; Parishar et al., 2021).

The VMP consists of projections from HVC (abbreviation used as a formal name; **Figure 1B** and **1D**) to RA (robust nucleus of the arcopallium; **Figure 1B**). Furthermore, another pallial region NIf (nucleus interfacialis nidopallii) projects to HVC. Whereas HVC and NIf strongly expressed δ-OR mRNA and could be clearly discerned from the surrounding nidopallium, δ-OR expression was lower in RA (robust nucleus of the arcopallium). Auditory areas including the auditory cortex (Field L), the thalamic nucleus Ov (nucleus ovoidalis) and MLd (nucleus mesencephalicus lateralis, pars dorsalis) of the auditory pathways also expressed low levels of δ-OR mRNA.

Despite the fact that there are lower levels of δ-ORs compared to μ-ORs in the zebra finch brain, these receptors are present across a number of cortical and subcortical structures. These findings suggest that δ-ORs may be important for modulating diverse brain functions such as cognition, spatial learning, movements and motor planning and vocalization, besides social interactions in zebra finches at different stages of development, and need to be investigated further.

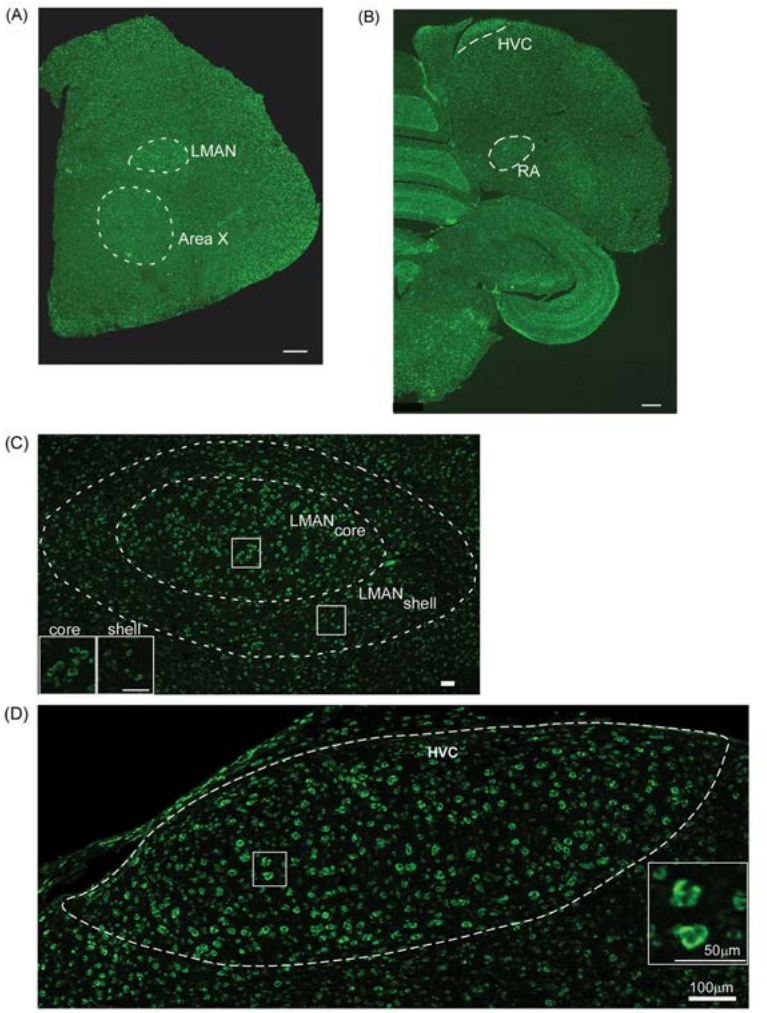

Figure 1: (A) Coronal section of the adult male zebra finch brain at the level of the anterior forebrain demonstrating that LMAN expresses higher levels of δ-OR mRNA than Area X. (B) At more caudal levels, HVC can be clearly demarcated on the basis of staining for δ-ORs. Whereas RA is also present in this section (ventral to HVC), lower levels of δ-ORs are expressed in this region. Scale bars, 200 μm. (C) A high magnification view demonstrating that magnocellular neurons in the core and parvicellular neurons in the shell of LMAN express δ-ORs. (D) Individual neurons in HVC express high levels of δ-OR expression. Scale bars, 100 μm for low magnification images and 50 μm for insets.

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1. Parishar P, Mohapatra AN and Iyengar S (2021) Investigating Behavioral Responses to Mirrors and the Mark test in adult male Zebra Finches and House crows. Frontiers in Psychology, April 15;12:637850. doi: 10.3389/fpsyg.2021.637850. eCollection 2021.

2. Parishar P, Sehgal N and Iyengar S (2021) The Expression of DOR mRNA in adult male zebra finches (*Taenopygia guttata*). PLoS ONE 16(8): e0256599. https://doi.org/10.1371/journal.pone.0256599, Published: August 31.

3. Singh UA and Iyengar S (2022) The Role of the Endogenous Opioid System in the Vocal Behavior of Songbirds and its Possible Role in Vocal Learning. Invited review, Front. In Physiology (Avian Physiology): Feb 22, 2022; Volume 13 | Article 823152; doi: 10.3389/fphys.2022.823152

Presentations

1. Soumya Iyengar: Brain-behaviour interactions in the 'Shining Raven'. 'Synapse', Symposium, IISER, Tirupati, Dec 4th, 2021.
2. Soumya Iyengar: The Avian Black Box - the Crow Brain. Theme: Recent trends in Brain research: Unlocking the mysteries of the brain, IBRO. IBRO Virtual Symposium (Institute of Home Economics, University of Delhi), March 22nd - 23rd, 2022.

Funding

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Collaborator

- Prof. S. Senthil Kumaran, Dept. of NMR, All India Institute of Medical Sciences, New Delhi.

Degrees Awarded (Ph.D.)

- Shankhamala Sen: (Thesis entitled "Neuroanatomical Studies of the House Crow (*Corvus splendens*) Brain" (Integrated MSc-Phd). Degree awarded: 3rd August, 2021.)
- Utkarsha Singh: (Thesis entitled "Role of Delta Opioid Receptors in Singing and Song Learning in Zebra Finches" (Integrated MSc-Phd). Degree awarded 14th February, 2022.)

Sourav Banerjee

RNA-based mechanisms of synapse development and memory storage

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Subcellular control of gene expression by regulatory RNAs is an emerging mechanism that drives development and functions of neural circuits. The localization of RNA, machineries required for protein synthesis as well as degradation and signaling molecules in neuronal dendrites create a microdomain to promote spatial control of synapse development and its functions. This localized control of gene expression drives structural and functional modifications of synapses that is necessary for memory storage as well as maintenance of network activity in the face of repetitive exposure to external stimuli. Motivated by these facts, the laboratory is investigating the mechanisms of synapse formation, Homeostatic and Hebbian forms of synaptic plasticity and memory storage by regulatory RNAs. Of particular ineterest, the laboratory has focused on two distinct classes of non-coding RNAs, microRNAs (miRNAs) and long non-coding RNAs (lncRNAs) that function as regulatory RNAs. The research programme employed a variety of cell biological, biochemical and electrophysiology approaches and used hippocampal neurons in primary culture or *in vivo* as a model system to study the RNA-based mechanism of synapse formation and memory storage in health and disease.

Regulation of synapse formation by lncRNAs

Growing body of literature on mechanisms of synapse formation have implicated activity-dependent transcriptional control and interactions between cell surface proteins. More recently, diverse factors that influence cell surface expression and interactions between cadherin and protocadherin family of proteins emerged as a key regulator of various stages associated with synapse development ranging from initial neuronal contact to synapse maturation. However, the role of regulatory RNAs in functional synapse development remains unexplored.

The research programme initiated by our laboratory has investigated the role of a subset of synapse-enriched lncRNAs in functional synapse development. These lncRNAs are identified from mouse hippocampus by our genome-wide transcriptomics

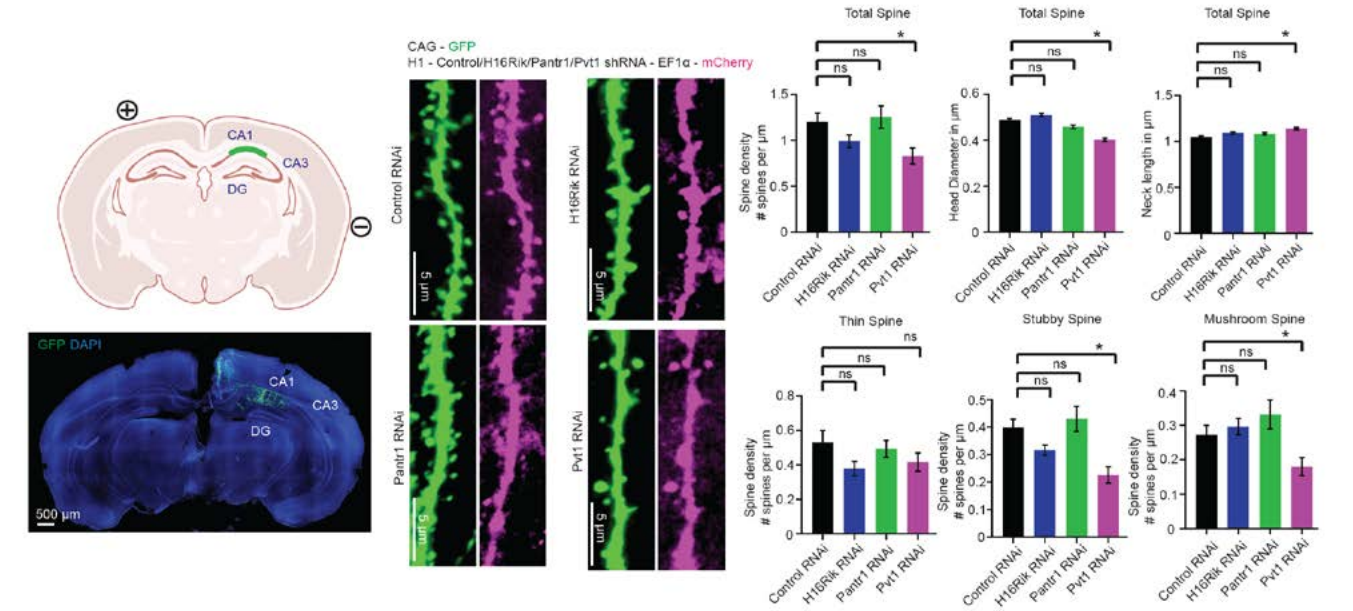

Figure 1: Long non-coding RNA regulates dendrite and spine development.

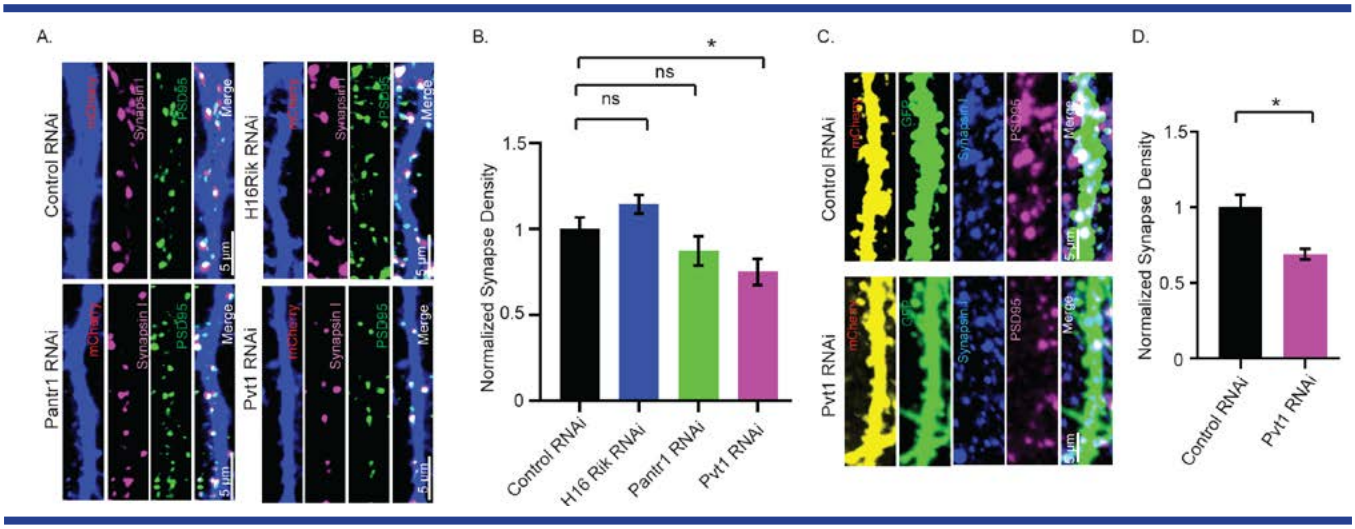

Figure 2: Long non-coding RNA influencing excitatory synapse development.

analysis. We have inhibited the expression of three highly abundant lncRNAs during embryonic development of brain (prior to initiation of synaptogenesis) using *in utero* electroporation.

We observed that inhibition of Pvt1 lncRNA led to reduction of dendritic complexity and spine shrinkage. Our study identied that Pvt1 regulates the expression of Rho family GTPase, RhoA and Rac1 to influence the development of dendnritic spines.

The knockdown of Pvt1 either in cultured hippocampal neurons or in CA1 region of the hippocampus led to a significant reduction of excitatory synapses. Transcriptomics analysis following knockdown of Pvt1 identified diverse synaptogenic factors. The Gene Ontology (GO) analysis of these factors indicated the involvement of diverse pathways necessary for synapse formations. Furthermore, our whole-cell patch clamp recordings showed that the knockdown of Pvt1 resulted in reduction in synaptic strength due to depletion of AMPA type glutametergic receptor on the synaptic surface.

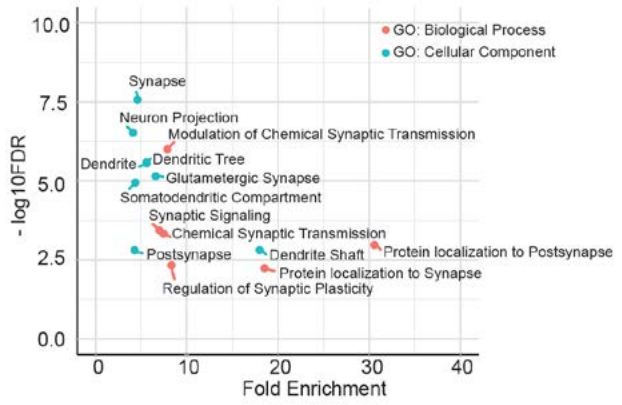

Figure 3: Synaptogenic pathways affected by knockdown of Pvt1.

Mechanism of homeostatic synaptic scaling by miRISC remodelling *via* coordinated control of protein synthesis and dedgradation

Neurons employ homeostatic synaptic scaling to counter the runaway excitation and subsequent loss of input specificity that occurs due to Hebbian plasticity. Systems level study of synaptic scaling has implicated a compensatory remodeling of synapses throughout the network while maintaining differences in their synaptic weightage. However, the molecular underpinning of homeostatic scaling is poorly understood. To gain an insight into molecular details of homeostatic scaling, the study investigated how the interplay between protein synthesis and degradation effectuates synaptic homeostasis. This study has demonstrated that a co-ordination between translation and degradation machineries *via* direct interactions is necessary for synaptic homeostasis. Furthermore, the study identified that the mTORC1 signaling plays a pivotal role in sensing the change in network activity and adjustment of synaptic strength by modulating synaptic level of surface AMPA receptor. This study illustrated that surface AMPA receptor expression is regulated by Arc *via* remodeling of the miRNA induced silencing complex (miRISC) (Srinivasan and Samaddar, PLoS Biology, 2021). This study provides a molecular basis for our understanding of how hyperexcitation could affect the physiological functions of synapses that occurs during brain disorders, such as epilepsy and autism.

Synapse-specific mechanism of memory involving non-coding RNAs.

Input-specific control of *de novo* protein synthesis at the synapses plays a pivotal role in regulating synaptic plasticity and memory. To gain a mechanistic insight into protein synthesis –dependent form of synaptic plasticity and memory, the research

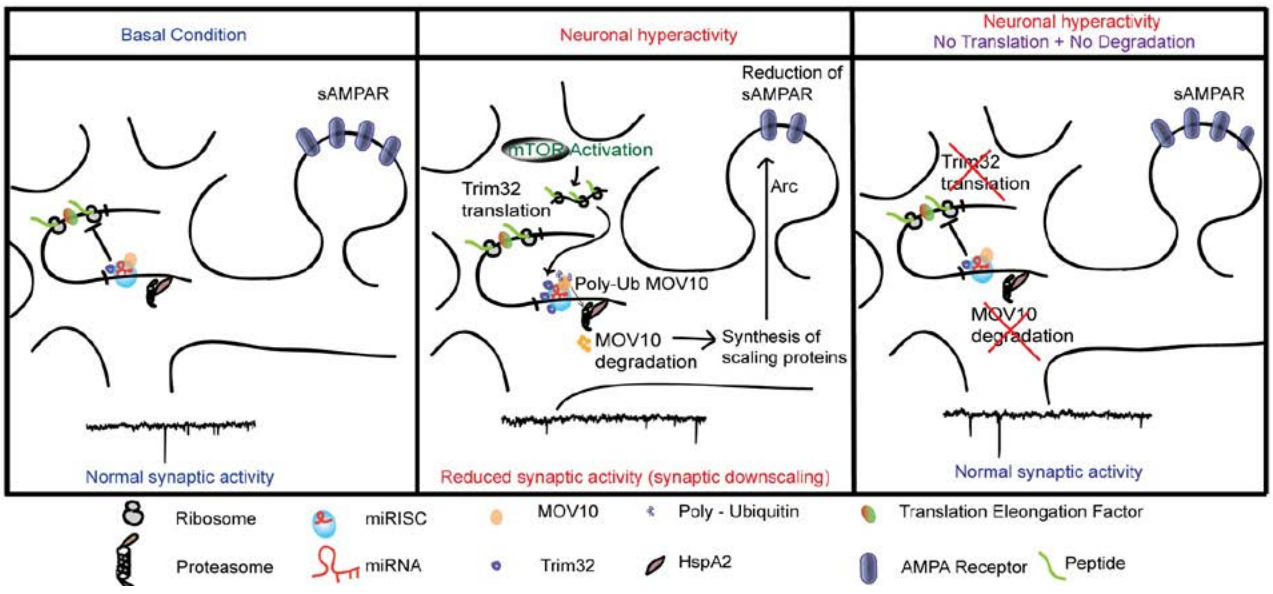

Figure 3: Schematic model of synaptic homeostasis regulation by miRISC.

programme is focused on activity-dependent functions of lncRNAs in neuronal dendrites.

The genome-wide screening of synaptic transcripts obtained from excitatory neurons of hippocampus identified a set of synapse-enriched long non-coding RNAs (lncRNAs >200 nucleotide). Our study has demonstrated that the contextual fear conditioning of mouse, a spatial learning paradigm, triggered the dendritic transport of specific lncRNAs. The research programme investigated the mechanism of memory storage by two lncRNAs, namely Pantr1 and H16Rik that showed significant dendritic enrichment upon contextual fear conditioning.

To gain a mechanistic insight, the research programme designed an *in silico* map of lncRNA-RNA binding protein (RBP) interactions based on compartive analysis of high througput studies of RNA-protein interactions. The dynamicity of the interactions was analyzed after contextual fear conditioning. We observed that lncRNAs

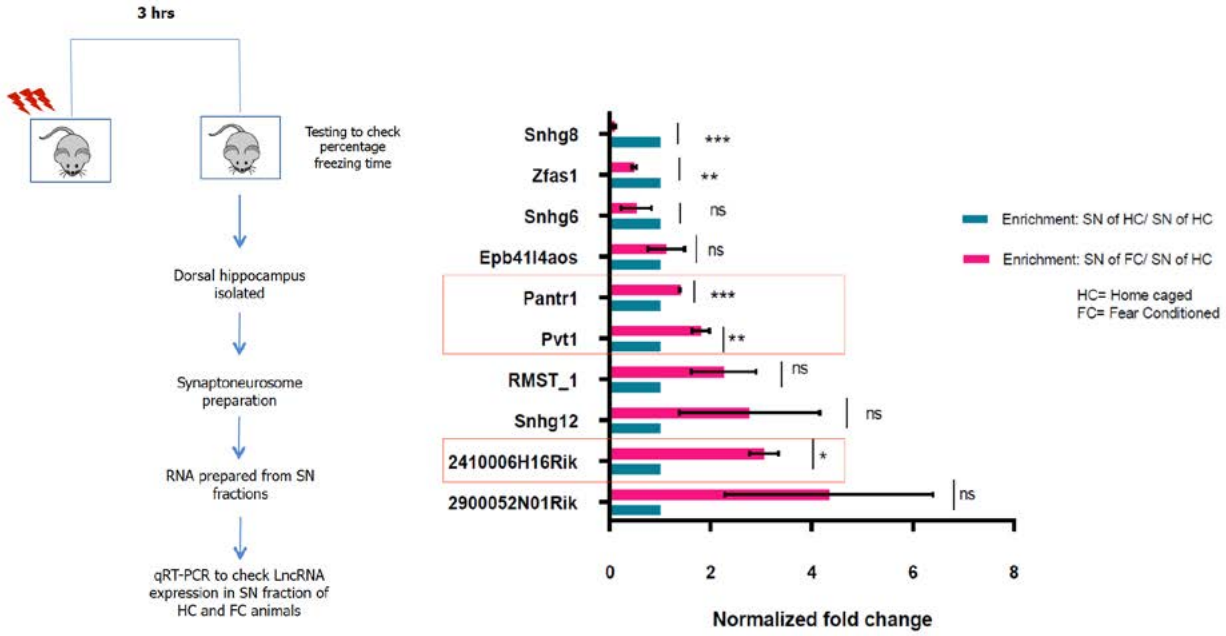

Figure 4: Dendritic enrichment of lncRNAs following contextual fear conditioning.

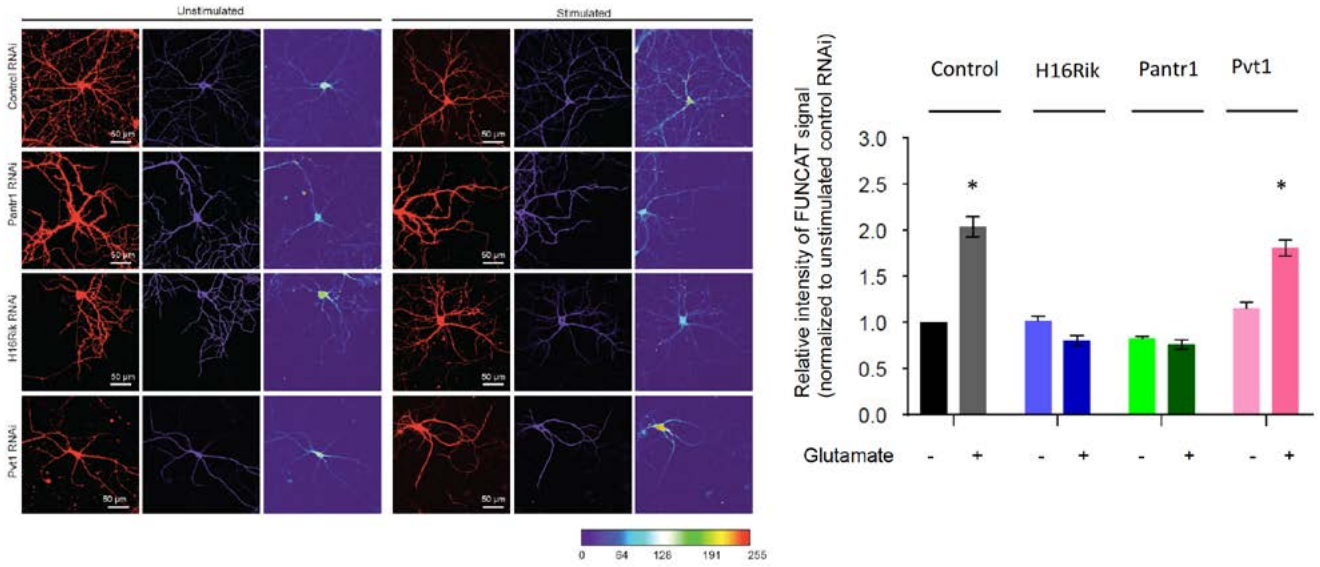

Figure 5: LncRNAs regulate neuronal activity-dependent protein synthesis.

function as RBP decoy to sequester or release these proteins to regulate dendritic translation. The fluorescent labelling of newly synthesized proteins (FUNCAT) revealed that the knockdown of dendritic lncRNAs, Pantr1 and H16Rik inhibited neuronal activity-dependent protein synthesis. The ongoing research aims to establish the importance of lncRNA-mediated control of dendritic protein synthesis in memory storage.

Publications

1. Balakumar Srinivasan, B.[$], Sarbani Samaddar, S.[$], Mylavarapu, S., Chelliah, J. P., and Banerjee, S. (2021) "Homeostatic scaling is driven by a translation-dependent degradation axis that recruits miRISC remodelling". doi: PLOS Biology 10.1371/journal.pbio.3001432. [$] Equal Contribution. ***Selected for Editor's choice with a short review as a "Primer"*** *"It takes two to tango: Concerted protein translation and degradation necessary for synaptic scaling" by Ana Luisa Carvalho PLOS Biology 10.1371/journal.pbio.3001448.* ***Highlighted by Nature India and F1000.***

2. Samaddar, S. and Banerjee S. (2021) Far from the nuclear crowd: Cytoplasmic lncRNA and their implications in synaptic plasticity and memory. Neurobiology of Learning and Memory. 2021 Sep 18:107522. doi: 10.1016/j.nlm.2021.107522.

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Presentation

1. Sarbani Samaddar, Balakumar Srinivasan, Kamakshi Garg, Dipanjana Banerjee and Sourav Banerjee. Decoding long non-coding RNAs in the neuron: Implications in development and synaptic plasticity." EMBO meeting on "RNA binding proteins: From RNA binding to condensation and aggregation." virtual meeting at NCCS, Pune, February 2021.

Funding

- Sciennce and Engineering Research Board
- Department of Biotechnology
- NBRC Core fund

Collaborators

- Dr Dasradhi Palakodeti, inStem, Bangalore
- Dr Sivaram Mylavarapu, RCB, Faridabad
- Dr James Chelliah, JNCASR, Bangalore
- Prof. Ted Abel, University of Iowa, USA
- Dr Timothy Bredy, University of Queensland, Australia

M.Sc Degree Award

Ms. Ojasee Bapat

Bhavani Shankar Sahu

Vesicular trafficking pathways in neurons/neuroendocrine cells and their consequent role in physiology, health and diseases.

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Sushma Dagar Postdoc

PhD student
Chandramouli Mukherjee,

MSc Student
Mohima Mukherjee

Project Assistant
Vinayak Ghosh,
Souren Sadhukhan

Technician
Mahendra Singh

Our lab investigates vesicular trafficking pathways in neuroendocrine cells. To understand the specialized vesicular trafficking pathways, we study a specific type called dense-core vesicles (DCVs). DCVs are specialized sub-cellular organelles in specific neurons/neuroendocrine cells and regulate diverse physio-metabolic functions. They undergo stimulus-dependent secretion, and the phenomenon is called “regulated secretion”. Components of regulated secretion include neuropeptides, neurotransmitters that regulate various physiological functions. Although the research on DCVs has been pursued for the past four decades, many aspects related to sub-cellular trafficking/ secretion are unknown, and we study this in our lab on two broad themes.

Research Theme I: Investigating DCV Biogenesis

Investigating the role of AP3 in regulated Secretion.

Regulated Secretion is an important phenomenon in certain specialized cells such as neuron and neuroendocrine cell lines. It is the release of biopeptides from the cell in the event of a physiological stimulus. Dense core secretory granule, a dense-core vesicle (DCV), is a repository of several biological peptides of paramount importance and are significant members of regulated Secretion. To that extent, several adaptor proteins exist that help sort cargo into the regulated secretion pathway, namely adaptor proteins 1 through 5. Of them, adaptor protein 3, or AP3, is an adaptor protein localized and associated extensively with the Golgi and the endosome. Moreover, it is the only adaptor protein that is evolutionarily conserved. In our study, we want to understand the role of AP3 in dense-core vesicle cargo sorting, biogenesis, and subsequent exocytosis to gauge its role in devising regulated Secretion.

Result summary: We have taken a professional secretory cell line, PC12 cell line, to study the role of AP3. AP3 loss of function approaches was implemented to understand its functionality by generating cell lines where AP3 can be knocked down through

induction by doxycycline. In our experiments, we have conducted stimulus coupled secretion assays through BaCl2 Secretogogue stimulation (BaCl2 depolarizes the membrane and releases all readily releasable DCVs) for studying the impact of AP3 in regulated Secretion. Upon stimulation, in AP3 knockdown (KD) cells, a significant impairment in Chromogranin B (a DCV marker) release was shown compared to wild-type cells. On knocking down AP3D1 (+DOX cells), we see a significant decrease in the number of responding puncta and an overall increase in the number of non-responding puncta. Furthermore, we also see a delayed response in the +DOX cells compared to the control cells, which may result from the failure of the regulated secretory machinery to deplete the AP3D1 subunit.

Regulated Secretion is affected in AP3 depleted cells:

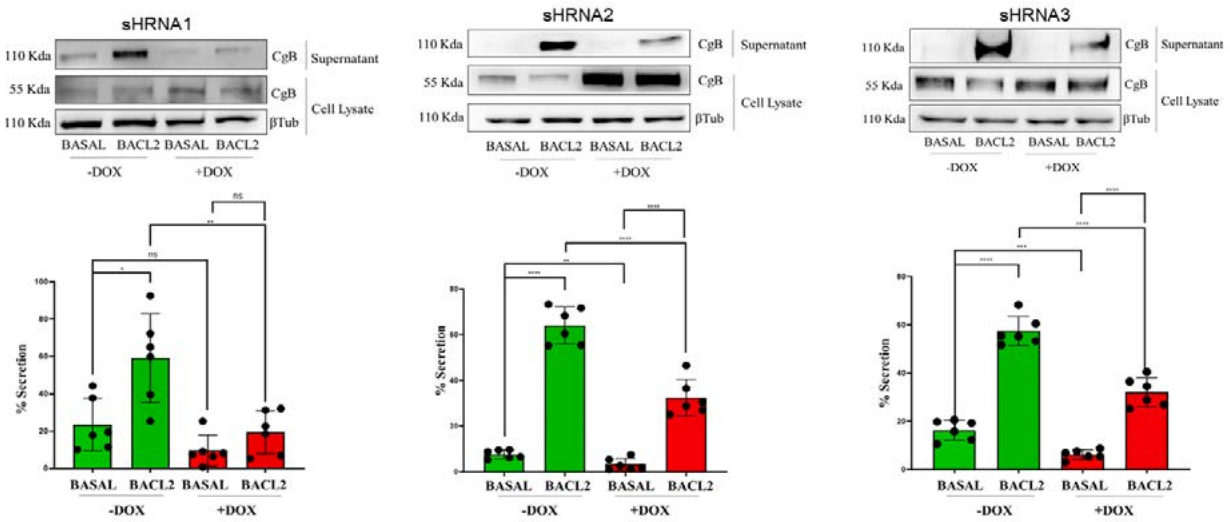


Figure 1: By using multiple cell lines harbouring multiple shRNA, we show that secretagogue induced regulated secretion is compromised when the adaptor protein 3 complex major subunit delta is knocked down (+DOX) as evident by the quantitative immunoblotting of Chromogranin B, a DCV marker protein released by the regulatory secretory pathway.

Adaptor Protein complex 3 affects the dynamics of regulated Secretion of DCV:

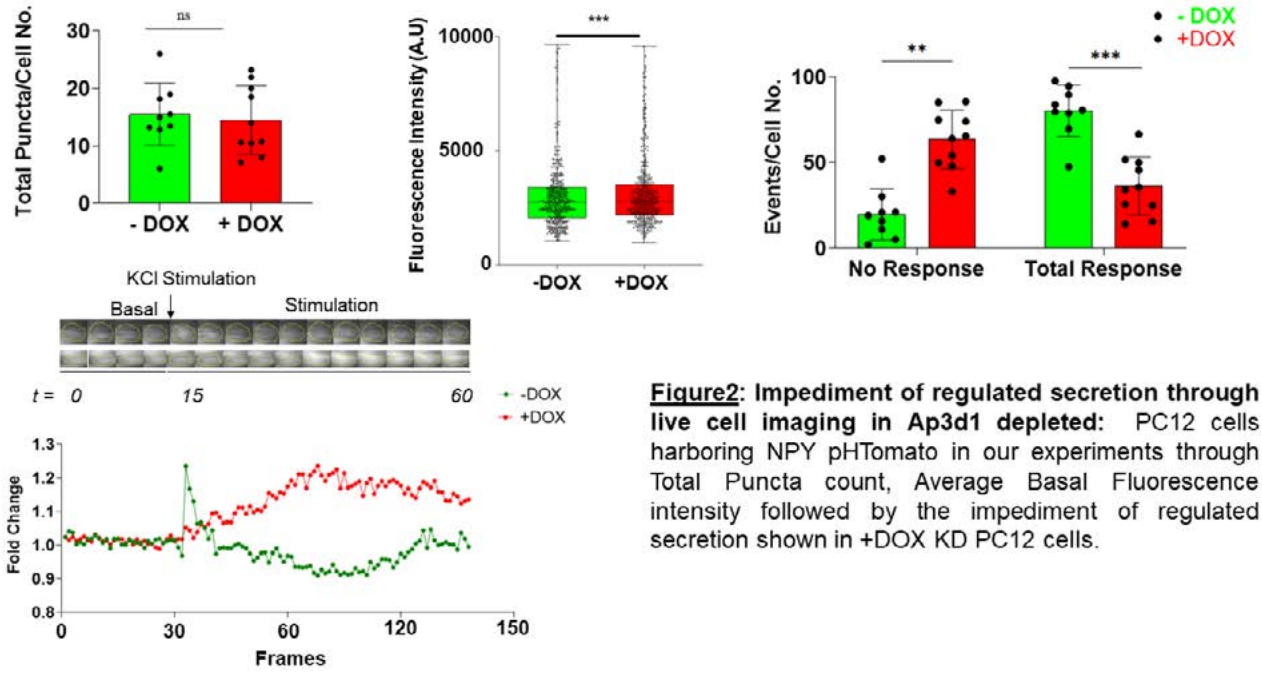


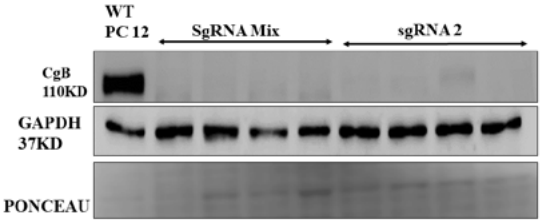
Figure2: Impediment of regulated secretion through live cell imaging in Ap3d1 depleted: PC12 cells harboring NPY pHTomato in our experiments through Total Puncta count, Average Basal Fluorescence intensity followed by the impediment of regulated secretion shown in +DOX KD PC12 cells.

Research Theme II: Investigating the contribution of the regulated exocytosis and neuroendocrine proteins in health and disease

Objective 2: Functionally Characterize the Cell-specific cargo in Secretory vesicles

The dense core secretory granules (or Dense core vesicle/DCV) are crucial for regulating biological functions, which are present in professional secretory cells like a neuron or neuroendocrine cells. The DCV matrix consists of at least one or more granin protein that regulates the functionality of the DCV. Among them, nine Granin have been discovered, and chromogranin B (CgB) is the most abundant one. Despite the emerging shreds of evidence pointing towards the possible role of CgB in various metabolic, organic and systemic disease pathology, the true molecular characterization to delineate the role of CgB in DCV biogenesis, maturation, and regulated exocytosis is yet to get determined. Our study aims to address those questions using advanced and sophisticated technical approaches.

The generation of CgB KO clones in PC 12 cells using CRISPR-Cas9 and Validation using IF and Western Blot



Transfection and PC12 CgB KO clone Validation:

The CRISPR constructs then Transfected in PC 12 cell using electroporation and selection pressure were applied after two days of transfection to generate stable PC12 CgB KO cell lines for all three sgRNAs. After completion of selection pressure single cell clones were taken using cloning cylinder. Then, each clone was screened using Western Blot and immunofluorescence to confirm the Knock out of the CgB from those cells.

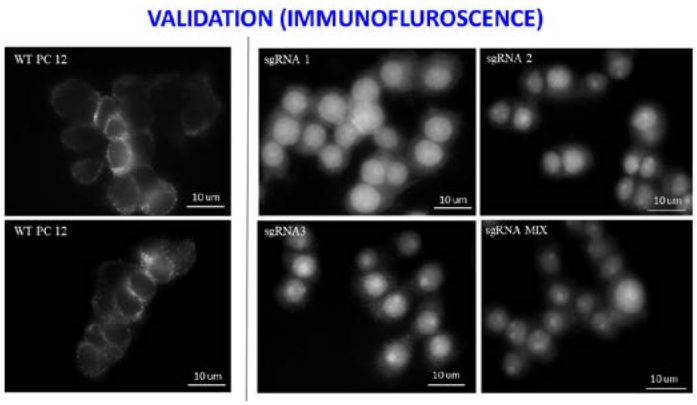


Figure 3: A: Screening of PC 12 clones which transfected using SgRNA 1 and SgRNA 3, absence of band (in comparison to WT) shows the absence of CgB. B: same clones screened using different commercially available antibody againt CgB. C: Screening of PC 12 clones which transfected using SgRNA 2 and SgRNA Mix (all SgRNA together), absence of band (in comparison to WT) shows the absence of CgB. {The round circle shows the clones which are taken for further experiments} **Figure 4**: Immunofluorescence screening of Different SgRNA PC12 CgB KO clones, absence of punctate staining in KO clones indicative of CgB knock out in respect to WT.

Secretory Phenotype

The regulated secretion is one of the fundamental aspect of normal physiology as DCV carries bio peptides, hormones to name a few. So defect in secretion could invariably leads to disease pathogenesis. To check for any phenotype in regulated secretion in CgB KO cells we performed secretion experiments where we incubated the WT and KO cells with basal and secretion buffer(to induce DCV exocytosis). And released proteins in cellular external environment in comparison with cell lysate in quantitative immunoblots shows the defective regulated secretion.

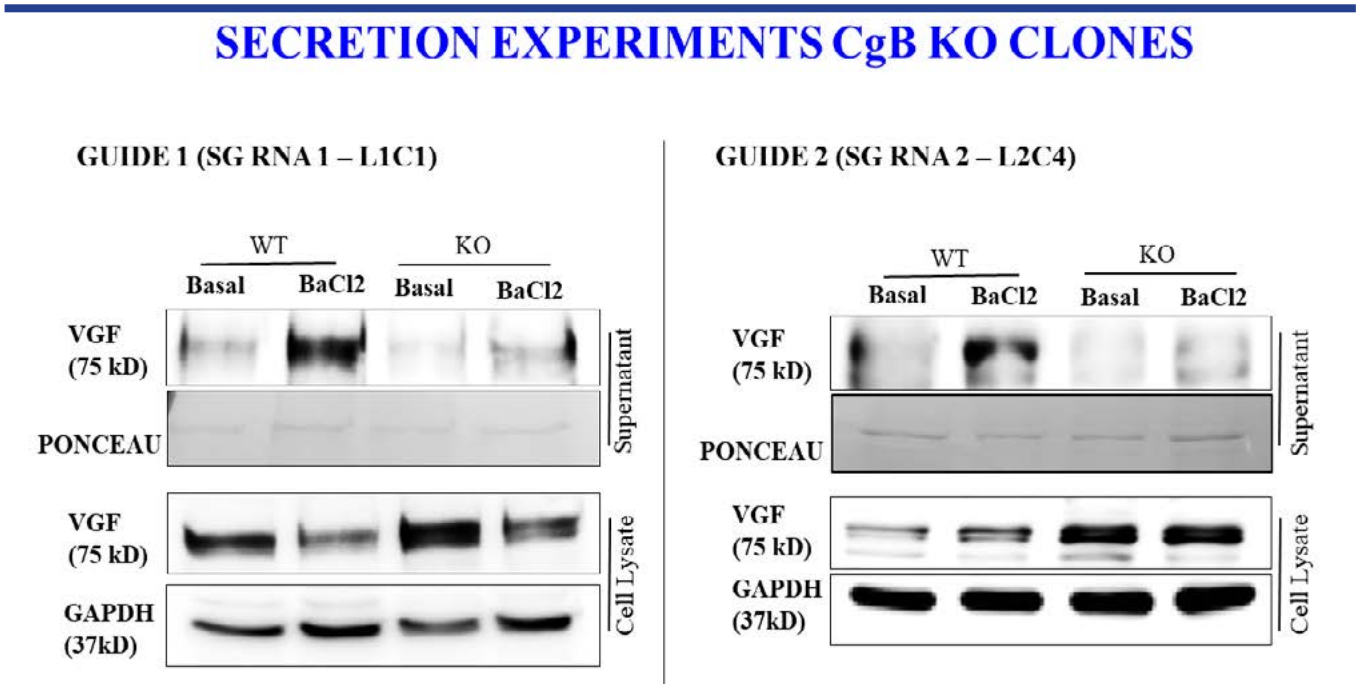


Figure 5: Shows impaired regulated secretion for VGF (known DCV Granin).Release of VGF to the supernatant is impaired in KO cells when treated with secretagogue ($BaCl_2$)

Presentation

Dr. B.S.Sahu: Webinar on Neuroendocrine regulation of metabolic physiology, GN Ramachandran Science club, Vigyan Prasar, MAC FAST, Kerala. (5 Sept. 2020)

Funding

- Department of Biotechnology,
- International Brain Research Organisation, Paris,
- ICGEB, Trieste
- NBRC core funds.

Collaborators

- Prof Anirban Basu, NBRC
- Professor Sushil Mahata, University of California, Sandiego, USA.
- Dr Alessandro Bartolomucci, University of Minnesota, Twin Cities, USA.
- Dr Sanjeev Upadhay, MS University, Baroda, India.
- Dr Saleem Mohammad, NISER, BBSR
- Dr Yusuf Akther, BR Ambedkar Central University, Lucknow.
- Dr Dileep Vasudevan, DBT- Institute of Life sciences, Bhubaneswar, India.

Awards

- DBT-Ramalingaswami fellowship award,
- IBRO(International Brain Research Organisation) start-up grant, ICGEB Trieste(Early career research award).

Degrees Awarded (M.Sc.)

Ms. Amna Jain

Mayanglambam Dhruba Singh

Drosophila models of human neurodevelopment and neurodegenerative disorders

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Bhavya Gohil,
Sanchi Ahuja

Our lab is interested in finding genetic targets that could modify human neurodegenerative disorders. We use Drosophila which is a powerful genetic model system to find the genetic targets with therapeutic potential. We focus on three neurodegenerative disorders such as Huntington's disease, Spinocerebellar ataxia-3, and Alzheimer's disease. As all these disorders do not have therapeutic molecules that could prevent the progression of neurodegeneration, it is pertinent to find novel molecular pathways that could reduce the pathogenesis of these disorders. To find the genetic modulators of these disorders, genetic screens are performed with Huntington's disease, Ataxia-3, and Alzheimer's disease models in Drosophila.

The Drosophila model system allows the expression of the human transgenes in a tissue-specific manner. Using the UAS-Gal4 bipartite system, the human disease-causing transgenes were expressed in the eye of the Drosophila. The Drosophila eye is not involved in survival; therefore, the expression of mutant human genes does not cause lethality. But the morphology and arrangement of the Drosophila ommatidial lattice were considerably perturbed. For example, expression of human ataxia-3 with 78 poly(Q) repeats induces the roughness and loss of pigmentation of the eye surface, and flies expressing human mutant huntingtin protein with 138 poly(Q) repeats caused defects in the arrangement of ommatidia. Using the external surface of the eye as the readout of phenotype, genetic screens are performed to discover novel modifier genes that could ameliorate the disease phenotype. The discovery of modifier genes and pathways is necessitated as no disease-modifying therapies are available which could prevent the progression of the disease. Our screen has identified potential genetic modulators of Ataxia-3, Huntington's disease, and tauopathy disorders. Currently, we are investigating the roles of the modifiers in the protection against neurodegeneration. We are checking the level of cell death in the Drosophila eye disc (Figure 1). Furthermore, we plan to study the improvement in mobility and lifespan in adult flies. Next, we will be investigating the level of protein aggregates and transcriptional status in the Drosophila

neuronal tissues. In addition, our lab is working on neurodevelopmental disorders caused by discs large (dlg1). Mutation of dlg1 in humans is associated with intellectual disability and epilepsy. In our study, the neurodevelopmental role of dlg1 will be investigated using the Drosophila model. Using the UAS-Gal4 system, knockdown of dlg1 caused rough eye, increased eye size, and climbing defects. Current work will focus on the finding of molecular mechanisms and genetic interactors which could have therapeutic potential in ameliorating the disease condition.

Funding

This work is supported by NBRC Core funds.

Meetings/Conference organized

Took part in DBT Science Setu webinar series organized by NBRC for 12 DBT STAR colleges from 15/04/2021 to 18/05/2021.

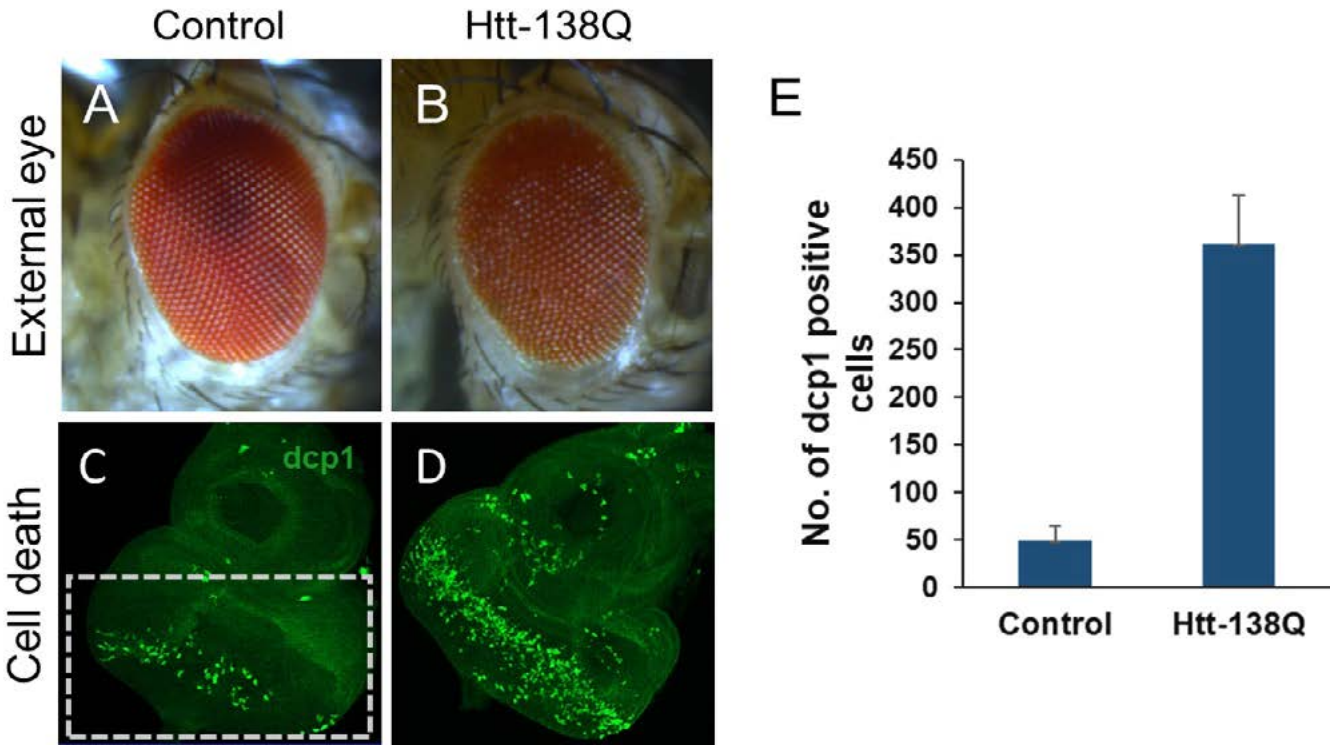

Figure 1. Overexpression of mutant huntingtin protein in Drosophila eye. (A) Control fly shows the regular arrangement of ommatidia. (B) Overexpression of Htt-138Q caused rough eye surface. (C-D) An increased level of cell death was observed due to overexpression of Htt-138Q. (E) Bar graph showing the level of cell death in Drosophila eye disc.

Dr. Nivethida Thirugnanasambandam

Characterizing interindividual variability in the output of the human motor cortex

PhD Students
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Background: Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation technique that works on the principle of Faraday's law of electromagnetic induction. A rapidly changing electric field in the coil generates a magnetic field that penetrates the skull painlessly and induces electrical current over the cortical area of interest. A suprathreshold TMS pulse usually activates both excitatory and inhibitory neurons within the primary motor cortex and therefore represents the net activity of the corticospinal pathway. By adjusting the TMS pulse intensity and waveform, it is possible to activate different classes of neurons, enabling the study of corticospinal excitability in much finer detail. Applying TMS pulses to the motor cortex offers the advantage of being able to elicit muscle contractions that can be measured noninvasively by surface electropmygraphy (EMG). TMS evoked muscle activity is measured in terms of motor evoked potentials (MEPs) that is representative of corticospinal excitability. However, the major challenge with TMS studies is the large variability in MEP amplitude both within and across individuals. Many studies have attempted to identify the factors driving this variability. Factors like age, gender, stimulation intensity and the stimulated hemisphere seem to be important contributors to the inter-individual variability. However, the findings have not been consistent across studies, most likely due to small sample sizes. Recent work by Corp et al. (2020) collated data from 35 studies revealed that the response of healthy individuals to interventional repetitive and to paired-pulse TMS protocols is best predicted by the baseline MEP amplitude. Leodori et al. (2021) showed that the variability in plasticity associated with theta burst stimulation, another interventional TMS protocol, depends partially on baseline corticospinal excitability.

Most TMS studies use the MEP amplitude at a single stimulation intensity equal to 120% RMT (MEP_{amp}) to measure baseline corticospinal excitability. Although the stimulation intensity could be optimized by using 120% RMT intensity across individuals, the variability in their response to TMS protocols still persists. Plotting the MEP amplitudes against the corresponding stimulation

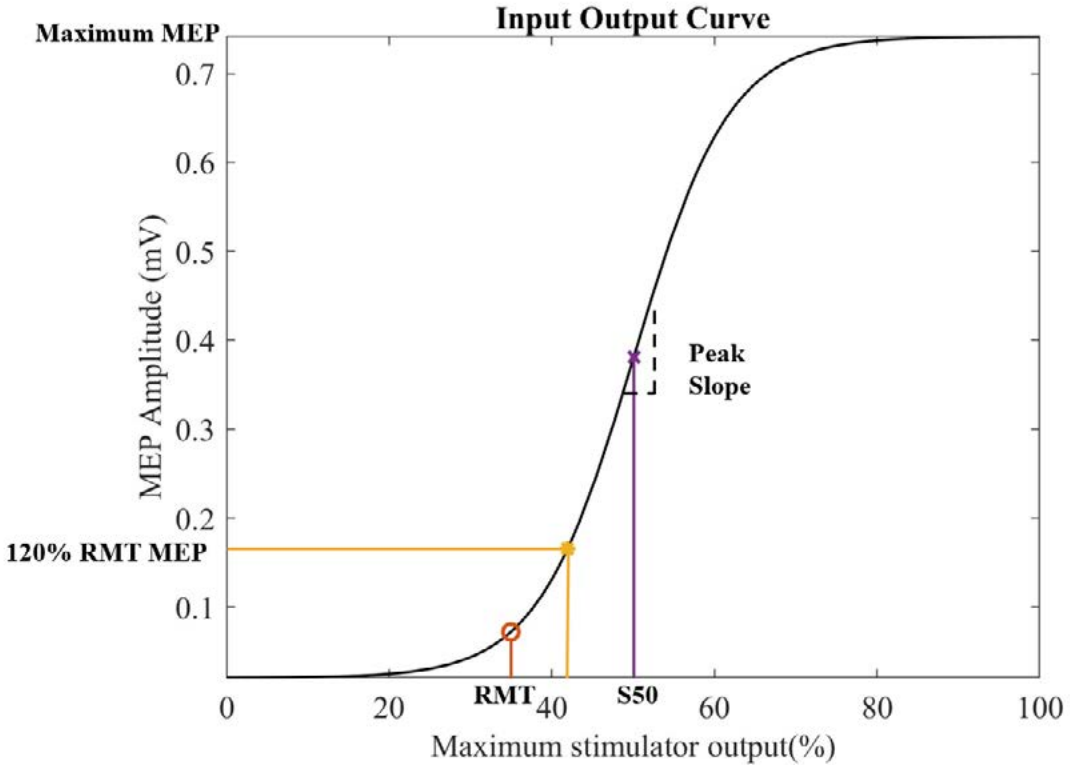

Figure 1. Input-Output Curve of one participant from this study. The labels describe the following parameters: (1) Resting motor threshold (RMT), (2) 120% RMT, (3) Intensity at half-maximum amplitude (S50) (4) MEP amplitude at 120% RMT (MEP_{amp}). The offset and MEP_{max} is visible the IOC as maximum and minimum MEP values respectively. Peak Slope (PS) is the maximum slope of the curve which can be obtained at S50

intensities yields an MEP recruitment curve or the Input-Output curve (IOC), which can be described by the Boltzmann sigmoid function equation. Different aspects of the IOC represent different physiological characteristics of motor excitability. Unfortunately, the majority of the studies do not record IOC, primarily due to time constraints.

In the current project, we aimed to identify the most important IOC parameters that can predict the MEP amplitude at stimulation intensity equal to 120% RMT. For this, we collated IOC data recorded from individuals who participated in three different studies at the Human Motor Control Section, NINDS, Bethesda, USA. This is the first study that has examined the role of IOC parameters in predicting the motor output using a relatively large sample size. We also intended to identify IOC parameters that drive the variability of MEPamp. Since the IOC offers a more detailed characterisation of corticospinal excitability, we expected to obtain valuable insights into the physiological processes that drive inter-individual variability in motor output, a problem that limits the clinical potential of noninvasive brain stimulation.

Methods: The IOC data from 84 healthy adult individuals (mean age: 38 ± 12 years; 39 females) who participated in three different TMS studies at the Human Motor Control Section, NINDS, Bethesda, USA were analyzed. All three studies were approved by the Combined Neuro Sciences IRB of the National Institute of Neurological Disorders and Stroke (NINDS) and conformed to the guidelines of the Declaration of Helsinki. All participants gave written informed consent before participation. None of the participants had any contraindications for undergoing TMS and no adverse events were reported. We excluded data from 6 subjects because their IOC did not saturate at 100% stimulator intensity. We also excluded 3 subjects whose

IOC parameters were beyond 3 standard deviations (or 99.73% confidence interval) from mean value. The data from the remaining 75 subjects were included for analysis.

To examine the inter-individual variability in MEP amplitude at 120% RMT, a General Linear Model (GLM) was built by taking the IOC parameters such as motor threshold (MT), intensity that elicits 50% MEP amplitude (S50), slope of the curve at the midpoint (PS) and maximum MEP amplitude (MEP_{max}) as independent variables. Z-score normalization was done on the independent variables before running the GLM.

We used coefficient of variation (CV) as a measure of inter-individual variability. For this, ee bootstrapped the data to estimate coefficients of variation of IOC parameters and included them in a GLM to identify the significant predictors of MEP amplitude variability. Bootstrapping was done without replacement by choosing subsamples of 50 subjects from a total sample size of 75 in 1000 iterations. This yielded 1000 CV values of MEP_{amp}, MT, PS, MEP_{max} and S50 that represented the distribution of inter-individual variability within our dataset. The bootstrapped CV values for each predictor variable were plotted against the CV values of MEP_{amp}. To identify the IOC parameters that best predicted the variability in MEP_{amp}, a GLM was built using the CVs of the bootstrapped variables.

Results: After removing non-significant and high collinearity variables, our GLM revealed MT, PS, and MEP_{max} as significant predictors of MEP_{amp}. Since all the predictors were z-score normalized, their coefficients indicate their level of importance in the linear model. PS showed the highest positive correlation with MEP_{amp} and was its best predictor. Our simple linear model with only the MT, PS, and MEP_{max} as predictors was sufficient to predict MEP_{amp} with good accuracy implying a strong linear relationship between these IOC parameters and MEP amplitude.

Further, we showed that variability in the MEP_{amp} across individuals is mainly driven by the PS and MEP_{max}, which reflect the recruitment gain and the maximum excitability

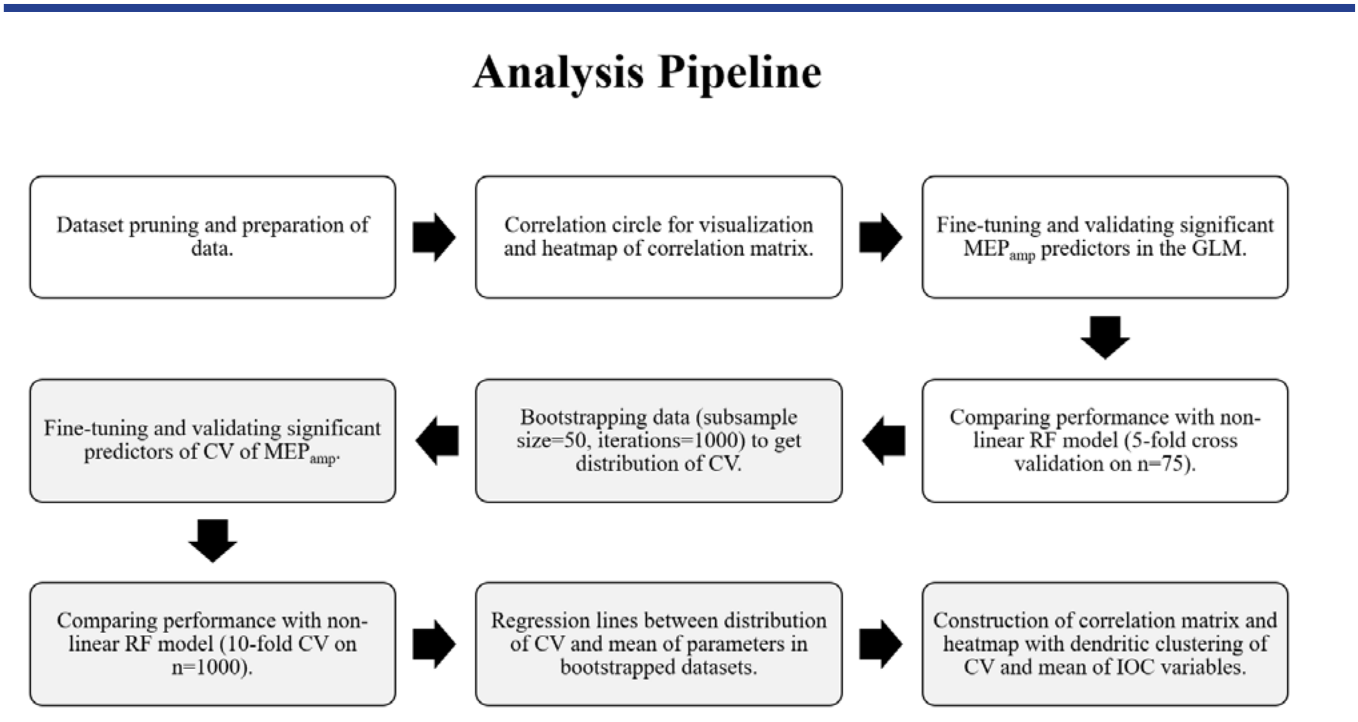

Figure 2. Flowchart of data analysis pipeline. (MEPamp = MEP amplitude at 120% resting motor threshold, GLM = General Linear Model, CV = Coefficient of Variation, RF = Random Forest, IOC = Input-Output Curve.)

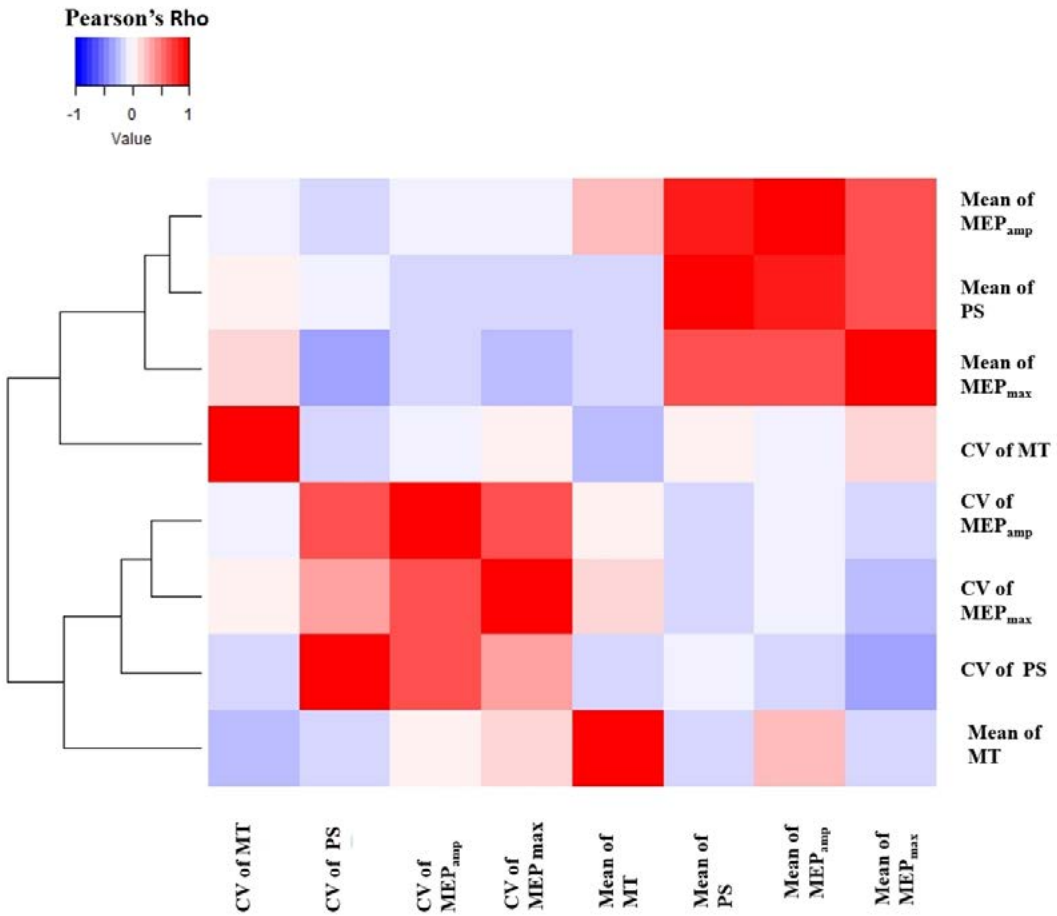

Figure 3. Correlation heatmap and dendrogram showing the relationships between the CV and the means of all IOC parameters.

of the motor neuronal pool at a certain brain state respectively. However, our GLM could explain only about 64% of variability in MEP_{amp} implying that the inter-individual variability in MEP amplitude can only be partially described by the inter-individual variability in IOC parameters.

Conclusion: In summary, we have shown that PS and MEP_{max} are the best predictors of MEP amplitude at 120% RMT. They are also the most important linear predictors of variability in MEP amplitude at 120% RMT intensity. RMT which is commonly used as a reference to individualize TMS stimulation is neither a good predictor of MEP amplitude at 120% RMT nor its variability across subjects. Our study shows that inter-individual variability of MEP amplitude can be accounted to a fair extent by the inter-individual variability of PS and MEP_{max}. We speculate that variability in motor output across subjects can be reduced by achieving a uniform IOC slope which may be possible by optimizing stimulation parameters.

Publications

1. **Shukla S & Thirugnanasambandam N (2021).** Tapping the Potential of Multimodal Non-invasive Brain Stimulation to Elucidate the Pathophysiology of Movement Disorders. **Front Hum Neurosci** 15:661396

Presentations

1. Thirugnanasambandam N. Probing the Pathophysiology of Movement Disorders using Noninvasive Brain Stimulation. NeuroFemIndia 2021 (virtual). April 2021.

2. Thirugnanasambandam N. Basic Functional Neuroanatomy. NeuroReHack Summer School (virtual). June 2021.
3. Thirugnanasambandam N. Training Workshop on TMS-EEG Methodology. NIMHANS, Bengaluru. July 2021.
4. Thirugnanasambandam N. Writing an Effective Grant Proposal. Science Communication Workshop of DBT/WT India Alliance (virtual). February 2022.

Funding

- DBT/WT India Alliance CPH Fellowship (Intermediate) – IA/CPHI/16/1/502624
- Har Gobind Khorana Innovative Young Biotechnologist Award 2020
- Finnish Indian Consortia for Research and Education (FICORE) grant
- EMBO funding for India|EMBO lecture course
- NBRC Core funds

Collaborators

- Dr. Arpan Banerjee, NBRC
- Dr. Roopa Rajan, Department of Neurology, AIIMS, New Delhi
- Prof. Risto Ilmoniemi, Aalto University School of Science, Finland

Degree Awarded

Anwesha Das (MSc in Neuroscience)

Meetings/Conferences organized:

- **NeuroFemIndia 2021 – a BiasWatchIndia Conference (Virtual)**

  As part of the BiasWatchIndia initiative, I was part of the organizing committee of the NeuroFemIndia 2021 conference that was held from 9-13 April 2021 in virtual mode. The aim of the meeting was to showcase the work and increase the visibility of women neuroscientists in India.

- **Gender Bias Workshop for Early Career Researchers (Virtual).**

  On account of International Women's Day, on behalf of the Indian National Young Academy of Sciences (INYAS), I organized a gender bias workshop targeted specifically towards early career researchers on 7th March 2022 in virtual mode. Prof. Mangala Subramaniam, Professor and Butler Chair, Director, Susan Bulkeley Butler Center for Leadership Excellence, Purdue University, USA was the rsource person. She spoke on "Potential strategies for addressing gender bias in academia: a focus on the Indian context".

Swagata Dey

Understanding cytoskeletal regulation during dendrite development and regeneration

Our sensory modalities define our behavior and their absence or dysfunction makes human life inconvenient and vulnerable. Neurons are polarized cells with distinct compartments like dendrites, axons, and synapses. As dendrites are the input processes, they define the quality and quantity of information that is processed by a neural circuit. Dendritic arbors are structurally diverse and their morphology correlates to the neuron type and function. Aberrant dendrite morphology is a hallmark of some chronic and acute neuropathologies like Autism, Schizophrenia, Alzheimer's disease, epilepsy, traumatic brain injuries, and drug abuse.

Unlike other compartments of the neurons, dendrites remodel extensively in response to various developmental, sensory, or pathological cues. For example, during pupa formation, *Drosophila* da neurons prune their dendrite arbor completely and reconstruct in a new geometry. Similarly, in vertebrates, sensory experience refines the connections of the mitral cells with a particular glomerulus. Neurite remodeling has been extensively studied using axon injury models and is facilitated by changes in the cytoskeletal architecture, rerouting of the polarized transport, and changes in the transcriptome. For example, axon injury causes a rise in the intracellular calcium which causes catastrophe of the microtubules and an increase in Cyclic Adenosine monophosphate (cAMP), Protein Kinase A (PKA), and Mitogen-activated protein kinase kinase kinase (MAPKKK) such as Dual Leucine Zipper Kinase (DLK-1). DLK-1 downregulates the microtubule depolymerization by KLP-7 (Kinesin-13) and promotes the formation of the growth cone facilitated by the actin turnover mechanisms. Dendrites and axons have a distinct molecular constitution and conventional axon regeneration pathways are not involved in dendrite regeneration. However, cytoskeletal effectors like AKT, ROR, and Wnt effectors have been implicated in the process.

The dendritic cytoskeleton is mainly composed of the microtubules and actin with scaffolding proteins like spectrins and septins. The core machinery for microtubule maintenance consists of

end binding proteins like EBP and Patronin, depolymerizing motor Kinesin-13, assembly factors like CRMP, and motors like Kinesin-1 that transport the majority of cargoes including tubulins and MT protofilaments. Similarly, actin is maintained by polymerization factors like Profilin, depolymerization factors Cofilin, and branching factors like Arp-2/3 and WASP/WAVE which have been implicated in the formation of the dendritic arbor. Dendritic arborization also depends on the microtubule and actin nucleators in the form of Golgi outposts, kinetochore proteins, endoplasmic reticulum, and actin blobs which enrich at the presumptive dendritic branch points. Due to dendritic complexity and lack of in vivo models, it is not well understood how neuronal cytoskeleton is organized and regulated for proper dendritic arborization during development or regeneration.

Using the PVD neurons, this study aims to understand

- The microtubule dynamics and role of its regulators during dendrite injury and regeneration.
- The role of actin and its regulators in the process of dendrite regeneration.
- Changes in the polarized transport during dendrite regeneration.

Among the microtubule regulators, we focused on understanding the role of KLP-7 (Kinesin-13), PTRN-1 (Patronin), and EFA-6 (ArfGEF). KLP-7 of the Kinesin-13 family depolymerizes the microtubules and is implicated in axon regeneration as it is downregulated by DLK-1. KLP-7 has also been implicated in the regulation of neuronal polarity and anatomy under the effect of Wnt signaling in the touch neurons of *C. elegans*. Furthermore, in *Drosophila* neurons, its ortholog Klp10a negatively regulates the dendrite pruning and the null mutant of its mouse ortholog Kif2a has abnormal neuronal morphology.

PTRN-1 is a minus-end binding protein and protects the minus ends of the microtubules against KLP-7-mediated depolymerization. It is also required for the maintenance of the microtubule polarity in the dendrites. PTRN-1 is required for axon regeneration in touch neurons of *C.elegans* and dendrite development, pruning, and regeneration in *Drosophila* da neurons.

EFA-6 is a cortical protein required for the regulation of both actin and microtubule cytoskeleton as well as vesicle trafficking. In *C.elegans* axonal injury can elicit an EFA-6 mediated DLK-1 independent pathway of regeneration.

Developmental changes in the PVD arbor from larval to adult stages

PVD neurons in *C. elegans* have a well-defined axon and stereotyped dendritic arbor. The branches are formed orthogonally in anatomy and hierarchy with a distinct cytoskeletal constitution.

The primary branches run in the anterior-posterior direction are mostly microtubule rich whereas the higher order branches have an actin based cytoskeleton. In order to understand the role of cytoskeletal regulators in dendrite arborization of PVD neurons, it is critical to observe the branch dynamics of different hierarchy at multiple stages of development. PVD is born during the L2 stage, and majority of arbor develops in the subsequent larval stages. I established a staging paradigm to understand branch formation at each of the hierarchical levels of dendrite arbor. The primary branches are laid out by L2 stage and they remain constant until the adult stage at 60 h AEL (Figure 1A-B). Excess primary branches developing during the adult stage fail to form higher order branches suggesting ectopic development (Figure 1A-B).

Majority of the secondary, tertiary, and quaternary branches are formed at the

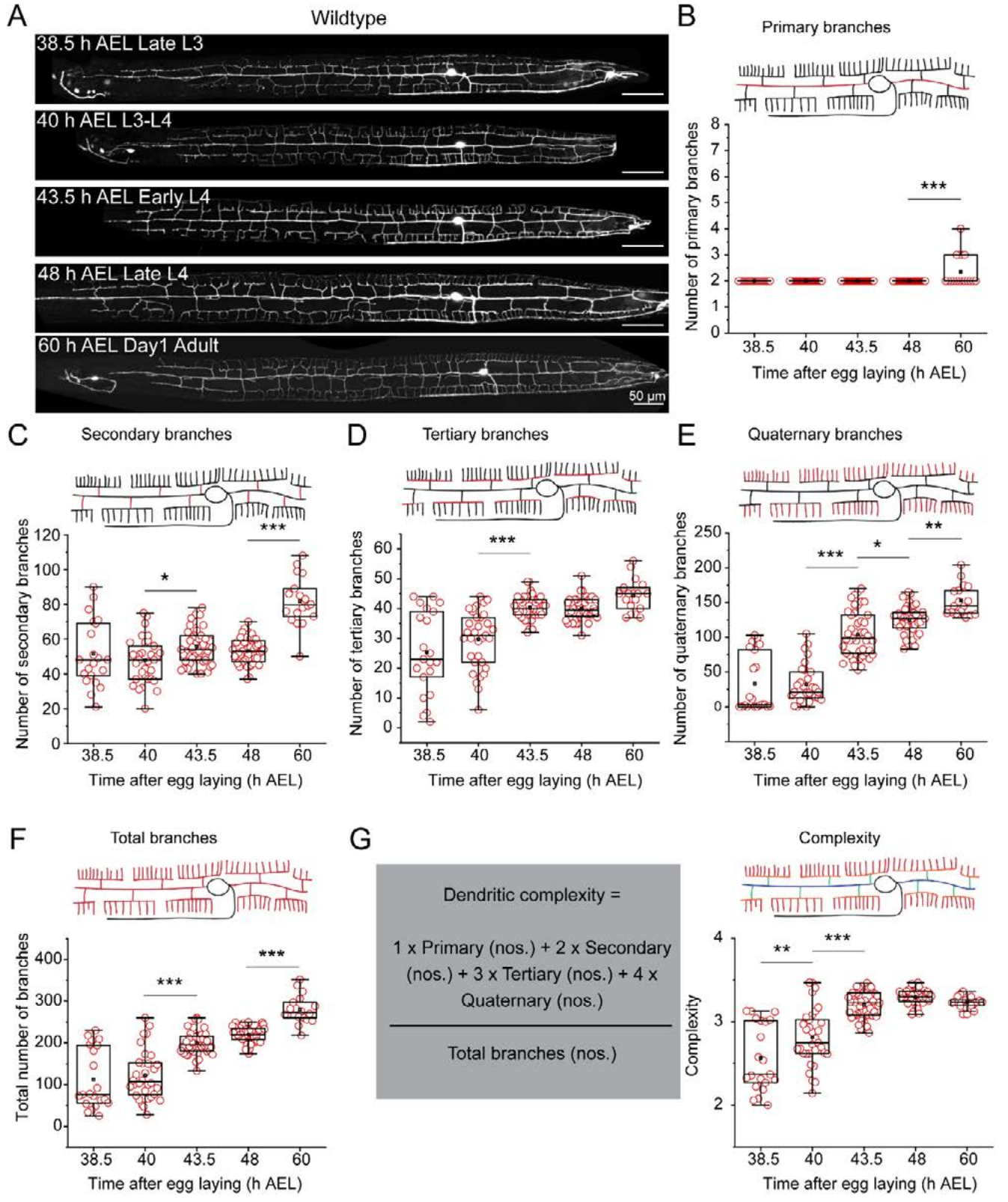

Figure 1: Developmental timeline of dendrite arborization in PVD neurons.

A. Representative images of GFP expressing PVD neurons at different developmental stages. **B-E.** Quantification of the total number of primary (B), secondary (C), tertiary (D), and quaternary (E) branches compared across different developmental stages. A comparison of means was done using ANOVA and Tukey's test. p<0.05*, 0.01**, and 0.001***. **F.** Cumulative number of branches at all hierarchical levels compared across different developmental time points. A comparison of means was done using ANOVA and Tukey's test. p< 0.001***. **G.** Comparison of the complexity of the branches at various stages as described on the left. Mean values were compared using ANOVA and Tukey's test. p<0.01**, and 0.001***.

beginning of L4 stage between 40 to 43.5 hours after egg laying (h AEL) which become part of the dendritic arbor (Figure 1A, 1C-D). During adult stages we observed an increase in the secondary branches (Figure 1C). Like the primary branches, these secondaries are offshoots of existing secondary and fail to form higher order branches. Tertiary branches are fully formed by 43.5 h AEL however, they are dynamic and show fragmentation or fusion (Figure 1D).

The quaternary branches further grow after 43.5 h AEL until adult stage after which we observed offshoot branching at the level of quaternary (Figure 1A, 1E) thus increasing the total number of branches (Figure 1A, 1F). As the dendritic complexity does not change significantly after 43.5 h AEL, we considered complete arbor formation by 48 h AEL of development (Figure 1A, 1G). We further focused on this stage to assess the role of cytoskeletal regulators.

KLP-7 and EFA-6 regulate the formation of secondary during dendrite development

KLP-7 is a motor of Kinesin-13 family that depolymerizes the microtubules at both its plus and minus ends. Loss of KLP-7 promotes axon regeneration in a DLK-1 dependent manner. Dendrite regeneration is independent of DLK-1 suggesting an alternate pathway. Loss of EFA-6 also promotes axon regeneration by partially bypassing DLK-1. Although both KLP-7 and EFA-6 are known as microtubule regulator, their role in the dendrites is not known.

We observed the dendrite arborization in *klp-7(0)* and *efa-6(0)* loss of function mutants along with *ptrn-1(0)*(Figure 2A). Patronin is required for maintenance of microtubule polarity in the dendrites of *Drosophila* neurons. We observed an increase in the number of secondary branches in the loss of function of *klp-7(0)* and *efa-6(0)* as compared to the wildtype (Figure 2A-B). Though both *klp-7(0)* and *efa-6(0)* showed an increase in the secondary dendrites, *klp-7(0)* mutant had secondary branches that failed to form any tertiary or formed an aberrant tertiary. Loss of ptrn-1 did not cause an increase in the secondary branches corroborating an earlier result.

We further assessed the number of secondary branches present per unit length of primary (Figure 2C). In *klp-7(0)* density of secondary branches was significantly higher than the wildtype during the L4 stages. This indicated a potential role of *klp-7* in limiting secondary branching in PVD neurons. As KLP-7 is a microtubule depolymerizing enzyme and has been implicated in regulating microtubule polarity in a neurite, we observed the microtubule dynamics using the plus end binding reporter EBP-2::GFP. Similar to previous studies, dynamic microtubules were localized to the axon and primary dendrites of the PVD neuron. The primary major branch has minus end out polarity of the microtubules. However, loss of function of *klp-7* caused the microtubules to also ingress into higher order branches like secondary and tertiary (Figure 2D). Furthermore, kymograph analysis showed a shift in the microtubule polarity in the major dendrite of PVD as compared to the wildtype (Figure 2E-G). These results show that *klp-7* is limiting dynamic microtubules to invade the secondary branches and may regulate microtubule polarity locally. We speculate that stabilization of microtubules and their ingression into the secondary branches may cause formation of ectopic processes in the *klp-7(0)* mutant. However, as the microtubule orientation was not changed drastically, KLP-7 is not the sole regulator of microtubule dynamics and orientation. Other microtubule regulators like Patronin and Kinesin-1 are known to regulate the microtubule dynamics and orientation in the PVD dendrites.

We will be investigating the microtubule polarity and dynamics in the *efa-6(0)* and *ptrn-1(0)*.

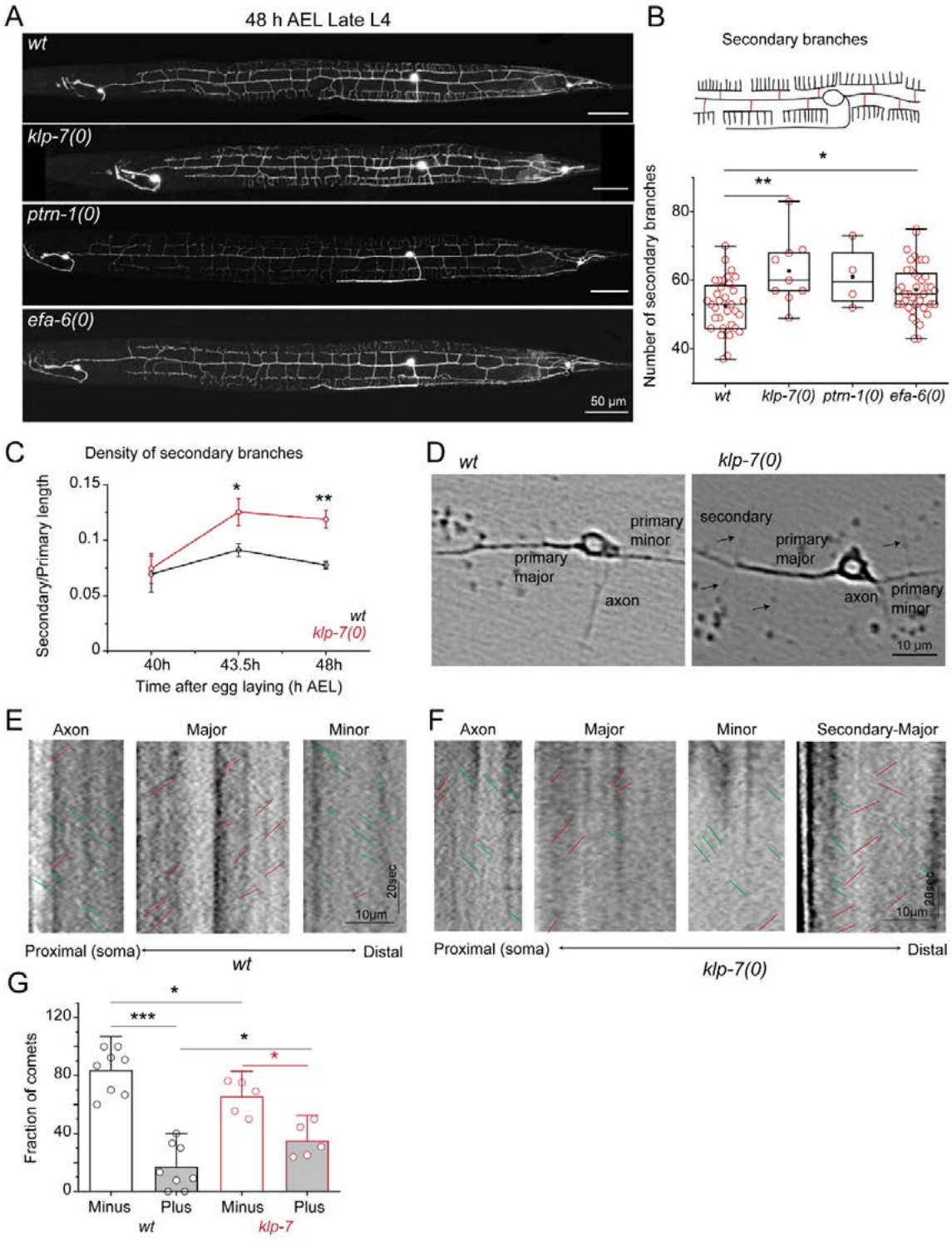

Figure 2: Dendrite arborization in mutants of microtubule regulators.

A. Representative images of the GFP expressing PVD neurons in wildtype (*wt*) animals and loss of function mutants of microtubule regulators, *klp-7*, *ptrn-1*, and *efa-6* with no major defects in the dendrite arbor at 48 h AEL. **B.** Quantification of the secondary branches shows an increase in the *klp-7(0)*, and *efa-6(0)* mutants as compared to the *wt* at 48 h AEL. **C.** Increase in the secondary branch density was observed in *klp-7(0)* during the development of the PVD neuron. Data is represented as Mean + SEM and compared using ANOVA and Tukey's comparison. p<0.05*, and 0.01**. **D.** Localization of dynamic microtubules marked by the reporter EBP-2::GFP in the PVD neurons of *wt* and *klp-7(0)* animals. **E-F.** Kymographs of EBP-2::GFP in the axon, major dendrite, and minor dendrite of *wt* (E) and *klp-7(0)* (F) PVD neurons. Additional comets were observed in the secondary dendrites (Secondary-major) of *klp-7(0)* mutant neurons represented in the F panel. Comets moving away from the cell body and towards the cell body are classified as plus end out (green traces) and minus end out (red traces), respectively. **G.** Quantification of the percentage of EBP-2::GFP comets in minus and plus end out orientation represented as Mean + S.D. Comparison of means was done using ANOVA and Tukey's test. p<0.05*, and 0.001***.

KLP-7 is required for proper tiling of the PVD menorah and formation of higher order branches

As previously mentioned, we observed aberrant tertiary branching in the *klp-7(0)* mutant. Unlike *efa-6(0)*, secondary branches in *klp-7(0)* made no or aberrant tertiary. The aberrant tertiary branches had multiple secondary branches associated with it (Figure 3A).

We estimated the total number of tertiary branches in the mutants of cytoskeletal regulators (Figure 3B). As compared to the wildtype, loss of *klp-7* mutant had less number of tertiary, and *efa-6* null mutant had higher number of tertiary branches. *ptrn-1(0)* showed comparable number of tertiary branches to wild type (Figure 3B). Also, the number of tertiary present per secondary was considerably lesser in *klp-7(0)* mutant than the wildtype indicating formation of aberrant tertiary in *klp-7(0)* mutant (Figure 3C). Around 10% of mature secondary branches in klp-7(0) mutant bear an aberrant tertiary as compared to the wildtype or *efa-6(0)* where many of the animals did not have any aberrant tertiary (Figure 3D).

Previous studies have found the role of F-actin in the remodeling of tertiary branches of PVD neurons. The F-Actin is downstream to various effector molecules like MIG-14/Wntless, KPC-1, Netrin-DCC signaling and Flamingo. However, it is unclear how KLP-7 may affect the tertiary branching.

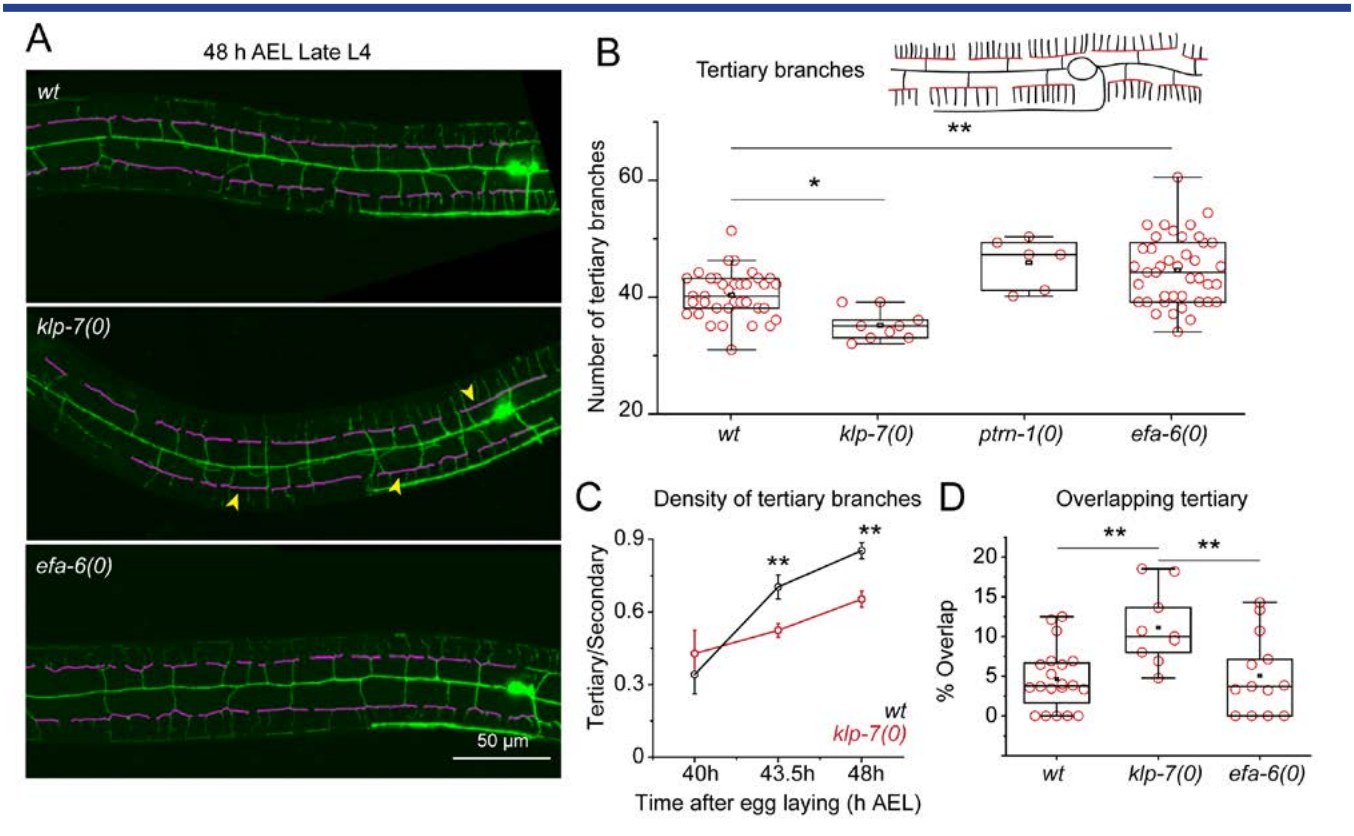

Figure 3. Effect of microtubule regulators in tertiary branch development.

A. Representative images of PVD arbors labeled by GFP in loss of function mutants of *klp-7*, and *efa-6* compared with the *wt* highlighting differences in the tertiary branches (magenta). **B.** Quantification of the overall number of tertiary branches in the *wt*, *klp-7(0)*, *ptrn-1(0)* and *efa-6(0)* animals. A comparison of means was done using ANOVA and Tukey's test. p<0.05*, and 0.01**. **C.** Density of tertiary branches per secondary decreased in the *klp-7(0)* mutant due to an increase in the overlap during the development of PVD neurons. Data is represented as Mean + SEM and compared using ANOVA and Tukey's comparison. p< 0.01**. **D.** Percentage of tertiary branches showing overlap were normalized with number of mature secondary (making tertiary) quantified in the major dendrite of *wt*, *klp-7(0)*, and *efa-6(0)* neurons. A comparison of means was done using ANOVA and Tukey's test. p<0.01**.

Along with tertiary branching, the quaternary branch formation was significantly affected due to loss of *klp-7*. We estimated the total number of quaternary branches in the *klp-7*, *ptrn-1*, and *efa-6* mutants (Figure 4A). While the number of quaternary branches in *ptrn-1(0)* and *efa-6(0)* were comparable to the wild type, it was significantly decreased in the *klp-7(0)* mutant at 48 h AEL (Figure 4A). Surprisingly, the number of quaternary branches in *klp-7(0)* at an earlier developmental time point (43.5 h AEL) were significantly higher than the wildtype (Figure 4B). This is also reflected in the density of quaternary branches per tertiary which was higher at 43.5 h AEL and lower at 48 h AEL in the *klp-7(0)* as compared to the wildtype (Figure 4C). The live imaging paradigm showed a growth and retraction of the quaternary branches in the wildtype. The dynamics of these branches was reduced in the *klp-7(0)*(Figure 4D).

We hypothesize that quaternary branches grow in a biphasic manner with phases of rapid growth followed by slow growth. Slow phase is a calibration to keep the branches with proper guidance complex. It is possible that the *klp-7(0)* mutant neurons have unstable protrusions as quaternary that are not stabilized due to stabilized microtubules or lack of actin or a combination of both. Alternatively, the receptor complex of DMA-1 and HPO-30 required for quaternary formation might be mislocalized or mistranported.

Though microtubule distribution has not been documented in the tertiary and quaternary branches of the PVD neurons, it is possible that the microtubule stabilization in *klp-7(0)* mutant

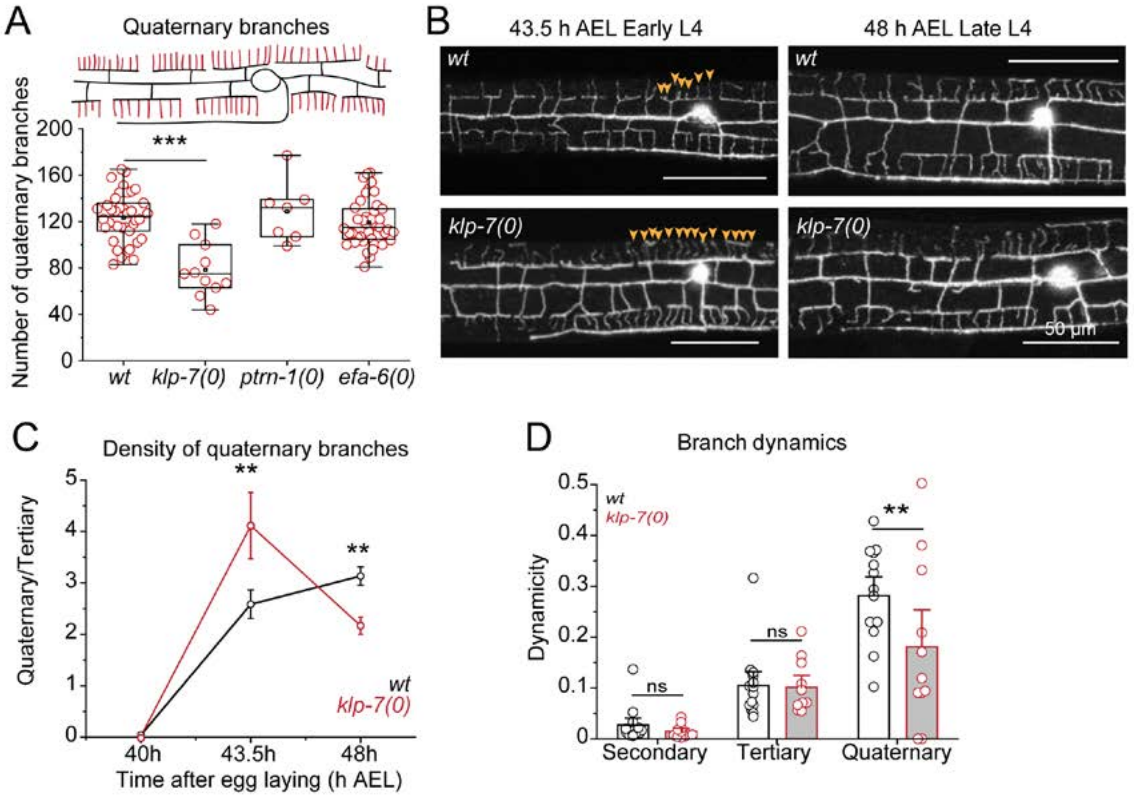

Figure 4. Effect of microtubule regulators in development of higher order branches.

A. Quaternary branches of PVD neurons of *wt*, *klp-7(0)*, *ptrn-1(0)*, and *efa-6(0)* animals quantified. A comparison of means was done using ANOVA and Tukey's test. p<0.001***. **B.** Representative images of the PVD neurons of *wt* and *klp-7(0)* in the early and mature stages of development. A differential change in the quaternary branches (yellow arrowheads) was observed in the *wt* and *klp-7(0)* PVD neurons. **C.** Density of the quaternary branches was altered in klp-7(0) mutant at different developmental stages. Comparison of means was done using ANOVA and Tukey's test. p<0.01**. **D.** Dynamicity of the branches were estimated from live imaging of the neurons in *wt* and *klp-7(0)* neurons. *klp-7(0)* mutants showed less dynamic quaternary branches than *wt* during development.

may change the cytoskeletal constitution in tertiary and thereby its formation. Also, using other microtubule reporters we will be validating this observation. Characterization of actin cytoskeleton in the *klp-7(0)* will help to test this hypothesis.

KLP-7 determines the axon-dendrite compartmentalization in the PVD neurons

Previous studies have documented a conversion of the dendrites to axon like identity as a consequence of the loss of Kinesin-13. We also made similar observations in the PVD neurons by using a axonal cargo reporter, mCherry::RAB-3. This reporter is present only in the axons of wild type neurons whereas in the loss of *klp-7* function, mCherry::RAB-3 was mislocalized to the secondary, tertiary and sometimes to the quaternary dendrites (Figure 5A-B). This dendro-axonal conversion is reminiscent of taxol treated developing neurons.

Since the overall dendritic morphology is maintained, it is possible that during the neuritogenesis of PVD in *klp-7(0)* mutant, the stabilized microtubules misdirected the axonal cargoes to the dendrites. On the other hand, loss of *efa-6* did not cause a mislocalization of mCherry::RAB-3 into the dendrites (Figure

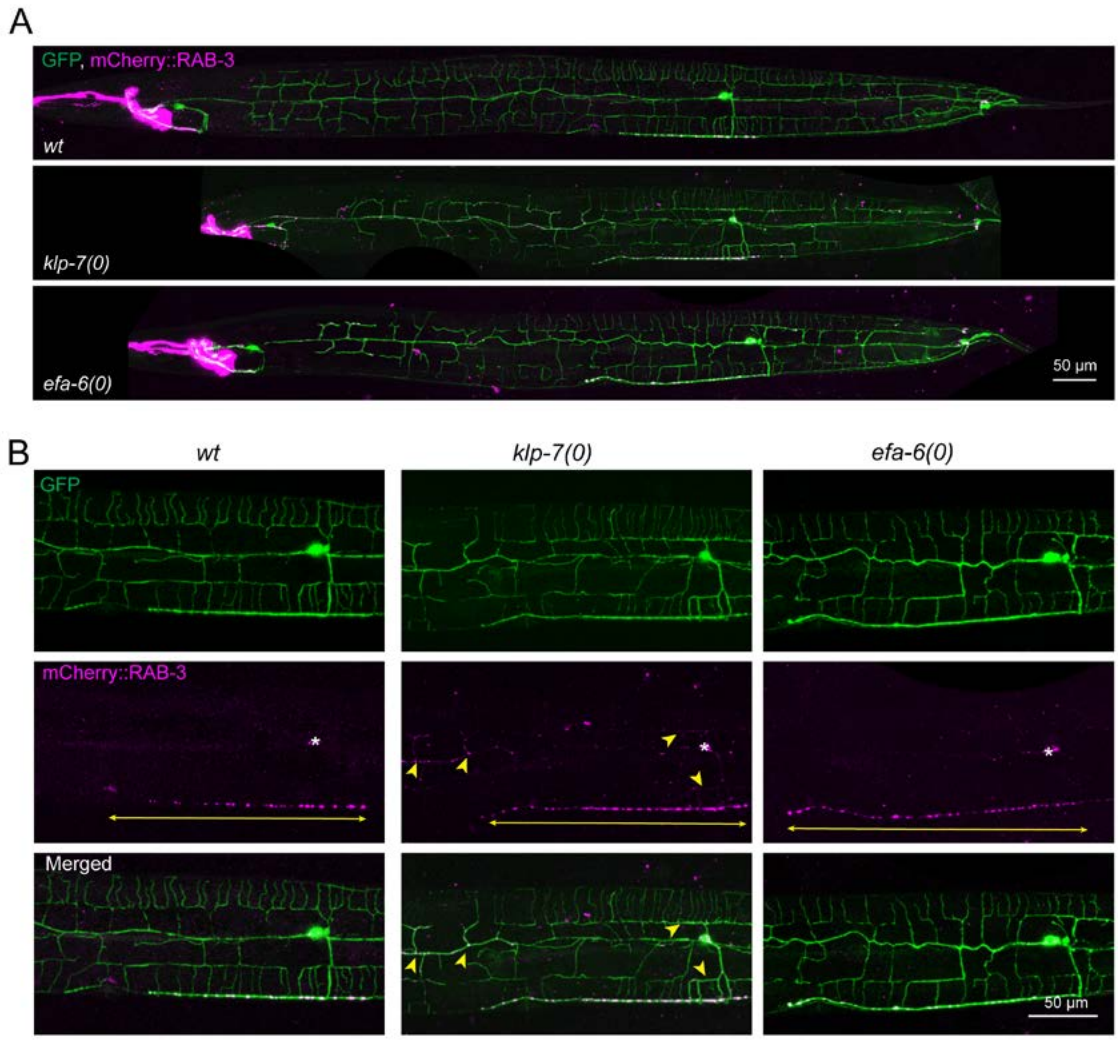

Figure 5. Loss of axon- dendrite compartmentalization in the *klp-7(0)* mutant.

A-B. Representative images (A) of PVD neurons expressing GFP and mCherry::RAB-3 in *wt*, *klp-7(0)*, and *efa-6(0)* animals with the magnified view of proximal arbor (B). Note the mislocalization of synaptic marker mCherry::RAB-3 to the dendrites of *klp-7(0)* mutant. Dendritic punctae of RAB-3 have been marked with yellow arrowheads whereas axonal distribution of RAB-3 has been denoted by yellow arrow.

5A-B). This indicates that microtubule stabilization might not be the cause of the loss of axon-dendrite polarity. Alternatively, microtubule stability in the presumptive axon ensures the formation of the diffusion barrier by TRIM46, UNC-44 (Ankyrin) at the axon initial segment which might have altered in *klp-7(0)* loss of function. Using a reporter of UNC-44 we will be testing this hypothesis.

Role of cytoskeletal regulators in dendrite regeneration

Apart from development, dendrites undergo extensive remodeling in acute clinical conditions. Though dendrite regeneration is independent of the conventional axon regeneration pathways, kinases like Akt, Ror, and Wnt effectors have been implicated in the process. Among various cytoskeletal regulators tested, Patronin and RacGTPase are necessary for dendrite regeneration. However, it is unclear what are the cytoskeletal requirements of dendrite regeneration.

To investigate further, we severed the major dendrite using a laser assisted transection and observed these after 24 hours. We tested *klp-7(0)*, *ptrn-1(0)*, and *efa-6(0)* mutants in this paradigm (Figure 6A). In the wild type worms, the major dendrite regenerates with extensive non-stereotype branching, reconnection between the proximal and distal sections of severed primary, and reconnection between

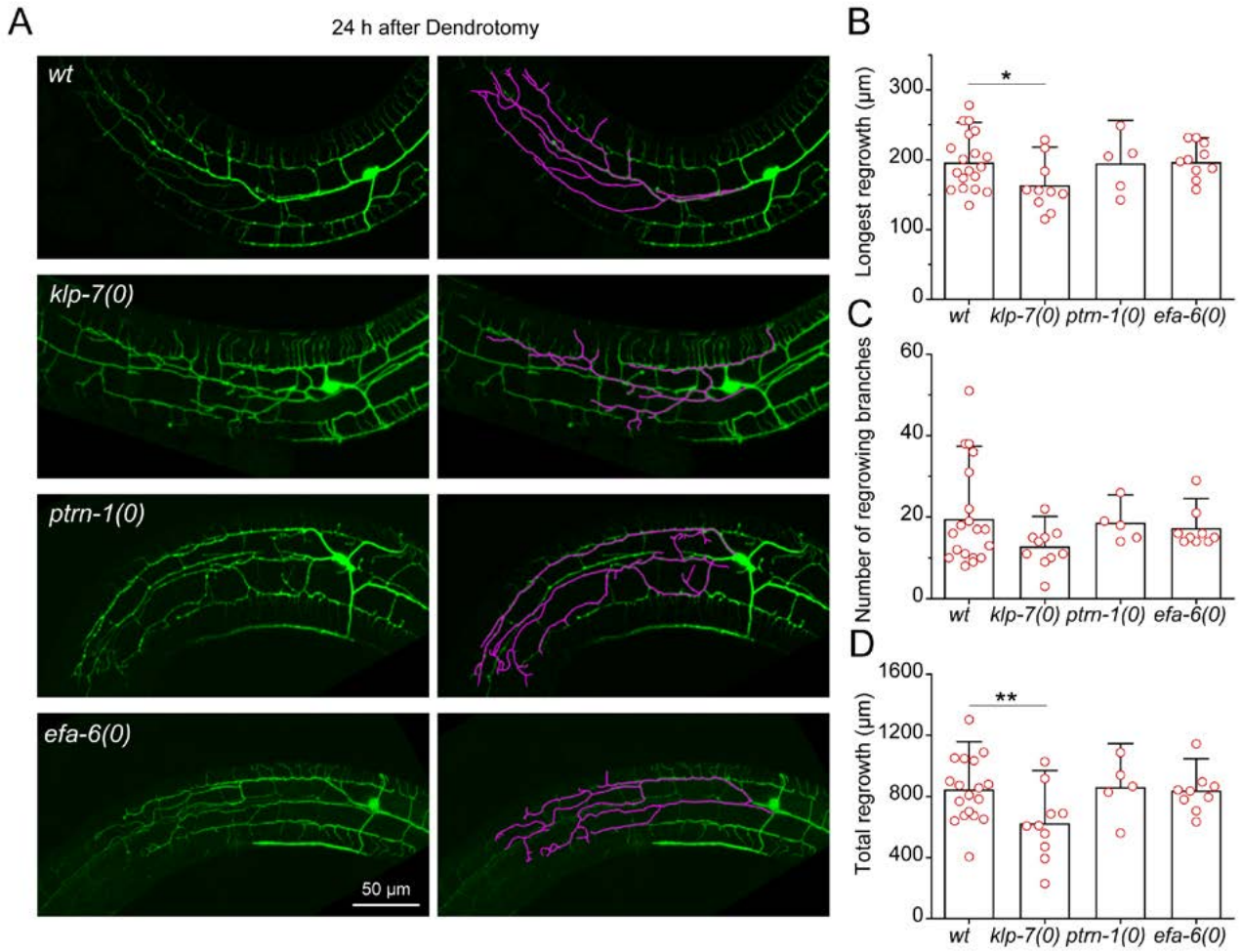

Figure 6: Role of cytoskeletal regulators in dendrite regeneration.

A. Representative images of the regenerated major dendrite of PVD neurons in *wt*, *klp-7(0)*, *ptrn-1(0)*, and *efa-6(0)* animals. On the right side, magenta traces represent the regenerated arbor in the corresponding mutants. **B-D.** Dendrite regeneration is quantified as longest regrowth (B), number of regrowing branches (C), and total regenerated arbor (D) in the cytoskeletal mutants. Data is represented as Mean + S.D. and mean values were compared using ANOVA and Fisher's test. $p<0.05$*, and 0.01**.

tertiary branches. Among the mutants tested, the *klp-7(0)* showed a reduced regenerated arbor (Figure 6A).

Quantification of longest regenerating branch and the sum total of all regrowing branches showed a reduction in the *klp-7(0)* mutant background as compared to wildtype, *ptrn-1(0)*, and *efa-6(0)* (Figure 6B, 6D). All the microtubule mutants had a tendency towards reduced number of regrowing branches (Figure 6C). We will be characterizing this further with microtubule reporters to understand their roles.

We found the Rac GTPase, CED-10 is required for the dendrite regeneration. CED-10 is a GTPase upstream to both actin and microtubules. To understand the organization of actin during dendrite regeneration, we explored the transgenic expressing GFP::Moesin in the PVD neuron. In the uninjured neurons, the GFP::Moesin is observable in the higher order dendrites mostly (Figure 7A). After the major dendrite was severed, we observed a drastic reduction in the intensity of GFP::Moesin in the distal severed portion within 3 hours (Figure 7A-B). Also, we found an enrichment of the GFP::Moesin in the regrowing end of the dendrite (Figure 7A-B). This indicates F-Actin turnover is required for the regrowth. Using this reagent, we will be testing other cytoskeletal regulators.

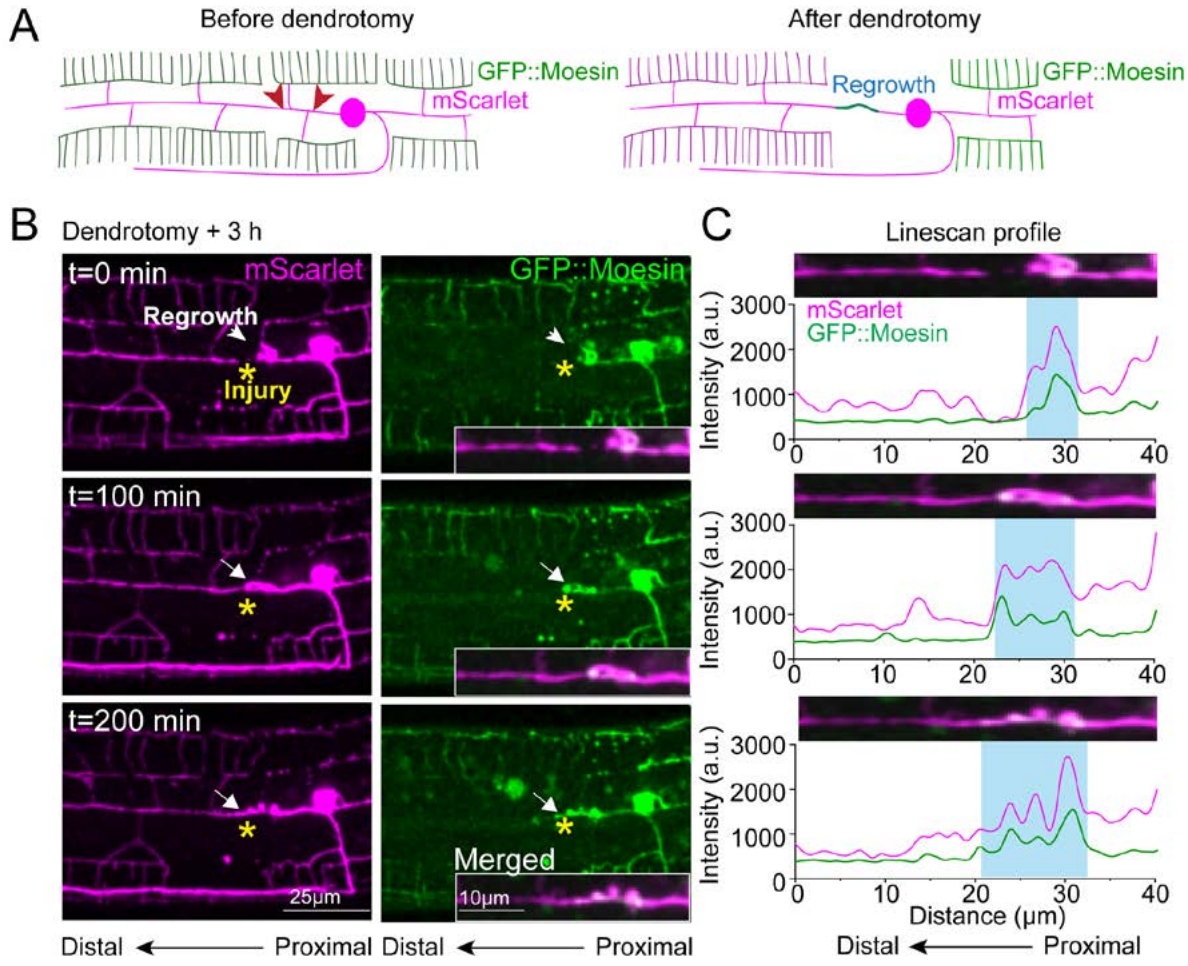

Figure 7. F-Actin enrichment in the regenerating dendrites of PVD neurons.

A. Schematic representing distribution of GFP::Moesin and mScarlet expressed in the PVD neurons before and after dendrotomy. GFP::Moesin is a reporter of filamentous actin (F-Actin) present in higher order dendrites of PVD neuron. **B-C.** Enrichment of F-Actin in the regrowth (white arrow, highlighted in linescan) from the severed dendrite at 3 hours post dendrotomy (yellow asterisk). Note the observable decrease in F-Actin in the distal severed portion of the dendrites.

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1. Swagata Dey: Kinesin-13 dependent dendrite arborization in the PVD neurons of *Caenorhabditis elegans*. Virtual, The Cytoskeleton of Neurons and Glia Webinar. March 2022.

2. Swagata Dey: Kinesin-13 regulates developmental pruning of dendrites in the PVD neurons of *Caenorhabditis elegans*. Virtual, 2021 Doorstep Meeting: The Cell Biology of Neurodegeneration and Repair. November 2021.

3. Swagata Dey: Kinesin-13 regulates growth and pruning of dendritic branches. Virtual, India Alliance Annual Conclave 2021. October 2021.

4. Swagata Dey, Nitish Kumar, Anindya Ghosh-Roy: Kinesin-13 mediated regulation of dendritic branch remodeling during the development of PVD neuron. Virtual, 23rd International Worm Meeting 2021. June 2021.

5. Swagata Dey: Revisiting the "Neuron Doctrine": Insights from live imaging. Virtual, NeuroFemIndia 2021. April 2021.

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Award

Featured in #365IndianWomenInSTEM series of TheLifeofScience.com (2021)

Major Research Programs

Dementia Science Programme

(A DBT Funded National Level Research Programme)

coordinated by National Brain Research Centre

Dementia is a devastating memory impairment condition. Alzheimer's disease (AD) accounts for majority of these cases. AD is a neurodegenerative condition. In the advanced stages of the disease, severe memory loss and impairment in other brain functions is observed. In addition to AD, there are other dementia conditions such as vascular dementia, dementia with Lewy body, and frontotemporal lobe dementia. According to the projections, the number of dementia cases are likely to increase tremendously in the coming decades. Out of these, majority of the cases are expected to be in low and middle-income countries such as India. This may tremendously increase the burden on the healthcare system as well as the society.

An urgent need was felt to understand different facets of dementia including AD. Towards this, National Brain Research Centre is coordinating a DBT-funded comprehensive and multi-centric Dementia Science Programme aimed at collecting data regarding incidence, prevalence, biomarkers, and risk and protective factors. This Programme involves basic scientists as well as clinicians from rural as well as hospital sites across the country. All the participating sites use robust and uniform criteria for diagnosis of dementia and its classification. These criteria are internationally accepted, and have been adapted and validated for the Indian context. It is expected that the results from the study may help in formulation of National levels policies for this major cognitive disorder. in the elderly population.

Participating Institutions (arranged alphabetically) in Dementia Science Programme are:

1. All India Institute of Medical Sciences, New Delhi
2. Bangur Institute of Neurosciences, Kolkata
3. University of Calcutta, Kolkata
4. The INCLEN Trust International, New Delhi
5. National Brain Research Centre, Manesar
6. National Institute of Mental Health and Neurosciences, Bengaluru
7. North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong
8. Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram

Director, NBRC is coordinating the Programme, with Dr. Shiv Sharma, NBRC, and Dr. NK Arora, INCLEN Trust International, as co-coordinators.

NBRC Flagship program: Comparative mapping of common mental disorders (CMD) over lifespan

Coordinator (Ex-officio, Director/ Director-in-charge NBRC): Prof Pravat Mandal

PIs (Brain Imaging): Dr Arpan Banerjee and Dr Dipanjan Roy

PIs (Bio-banking and genetic analysis): Dr Shiv Kumar Sharma and Dr Anindya Ghosh Roy

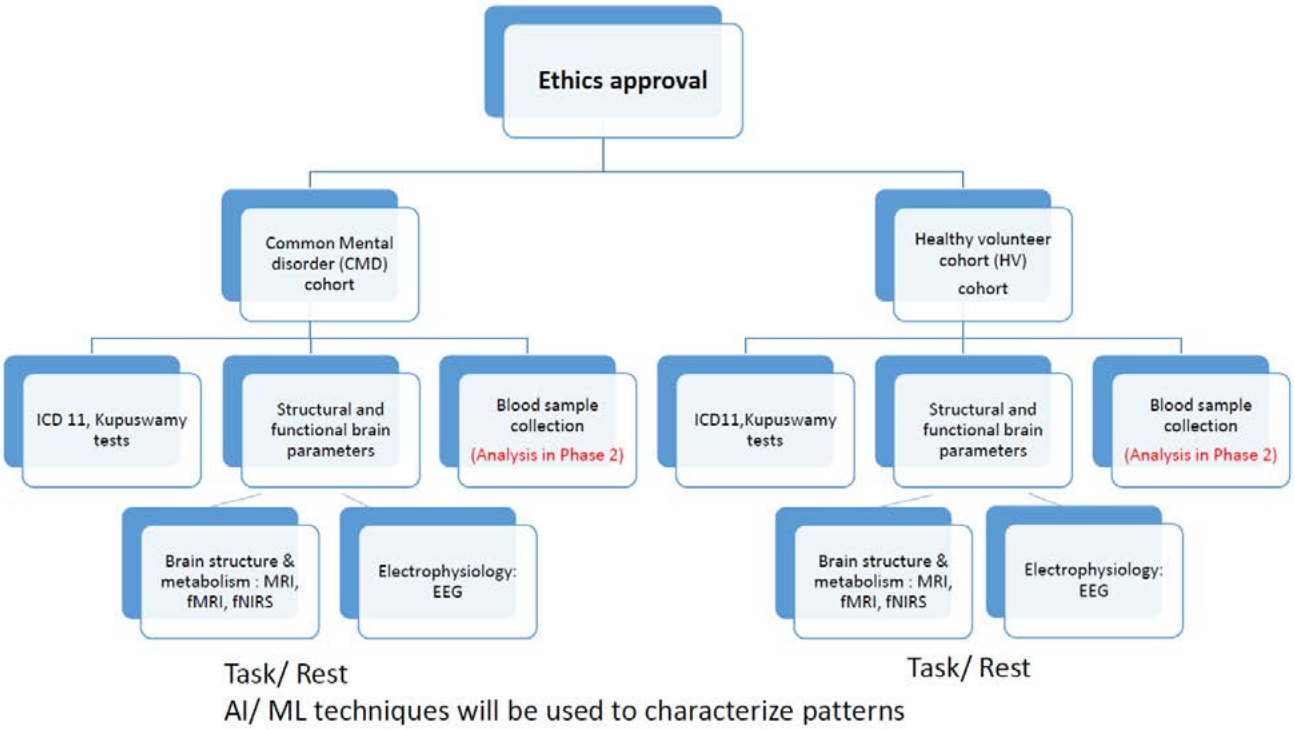
NBRC has secured funds from Department of Biotechnology in support of its flagship program for brain mapping of common mental disorders (CMD) of India. In Phase 1 the project involves collection of brain imaging and biological sample by building cohorts and identifying imaging phenotypes from anxiety, depression, bipolar and post-traumatic stress disorder (PTSD) – together defined as CMD. In Phase 2, the project will involve linking of brain imaging and molecular phenotypes by Artificial intelligence / machine learning tools. Goals of the flagship program (Phase 1) are following

- To build a new big-data repository comprising of brain imaging (structural and functional) data of normal **and patients with common mental disorders (CMD) comprising of anxiety, depression, OCD and PTSD,** where *AI-based techniques can be implemented over the long-term.*
- Quantification of changes in brain's structural and functional networks during resting state and with naturalistic stimuli in a cross-sectional adult life span data from general population (in the age range between **18-80 years**)
- Identification of parameters to differentiate between different etiologies of cognitive impairment **in CMD subtypes comprising of anxiety, depression, OCD and PTSD**.
- Predictive regression based model to extract relationship among mental health measures in different phases of CMD in the age range between 18-80 years and overlapping brain connectivity patterns
- Collection of blood samples to build a biobank for genetic analysis in Phase II

The flagship project is of immense clinical and research importance to the nation and will be impactful in patient treatment and drug discovery. The project will provide normative data in populations that has not been accessed by previous studies and be an important resource hub for a variety of researchers from eminent technological institutions in the country. The expected outcome from this project are following:

1. **Creation and dissemination of a public database** that will include normative data from 200 healthy volunteers and 200 mental health affected patients.
2. **Several imaging derived phenotypes (IDP)** that include information about specific brain structures and their connections by the end of Phase 1.
3. **Creation of a bio-bank in Phase 1** that will store blood samples from healthy and patient participants. **In phase 2 genomic DNA** will be prepared from the blood samples and subsequently whole-genome sequencing and analysis will be done.

Implementation road map



Current status: Ethics protocol obtained, healthy volunteer cohort development in process, protocols for MRI scans and behavioral study design is finalized.

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Report prepared by Dr Arpan Banerjee, Scientist V, NBRC.

Prepared by Dr. Arpan Banerjee

Publications, Patents & Presentations

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Presentations

1. Anindya Ghosh Roy 25th Feb 2022, IN-EMBO webinar series. "*C. elegans* as a model for nerve regeneration study"
2. Anindya Ghosh Roy Brain Awareness Week, March 14 to 20 at DBT-InStem, organized by InStem, Bangalore, "Study of neuronal regeneration using *C. elegans*"
3. Anirban Basu Primary Cell Culture model: An excellent tool to study the effects of Viral Infection of CNS; 6th International Brain Research School, Suleyman Demirel University, Isparta, Turkey, 21-27 June 2021. (*on line mode*)
4. Anirban Basu Innate Immunity in the central nervous system: Redefining the relationship between "Immune system" and "Nervous system" School of Life science, JNU, 31st July 2021. (*on line mode*)
5. Anirban Basu Drug repositioning/ repurposing: Promising strategy to develop therapy against viral infections; Annual Meeting of the Indian Academy of Sciences 12-14th November 2021. (*on line mode*)
6. Anirban Basu Biosecurity: Developing a healthy Immune system. Ted^{X}XIMUniversity, 13th of February, 2022. (*on line mode*)
7. Anirban Basu Molecular basis of virus-induced acute flaccid paralysis; Correlation with motor neuron dysfunction; INDO-US Symposium on Molecular Virology, IIT-Mandi; 15-17th February, 2022. (*on line mode*).
8. Anirban Basu Modulation of Neural Stem/Progenitor Cells fate following Japanese Encephalitis Virus infection 6th International Anatomical Sciences and Cell Biology Conference, National University of Singapore, Singapore, 21-23 February 2022. (*on line mode*)
9. Dr. Arpan Banerjee: Brain, mind, and behavior: The ethereal triumvirate. Invited speaker for Brain Awareness week IISER Behrampore (March 2022)
10. Dr. Arpan Banerjee: Career in Sciences, DAV Model School, Durgapur. (Dec 2021)
11. Priyanka Ghosh: Distinct roles of MMN and P300 in processing prediction errors across modalities; *NeuroCog* , University of Louvain, Belgium
12. Dr. B.S.Sahu: Webinar on Neuroendocrine regulation of metabolic physiology, GN Ramachandran Science club, Vigyan Prasar, MAC FAST, Kerala. (5 Sept. 2020)
13. Dipanjan Roy Invited Speaker Psychology Departmental seminar series at Ashoka University "Lifespan associated change in coherent communication and behavior and cognitive processing" 03rd December 2021
14. Dipanjan Roy Invited Speaker Cognitive Science Colloquium series at IIT Delhi Cognitive Science Department 29th October 2021.
15. Ellora Sen "Molecular Clock in Linking inflammation-metabolism axis in cancers". Amity University Manesar, 16th April 2021
16. Ellora Sen "Inflammation in diseases". National webinar on diversity in zoology - classical and modern. Dept. of Zoology, Mithibai College, Mumbai 28th July 2021
17. Ellora Sen "Influence of dysregulated metabolism on immune evasion and cellular circadian rhythm in glioma" Cell and Molecular Biology Seminar Series, IISER, Kalyani 14th August, 2021
18. Ellora Sen "Reprogramming the tumor microenvironment: Implication in cancer therapy". World Cancer Day, 4th Feb 2022, CNCI Kolkata

19. Ellora Sen "Epiphany of the Self: Identity with pure existent". Concept of Consciousness: Neuroscience & Indian Philosophical Perspective. Organized by Centre for consciousness studies NIMHAS & Indian Council of Philosophical Research (ICPR), September 2021.

20. Ellora Sen "Viewing Women Leadership in Science through the lens of Existential philosophy". International Conference on "Women's Leadership in Science and Technology" NIT, Durgapur, October 2021

21. Ellora Sen "Resurgence of Ayurveda: Sharing the learning." Vigyan Sarvatra Pujyate, Azadi ki Amrit Mahotsav, Kurukshetra Feb 28, 2022

22. Ellora Sen Women in Science: Dethroning the myth of Femininity. Women's day 2022, IITR Lucknow

23. Ellora Sen Existentialism and the future of Women Leadership in Science. Women's day 2022, NBRC

24. Pravat Kumar Mandal: Diagnostic Biomarker for Alzheimer's Disease, Science Setu, Govt. Raj College, Jargan, West Bengal, September 2021.

25. Soumya Iyengar: Brain-behaviour interactions in the 'Shining Raven'. 'Synapse', Symposium, IISER, Tirupati, Dec 4th, 2021.

26. Soumya Iyengar: The Avian Black Box - the Crow Brain. Theme: Recent trends in Brain research: Unlocking the mysteries of the brain, IBRO. IBRO Virtual Symposium (Institute of Home Economics, University of Delhi), March 22nd - 23rd, 2022.

27. Sarbani Samaddar, Balakumar Srinivasan, Kamakshi Garg, Dipanjana Banerjee and Sourav Banerjee. Decoding long non-coding RNAs in the neuron: Implications in development and synaptic plasticity." EMBO meeting on "RNA binding proteins: From RNA binding to condensation and aggregation." virtual meeting at NCCS, Pune, February 2021.

28. Swagata Dey: Kinesin-13 dependent dendrite arborization in the PVD neurons of *Caenorhabditis elegans*. Virtual, The Cytoskeleton of Neurons and Glia Webinar. March 2022.

29. Swagata Dey: Kinesin-13 regulates developmental pruning of dendrites in the PVD neurons of *Caenorhabditis elegans*. Virtual, 2021 Doorstep Meeting: The Cell Biology of Neurodegeneration and Repair. November 2021.

30. Swagata Dey: Kinesin-13 regulates growth and pruning of dendritic branches. Virtual, India Alliance Annual Conclave 2021. October 2021.

31. Swagata Dey, Nitish Kumar, Anindya Ghosh-Roy: Kinesin-13 mediated regulation of dendritic branch remodeling during the development of PVD neuron. Virtual, 23rd International Worm Meeting 2021. June 2021.

32. Swagata Dey: Revisiting the "Neuron Doctrine": Insights from live imaging. Virtual, NeuroFemIndia 2021. April 2021.

Externally Funded Research Projects

List of Extra Mural Projects

S. No.	Name of P.I.	Project S.No.	Name of Project	Name of the Implement-ing Agency	Date of Sanction of Project	Actual Sanctioned/ Release Amount for F.Y. 2021-22	Original Sanctioned Cost (Rs. In Lakh)	Date of Completion	Sanction No.
1	Prof. Anirban Basu	1	Deciphering ANTIVIRAL Properties of Statins against Japanese Encephalitis Virus Infections	D.B.T.	26.12.2018	3.76	30.00	25.12.2021	BT/PR27796/ MED/29/1301/2018
		2	MicroRNA mediated regi;ation of neural stem/progenitor cell fate in neurotropic flaviviral infection	D.B.T.	29.12.2017	0.00	77.07	28.06.2021	BT/PR22341/ MED/122/55/2016
		3	Understanding the therapeutic role of adult stem cell derived exosome in combating virus induced neurodegenerative disease	D.B.T.	20.03.2018	0.00	25.50	19.03.2022	BT/PR15984/ MED/31/325/2015
		4	Elucidating the role of long non coding RNAs (IncRNAs) in neuronal cell death during Japanese Encephalitis (JE)	D.B.T.	05.03.2019	0.00	19.00	04.03.2022	BT/PR26590/ MED/122/133/2017
		5	J.C Bose Fellowship	S.E.R.B	09.10.2021	19.00	95.00	08.10.2026	JCB/2020/000037
2	Dr. Ellora Sen	6	Non canonical function of metabolic genes in sculpting glioma tumor microenvironment	S.E.R.B	28.03.2022	12.70	38.10	27.03.2025	PDF/2021/000199
3	Dr Soumya Iyengar	7	Exploring Auditory Perception in House Crows using Functional Magnetic Resonance	D.S.T. (SERB)	20.05.2020	8.00	21.86	19.05.2023	CRG/2019/002672
		8	Autism spectrum disorders, genes and the gut microbiome: Utilizing song birds (Zebra Finches) as a model system	D.S.T.	24.02.2021	0.00	41.45	23.02.2024	DST/CSRI/2017/69
		9	The sensitive period of the human auditory cortex a neuroanatomical study	ICMR	25.09.2019	0.00	42.10	24.09.2022	51/4/2019-ANA/ BMS
4	Dr. Pankaj Seth	10	Hypoxia Induced Changes in Blood Brain Barrier	D.B.T.	12.09.2018	0.00	34.66	11.09.2021	BT/PR23625/ MED/122/77/2017

S. No.	Name of P.I.	Project S.No.	Name of Project	Name of the Implement-ing Agency	Date of Sanction of Project	Actual Sanctioned/ Release Amount for F.Y. 2021-22	Original Sanctioned Cost (Rs. In Lakh)	Date of Completion	Sanction No.
		11	Effect of hypoxia on different neural cell types in vitro-a model to design therapeutic strategies against cerebral palsy in preterm infants	D.B.T.	16.10.2018	0.00	66.96	15.10.2021	BT/PR21413/ MED/122/40/2016
		12	Role of FAM43A,the duslexia and ADHD gene, in brain development and signaling in the brain	S.E.R.B	01.02.2022	5.58	16.74	31.03.2025	PS/SERB/0222/116
		13	Role of Ephrins/Eph receptors in HIV mediated neuropathogensis	D.B.T.	27.06.2019	13.02	73.16	26.06.2022	BT/PR27512/122 /146/2018
5	Dr. Dipanjan Roy	14	Role of default mode brain network is normal cognitive function-Ramalingaswamy	D.B.T.	26.05.2016	0.00	88.00	26.05.2021	BT/RLF/Re-entry/07/2014
		15	Dementia Science Program-Tissue MRI Studies	D.B.T.	18.12.2017	0.00	35.41	17.06.2023	BT/HRD/ Dementia/2017
6	Dr. Pravat Kr. Mandal	16	Unravelling the causes of stroke and cognitive decline in general population A cross-Cultural perspective (DBT Netherland Grant)	D.B.T.	21.04.2016	15.40	73.66	20.04.2022	BT/IN/ Netherlands/03/ KP/2012
		17	Dementia Science Program-Imaging Studies	D.B.T.	18.12.2017	0.00	35.41	17.12.2021	BT/HRD/ Dementia/2017
		18	Artificial intelligence for early predictive diagnosis of alzheimer's disease using multi model imaging data	Meity	17.09.2019	14.45	59.96	16.09.2022	4(5)/2019-ITEA
7	Dr. Sourav Banarjee	19	Regulation of Fear memory formation by long non-coding RNAs and RNA biniding protiens: Mechanism of combinational control	D.S.T. (SERB)	25.03.2019	14.00	52.39	24.03.2022	SERB/F/ 12655/2018-19
		20	CRISPR-Cas13- mediated engineering of endogenous long non-coding RNAs for fluorenscent tagging to study RNA dynamics	D.B.T.	29.02.2020	13.17	72.00	28.02.2023	BT/RLF/PR31811/ GET/119/285/2019

S. No.	Name of P.I.	Project S.No.	Name of Project	Name of the Implement-ing Agency	Date of Sanction of Project	Actual Sanctioned/ Release Amount for F.Y. 2021-22	Original Sanctioned Cost (Rs. In Lakh)	Date of Completion	Sanction No.
8	Director NBRC	21	Magentoncephalography (MEG) Resource Facility	D.B.T.	27.03.2018	0.00	1498.86	26.03.2023	BT/MED/122/ SP24580/2018
		22	Delcon (E- Laibrary Consortia) Project	D.B.T.	18.03.2009	4184.72	37123.67	31.3.2023	BT/BI/12/053/2012
		23	Comparative Mapping of common mental disorders (CMD) over lifespan	D.B.T.	29.09.2019	0.00	477.05	28.09.2022	BT/MED/-III/ NBRC/Flagship/ program/2019
		24	Demetia Science Programme-Coordination Administration & Management setup at DBT	D.B.T.	18.12.2017	0.00	530.42	17.06.2023	BT/HRD/ Dementia/2017
9	Dr. Shiv Kumar Sharma	25	Demetia Science Programme-Basic Biology Studies (i) Genetic Studies at lab	D.B.T.	18.12.2017	0.00	106.64	17.06.2023	BT/HRD/ Dementia/2017
10	Dr. Arpan Banerjee	26	Early Diagnosis of Structural and Functional Decline in Brain Circuits Stemming from Traumatic Injuries in Professional Athletes Playing Centact Sports	MYAS	14.02.2019	0.00	40.00	13.02.2022	K-15015/42/2018/ SP-V
11		27	Study of Neuronal Regeneration after Injury using Caenorhabditis Elegans	SERB	20.05.2020	0.00	50.72	19.05.2023	CRG/2019/002194
12	Dr. Bhavani Shankar Sahu	28	Understanding the regulated secretory pathway and its role regulating physio-metabolic fuctions	D.B.T.	16.12.2019	18.69	_	15.12.2021	BT/RLF/Re-entry/38/2016
		29	IBRO Returned Home Start-up Grant	IBRO	19.06.2020	0.00	4500 Euro	18.06.2022	IBRO Return Home Program 2018
		30	ICGEB Research Grant	ICGEB	01.12.2020	0.00	12.95	31.12.2024	BSS/ ICGEB/0121/122
13	Dr. Swagata Dey	31	Wellcom Trust/DBT Indian Alliance	D.B.T.	01.01.2020	0.80	167.73	31.12.2025	IA/E/18/1/504331
14	Dr. Nivethida	32	Wellcom Trust/DBT Indian Alliance	D.B.T.	01.07.2017	50.75	378.7	30.06.2022	IA/ CPHI/16/1/502624
15		33	Modulating effective connectivity in the agency network of humans	D.B.T.	16.08.2021	26.61	60.43	15.08.2024	BT/13/ IYBA/2020/12
16	Dr Suman Saha	34	N-PDF	SERB	14.02.2022	9.60	19.2	15.02.2024	CRG/2021/0585

Distinctions, Honors, & Awards

Course-Work

M.Sc. 2020 batch

Ms. Mohima Mukherjee

M.Sc. student, has been awarded first rank upon completion of Course-Work during the year 2021-22 and a certificate was given to her.

Ms. Mrittika Dey

M.Sc. student, has been awarded second rank upon completion of Course-Work during the year 2021-22 and a certificate was given to her.

Dr. APJ Abdul Kalam Memorial Award

Mr. Anagh Pathak (M.Sc.-Ph.D. Integrated student 2016 batch)

M.Sc.-Ph.D. Integrated student, has been awarded as Dr. APJ Abdul Kalam Memorial Award during the year 2021-22 and a certificate was given to him.

Ms. Mukta Kumari (Ph.D. student 2014 batch)

Ph.D. student, has been awarded as Dr. APJ Abdul Kalam Memorial Award during the year 2021-22 and a certificate was given to her.

Ms. Kirti (M.Sc.-Ph.D. Integrated student 2016 batch)

M.Sc.-Ph.D. Integrated student, has been awarded as Dr. APJ Abdul Kalam Memorial Award during the year 2021-22 and a certificate was given to her.was given to her. year 2019-20 and a certificate was given to her.

Academic Programmes

ACADEMIC PROGRAMMES

NBRC was awarded Deemed University status (de-novo category) in 2002 under Section 3 of UGC Act, 1956 (3 of 1956) vide notification No.F.9-52/2001-U.3 dated 20th May, 2002 issued by Ministry of Human Resources Development, Government of India. NBRC is the first autonomous Institution to attain the status of Deemed University among the other Institutes of the Department of Biotechnology. The 'Deemed to be university' status of NBRC has been reviewed by the Committee duly constituted by the UGC and also by an independent Committee constituted by Ministry of HRD, on completion of five years as Deemed University. The committee recommended extension of Deemed University status and placed NBRC under "A" category.

1. Ph.D. in Neuroscience

NBRC has a Ph.D. Programme in Neuroscience to develop trained manpower having a broad overview of different aspects of Neuroscience.

NBRC provides a fellowship of ₹ 31,000/- per month for Junior Research Fellows and ₹ 35,000/- per month for Senior Research Fellows.

2. M.Sc. in Neuroscience

NBRC is one of the first Institutes in the country to develop an integrated multidisciplinary teaching programme in Neurosciences. During the academic year 2015-16 NBRC reintroduced the M.Sc. (Neuroscience) programme to develop trained manpower having a broad overview of different aspects of Neuroscience.

M.Sc. (Neuroscience) students are provided a fellowship of ₹ 12,000/- per month.

NBRC inducts students for its M.Sc. (Neuroscience) and Ph.D. programmes from diverse backgrounds having Bachelors or Masters degree in any branch related to Neurosciences, Psychology or M.B.B.S., B.E., or B.Tech. NBRC recognizes that understanding brain functions requires a fusion of knowledge from multiple disciplines.

Summer Training and Short-term Programmes

NBRC conducts Summer Training Programme for the Students, recommended through three National Science Academies viz: (1) Indian Academy of Science, Bangalore (2) Indian National Science Academy, New Delhi (3) National Academy of Sciences, Allahabad. The summer training is for a period of eight weeks and the trainees are provided with shared accommodation at NBRC hostels. Summer trainees are encouraged to attend seminars and journal clubs organized at the Institute. The summer training projects provides an exposure to Neuroscience and motivates trainees to consider it as a future career option.

NBRC Facilities

COMPUTING FACILITY (CF)

The Computing Facility of the National Brain Research Centre manages the overall Information and Communications infrastructure of the Institute apart from aiding in R&D activities. Computing Facility manages the campus converged network (data and voice traffic), communications links (Network and PSTN), Institute's Data centre, cloud resources running from NIC cloud, application servers, software development, ICT Modernization, e-Governance initiatives, technical support to users, common computing facility, etc. Some of them are summarized as under:

A. Campus Converged Network *(NBRC-IntraNet)* The NBRC campus network consists of a campus-wide Local Area Network running on a 10Gbps fiber optic backbone with redundant paths over manageable switching fabric which is further integrated with wireless access points managed through a central controller for mobility needs. The redundancy and robustness are built into the network architecture. The network is supplemented with a secure firewall/UTM cluster for network safety, intrusion detection system, gateway level antivirus, VPN facility, managing IT policy and detailed auditing/ logging, etc. The campus network is IPv6 compliant and IPv6 services are functional in the dual stack. The wireless network of the institute has further been integrated with Eduroam service by integrating it with National NREN (ERNET-India), the Eduroam service provides visiting scientists and researchers seamless secure wireless access in all participating institutions across the world.

The campus converged network of the institute is integrated with National Knowledge Network (NKN), on a 1 Gbps optical fibre link provided by BSNL that is further supplemented with a 50Mbps backup radio link for redundancy. The NKN linkage is instrumental in the running of several scientific projects for multi-site high-volume data applications like the NBRC-AIIMS data pipeline for MEG as part of the collaborative Centre of Excellence in Epilepsy project funded by DBT.

The campus converged network not only carries data traffic but also the Voice traffic from the IP-PBX system as well as the Video traffic from the IP-CCTV system.

B. IP-PBX facility The telecommunication systems of the institute are running on IP-PBX and the campus network is used to carry the voice traffic along with data traffic, the user endpoints are IP-Phones connected to LAN. The facility is running on automatic failover mode on virtualized servers from the institute's data center. The external incoming and outgoing voice traffic is routed on E1-PRI of BSNL. The users are also provided with various facilities like multi-point conferencing, voicemail, directory, call forwarding, etc. over the provided endpoints.

C. Institute Core and Application Servers The computing facility manages and maintains the server infrastructure of the institute which is housed and maintained in the data centre facility. In essence, the institute currently has **five** fully utilized 42U server racks in the data center facility. The various services running on these servers can be classified as follows:

- Web servers for the institute and various web servers related to ongoing computational projects and applications of various scientific groups. The primary web server for the official website is running from VMs installed on the NIC cloud.
- Acting as liaison with NIC for maintaining emails of core employees

on NIC mail services (gov.in/nic.in). Management of in-house email on list server (nbrc.ac.in) for temporary staff, students, and project personnel for broadcast and academic purposes.

- DNS servers for the official and hosted domains that are running from NBRC datacenter as well as VM's hosted on NIC cloud.
- Virtualization servers for providing virtualized hardware to run various applications and services in a more systematic manner and to consolidate and utilize the existing physical server infrastructure.
- Central Storage servers of 400TB have been installed and it is working along with backup servers handling storage requirements of the users and laboratories for online central storage and data processing. Major steps have been taken for upgrading the central storage infrastructure.
- Radius and authentication servers for access, accounting, and authorization of computing resources
- License management servers for managing institutional site/network/ concurrent licenses.
- Application servers running on windows and Linux platforms for common computing requirements of the users and also other specialized computing servers for specific data processing requirements of various laboratories.
- Antivirus and security servers for providing protection to user end-points across the campus.

D. Other Facilities & Services

- *NIC Cloud and Email Services :* The CF also manages the Virtual Machines on the NIC Cloud for better availability of web resources (especially the official website http://www.nbrc.ac.in and public DNS). Similarly, users having GOV.IN email ids on NIC platform for better availability.
- *Central Documentation Facility:* The central documentation facility provides round-the-clock availability to users for various computational needs like a facility for printing, scanning, poster-printing, etc. apart from providing data-processing computational nodes.
- *ICT Support & Service:* The computing facility also provides support and manages maintenance activities for the entire computing infrastructure of the institute which also includes user endpoints like computers, peripherals, software etc. An online support ticketing system with automated workflow management is functional for support activities.
- *CCTV Monitoring and Management:* More cameras are added to the surveillance system to enhance coverage of the campus. The installed IP Cameras are connected to the core network which is enhanced the security and monitoring of the campus. Most entry/exit points of the buildings are covered with the Central CCTV system.
- *Software Development:* The computing facility also undertakes software development activities in line with the institute's requirements, several scientific and e-Governance applications have been developed in-house.
- *Infrastructure Improvement:* The computing facility also undertakes planning and implementation of new computational infrastructure facilities and services, software/hardware/ network upgradations of Institute computers/peripherals, etc., and also planning to upgrade our mailing system with enhanced security.

- *Video-conferencing:* Computing Facility conducted online meetings/interviews/ lectures/workshops events during the covid-19 pandemic and purchased licensed online conference/meeting tools to do the institute's activity smoothly and Management video-conferencing for official meetings, interviews, and academic activities.

Animal House

NBRC is an autonomous institute of Department of Biotechnology, Govt. of India, with a mandate of carrying out frontline research to understand brain function in health and disease. As part of the infrastructure, NBRC has a state of the art animal facility to meet the requirements of the scientists for advanced neuroscience research.

The Institute recognizes that use of laboratory animals in research is an important privilege accompanied by a great ethical responsibility to ensure humane care and use of these valuable subjects. To ensure appropriate care and use, detailed programs of excellent veterinary and husbandry care, and programs for peer-reviewed evaluation of all activities prior to use of any animal in research are in place. NBRC is committed to the highest standards of research and recognizes that laboratory animals must receive the best possible care, not only to obtain valid research data, but also to ensure the health and safety of animals, researchers, and animal caretakers. Qualified and trained veterinarians oversee all the animal health concerns, and provide all necessary veterinary care to ensure that healthy animals are available for research.

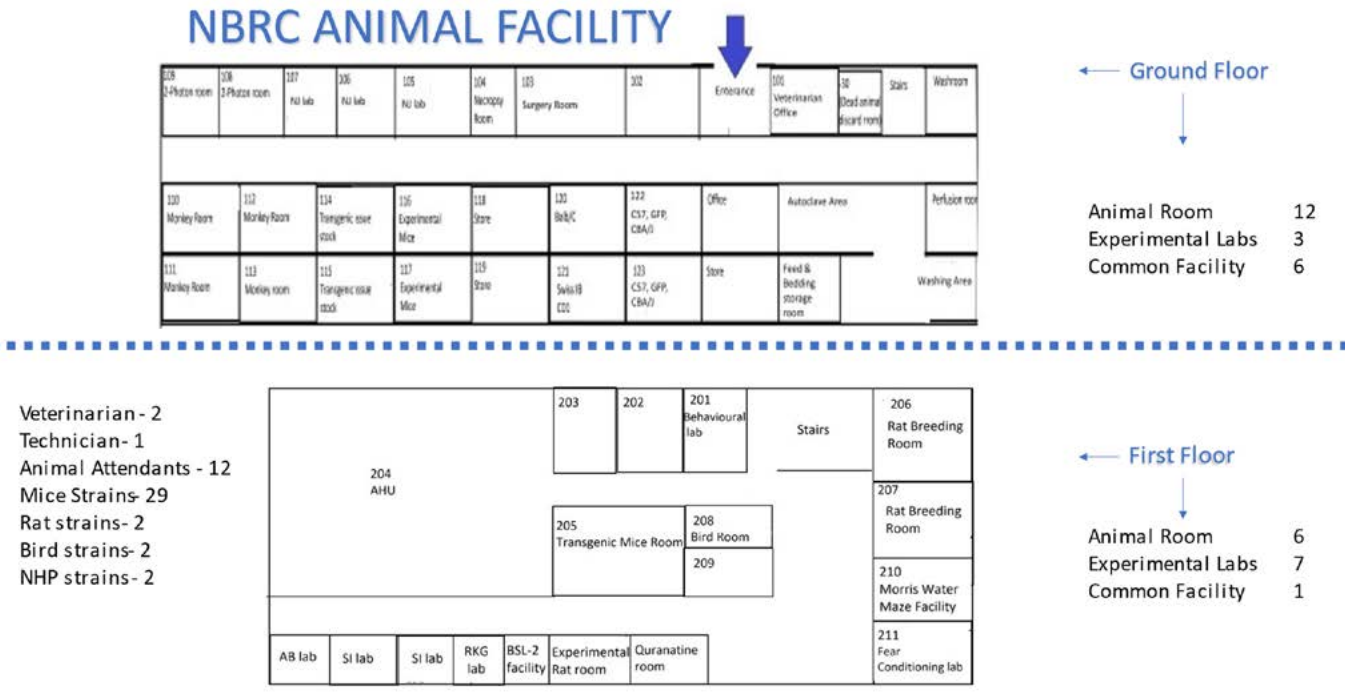
The Animal Facility is registered with the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Fisheries, Animal Husbandry and Dairying, Government of India, New Delhi. (Registration number: 464/GO/ReBi-S/Re-L/01/CPCSEA; initially registered on 24/08/2001. All activities of the Animal Facility are carried out as per standard operating procedures (SOPs). The Animal Facility maintains the records of day-to-day activities as well as breeding, maintenance and experimentation as per the statutory requirement of CPCSEA.

The main activities of Animal Facility are to procure and breed a wide variety of species of laboratory animals and supply quality animals to in-house researchers, which are used as animal models for understanding the human brain in health and disease. A high degree of hygienic conditions are maintained in the animal house by regular cleaning and sterilization of the cages, water bottles, bedding and feed. The animal rooms are also regularly disinfected. Heavy-duty steam autoclaves have been installed for these purposes. A hot vapour jet machine is used for cleaning the large monkey cages. The staff is required to take shower, and change to work-overalls before entering the animal rooms, and again in the evening after finishing the work. All users are required to use appropriate PPE before handling animals.

The facility is spread over two floors and is designed and built for accommodating animal species, which include rats, mice, birds (crow and zebra finches) and non-human primates. The ground floor houses rooms for rodents and non-human primates and transgenic animals, birds and rats are housed on the second floor. The Animal Facility also houses the 2-Photon imaging facility and is connected

to the MRI building, making it convenient to move animals for experiments if required.

All the animal species are housed in species appropriate cages, which are designed as per the CPCSEA guidelines The outdoor play area for non-human primates has six large interconnected enclosures that provide a flexible layout for optimising enrichment and social interactions. The transgenic, knock out and mutant mice are housed under germ-free conditions in filter top cages and individually



ventilated cages (IVC). Such animals are handled in laminar hoods, and then moved to fresh cages in cage-changing station under hepa-filtered air.

The animals are maintained under controlled environmental conditions as specified in CPCSEA guidelines, with temperature maintained between 22 ± 2° C, relative humidity between 45-55%, 12:12 hr light-dark cycle, and 12-15 air changes per hour. The air-handling system uses 100% fresh air for each change.

All animals are procured as per CPCSEA guidelines. A health surveillance program for screening incoming animals is carried out to assess animal quality. Animals procured from other places are kept in quarantine to minimize risk for introduction of infection in established colony.

The animal facility has a state-of-art surgical suite equipped with intensity controlled surgical lights, advanced surgical microscopes, gas anesthesia machines, equipment for monitoring the physiological state of the animals, including heart rate monitor, pulse oximeter and rectal thermometer. For cleaning and sterilization of the surgical instruments there is an ultrasonic instrument cleaner, glass bead sterilizer and ethylene oxide gas sterilizer.

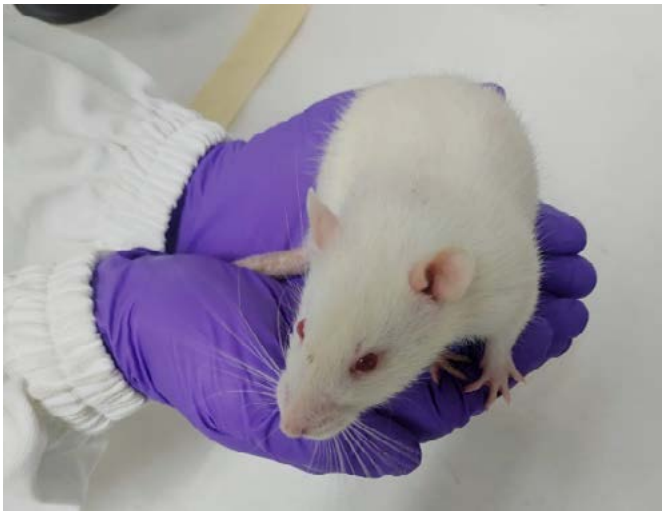
The animal facility has a necropsy room, perfusion room with a perfusion hood, deep freezer for carcass storage, and incinerator for disposal of the animal carcass.

The animal facility has been equipped with a card reader security system. The access is restricted to the animal house staff, maintenance staff and the investigators who are listed in the IAEC approved protocols. All the personnel who handle animals are required to have a current tetanus vaccination, and those who handle non-human primates (NHP) are regularly screened for tuberculosis. Everyone handling NHP's is trained in the procedures for the first-aid in case of an injury from an animal bite or scratch.

Close circuit monitoring cameras have been installed at various locations in the facility to help in effective monitoring of the animal facility.

The Veterinary staff of Animal Facility also conducts short-term training for M.Sc. and Ph.D. students, Project Assistants and other scientific staff in the field of laboratory animal science covering ethical and statutory guidelines that regulate scientific experiment on animals, general biology and reproduction of the laboratory animals, *animal identification techniques, blood collection, injections, anesthesia and monitoring, handling and restraint, husbandry and care, sex differentiation, humane euthanasia, etc*

The animal facility is currently maintaining the following species and strains of laboratory animals.



Mice Strains

- SWISS
- BALB/c
- C57BL/6J
- CD1

Transgenic Mice

- B6C3-Tg (APP695)85DboTg(PSEN1)85Dbo (Alzheimer disease model)
- UBC-GFP (Green fluorescent protein)
- B6CBA-Tg (Hdexon1) 62Gpb/3J (Huntington disease model)
- B6;129P2Pvalb< tm1(cre)Arbr>/J
- B6.CgGt(ROSA)26Sor<tm9(CAGtdTomato)
- B6.CgTg(Scnn1acre)3Aibs/J
- STOCK Gad2<tm2(cre)Zjh>/J
- B6.CgTg(Camk2a-cre)T29-1Stl/j
- B6.129-Rp122<tm1.1Psam>/j
- STOCK Tg(Thy1-EGFP)MJrs/J
- B6.Cg-Tg(Thy1-YFP)16Jrs/J
- B6.Cg-Tg(Thy1-YFP)HJrs/J
- B6;129S6-Tg(Camk2a-cre/ERT2)1Aibs/J
- STOCK *Sst*$^{tm2.1(cre)Zjh}$/J
- B6.Cg-*Gt(ROSA)26Sor*$^{tm6(CAG-ZsGreen1)Hze}$/J
- B6:129X1-Gt(ROSA)26Sor<tm(EYFP) Cos>/j
- C57Bl6-Tg(Nes-cre/ERT2)Keise/j
- C57BL/6J-Tg(Thy1-GCaMP6s) GP4.3Dkim/J
- B6;129S6-Gt(ROSA)26Sortm96(CAG-GCaMP6s)Hze/J
- C57BL/6J-Tg(Thy1 GCaMP6s) GP4.3Dkim/J

Knock Out Mice

- UBE3A null mice (Angelman syndrome model)

Rat Strains

- Long Evans
- Sprague Dawley

Non-human primates

- Rhesus Monkeys (*Macaca mulatta*)
- Bonet Monkeys (*Macaca radiata*)

Birds

- Zebra finches (*Taeniopygia guttata*)
- House crows (*Corvus splendens*)

All the mice strains are maintained by inbreeding and the rat strains by out breeding. Zebra finch colonies are maintained by out breeding. The transgenic and knockout mice are maintained under a specialized breeding program after the investigators provide the molecular genotyping of these strains based on presence or absence of the gene of interest.

Digital Library

The NBRC Library plays a vital role in the collection, development and dissemination of scientific and technical information to meet the present and future needs of the Centre and also provides facilities and support to the scientists, researchers, students, staff and NBRC's networked centers. The Library is housed in a spacious two-storey building, with reading room, reference room, video conferencing, online journal access facility, book section, internet access and reprographic facilities etc. The main aim of the NBRC Library staff is to provide excellent services to users in NBRC and all centers associated with the Institute. The NBRC library has a large collection of Journals, books and other relevant research materials on Neuroscience, Biochemistry, Genetics, Molecular Biology, Immunology & Microbiology, Pharmacology and Toxicology, Psychology, Physics, Mathematics, Computer Science and general subjects. The NBRC Library currently subscribes to 994 online journals through the DBT e-Library Consortium (DeLCON), 3 specialized journals, and 122 freely accessible online journals. It also maintains digital archives and news clips about the Centre and subscribes to Newspapers and News Letters. The collection of the NBRC Library is growing day-by-day along with new developments in research and knowledge in the field of Neuroscience and related areas. To provide optimum service to all users, the NBRC library is currently digitizing its list of collections using the LSEASE software, to which all users will have full access. A barcode technology has also been installed for accurate and speedy circulation and the management of all library documents. The new software will also help in efficient library operations viz. administration, acquisition, circulation, serial control, cataloguing and information retrieval. The Library has set up 22 Computers with Internet facility to provide services for use of researchers and students in the NBRC Common room and has been providing electronic access to the subscribed journals through the campus portal. The NBRC Library also provides Inter Library Loan Services to NBRC's 48 networked centres all over India. Researchers at different centres send their requirement for research material or journal articles through email to NBRC Library library@nbrc.ac.in or to the Librarian Dr. D. D. Lal, ddlal@nbrc.ac.in which are then downloaded and sent to them free of cost. The library entertains an average of approximately 450 requests for articles and this number is increasing every year. The NBRC Library regularly evaluates its information services to ensure that the Institution's requirements are met. It promotes resource sharing and cooperation activities among libraries by providing an efficient and reliable means of resource sharing, that is, the inter library loan for the maximum use of resources, by providing copies of documents which are not available to researchers at centres outside the institute.

MAIN ACTIVITIES OF NBRC LIBRARY

1. Book Acquisition
2. Periodicals Acquisition
3. Selective Dissemination Information (SDI),
4. Current Awareness Services (CAS)
5. Inter Library Loan
6. Resource Sharing
7. Circulation services
8. Reference Services, Bibliographic services
9. Indexing and Special Services
10. Collects maintains, store and retrieves information and data keeping in the view of evolving needs of its researchers
11. Help to Network Centres.

DBT's Electronic Library Consortium (DeLCON)

DeLCON CONSORTIUM: A NATIONAL LIBRARY CONSORTIUM FOR LIFE SCIENCES & BIOTECHNOLOGY HOSTED AND ADMINISTERED BY NBRC AND SPONSORED BY DEPARTMENT OF BIOTECHNOLOGY (DBT)

The DBT Electronic Library Consortium (DeLCON)' is a major initiative of the Department of Biotechnology (DBT) to provide unlimited access to most of the relevant periodicals to the researchers at participating institutions. It was initiated in the year 2008 and finally launched in the month of January 2009 with 10 DBT core member institutions (including DBT H.Q. & ICGEB) enabled with a centralized subscription to a large number of high impact online journals. It is a national initiative for providing access to scholarly electronic resources including full-text and bibliographic databases in all the life sciences disciplines to the DBT institutions.

It facilitates the access to high quality e-resources to the faculties, scientists, research scholars, students and Project Assistants of the DBT research Institutions in the country to improve teaching, learning and research. DeLCON consortium was extended in three phases; and in the second phase 17 DBT Institutions were added, in the year 2010. Subsequently 7 more institutional members were added in the 3rd phase of extension in the year 2011. In the year 2012, DBT merged all the phases and it became a single 'DeLCON Consortium' with 33 members.

In the year in 2019, the DBT added one new Institute i.e. Institute for Stem Cell Science and Regenerative Medicine (InStem) under DeLCON Consortium. Currently DeLCON has a total of 35 members. The 'DeLCON Consortium' provides current (presently 994 online resources) as well as archival access to more than 1176 core peer-reviewed journals and one bibliographic database (SCOPUS Database) in different disciplines from 21 foreign publishers.

The DeLCON comprises the following 35 member institutions:

List of DBT & NORTH EAST REGIONAL (NER) INSTITUTIONS

DBT Institutions

1. Department of Biotechnology (DBT), New Delhi
2. National Brain Research Centre (NBRC), Manesar
3. National Institute of Plant Genome Research (NIPGR), New Delhi
4. National Institute of Immunology (NII), New Delhi
5. National Centre for Cell Science (NCCS), Pune
6. Institute of Life Sciences (ILS), Bhubaneshwar
7. Institute of Bioresources and Sustainable Development (ISBD), Imphal
8. Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad
9. Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvananthapuram
10. International Centre for Genetics Engineering and Biotechnology (ICGEB), New Delhi
11. National Agri-Food Biotechnology Institute (NABI), Mohali, Punjab
12. National Institute of Biomedical Genomics (NIBMG), Kalyani, Kolkata DBT's Electronic Library Consortium (DeLCON) NBRC Annual Report 2016-17 129

13. National Institute of Animal Biotechnology (NIAB), Hyderabad
14. Regional Centre for Biotechnology (RBC), Faridabad, as a part of NCR Biotech Science Cluster (BSC)
15. Transnational Health Science & Technology Institute (THSTI), Faridabad, as a part of NCR Biotech Science Cluster (BSC)
16. Biotechnology Industry Research Assistance Council (BIRAC), New Delhi
17. Institute for Stem Cell Science and Regenerative Medicine (InStem), Bangalore.

North Eastern Region (NER) Institutions

18. Dibrugarh University, Assam
19. Assam University, Silchar
20. North Eastern Regional Institute of Science & Technology, Arunachal Pradesh
21. North East Institute of Science & Technology, Assam
22. Mizoram University, Mizoram
23. D. M. College of Science (DMC), Manipur*
24. Sikkim University, Gangtok
25. College of Veterinary Science, Assam Agricultural University, Guwahati
26. Guwahati University, Assam
27. Manipur University, Imphal
28. College of Veterinary Science & Animal Husbandry Central Agricultural University, Mizoram
29. Rajiv Gandhi University, Arunachal Pradesh
30. Nagaland University, Nagaland
31. North-Eastern Hill University (NEHU), Shillong
32. St. Anthony's College (SAC), Meghalaya*
33. Indian Institute of Technology Guwahati, Assam
34. Tezpur University, Tezpur, Sonitpur, Assam
35. Sikkim State Council of Science and Technology, Gangtok, Sikkim

(*= DMC is a part of Mizoram University & SAC is a part of NEHU)

In terms of number of users, the DBT's Electronic Library Consortium (DeLCON) is the largest Consortium in India constituted in the area of Biotechnology and Life Sciences with a vision and plan to reach out to all DBT Institutions departments, research institutions, universities and their colleges affiliated to DBT.

The complete list of full-text resources (e-Journals) and bibliographic databases subscribed under the DeLCON Consortium is given below.

LIST OF JOURNALS UNDER DeLCON CONSORTIUM

Name of Publishers → Journals → Hyperlink of the publishers → No. of Journals

- American Association for Cancer Research (AACR) → http://www.aacr.org → 8 Journals
- American Society For Microbiology (ASM) → http:// www.asm.org/ → 16 Journals
- Cold Spring Harbor Laboratory Press (CSHL) → http://www. cshl.edu → 4 Journals
- Taylor & Francis (T&F) → http://www. informaworld.com → 40 Journals
- Nature Publications → http:// www. nature.com → 34 Journals
- Oxford University Press (OUP) → http:// www.oxfordjournals. org → 22 Journals
- Springer India → http://www. springerlink. com → 343 Journals
- Microbiology Society (MBS) → http:// mic.

sgmjournals.org → 3 Journals

- Wiley-Blackwell → http:// www3.interscience.wiley.com/cgi-bin/home → 86 Journals
- Elsevier Science (ScienceDirect) → http:// www.sciencedirect.com → 434 Journals
- American Association of Immunologist (AAI) → http:// www.aai.org/ → 1 Journal
- Proceedings of National Academy of Sciences (PNAS) → http://www.pnas.org → 1 Journal

Archives only

- Lippincott William & Wilkins/Wolter Kluwer/OVID→ http://ovidsp.ovid.com → 11 (Only Archives from 2009-2011)
- Marry ANN Liebert (MAL) → http://www.liebertonline.com → 92 (Only Archives from 2009-2018)
- American Chemical Society(ACS) → http:// pubs.acs.org→ 47 Journals (Only Archives from 2009-2016)
- Annual Reviews (AR) → http://www.annualreviews.org → 23 Journals (Only Archives from 2009-2011)
- The New England Journal of Medicine (NEJM) → http:// www.nejm.org → 1 (Only Archives from 2009-2018)
- American Association for Advancement of Science(AAAS)→ http://www.sciencemag.org → 3 Journals (2009-2019)
- American Society for Biochemistry and Molecular Biology (ASBMB)→ http://www.jbc.org → 2 Journals (2009-2020)
- American Society for Hematology (ASH) → http://bloodjournals.hematologylibrary.org → 1 Journal (2009-2019)

BENEFITS OF DELCON CONSORTIUM (GENERAL)

The consortia-based subscription to e-resources is a viable solution for increasing the access to electronic resources across DBT institutions at a lower rate of subscription. Major benefits of DeLCON Consortium are:

- DeLCON acts as a single window service for a large number of DBT Institutions with their diverse research and academic interest.
- DeLCON with its collective strength of participating institutions, attracts highly discounted rates of subscription with most favourable terms of agreement for a wider range of e-resources. Most of the e-publishers have responded positively to the call of the Consortium. The rates offered to the consortium are lower by 66% to 99% depending upon the category of DBT institutions.
- DeLCON has triggered remarkable increase in sharing of electronic resources amongst participating DeLCON members
- The research productivity of DBT institutions has improved with increased access to international full text resources (Journals and database).
- Users have immediate access to material previously not subscribed to, at no incremental cost for accessing back files.
- It improves the existing library services and reduced the subscription cost.
- DeLCON is open so that other DBT institution can also join the DeLCON Consortium.
- DeLCON offers better terms of agreement for use, archival access and preservation of subscribed electronic resources, which would not have been possible for any single institutions.
- Members of the DeLCON Consortium have the benefit of cap on the annual increase in the rates of subscription. While the usual increase in price of e- resources is vary from 15% to 20%, but the DeLCON

members enjoy a cap on increase in price ranging from 5% to 7%.

- Since the subscribed resources is accessible online in electronic format, the DBT institutions have less pressure on space requirement for storing and managing print based library resources.

MAJOR ADVANTAGES OF 'DELCON FOR CONSORTIUM MEMBERS

Some of the important advantages of the DeLCON consortium provides to members as given below:

- Consortia-based subscription to electronic resources provides access to wider number of electronic resources at substantially lower cost.
- Optimum utilization of funds.
- Facilities to build up digital libraries
- Helpful in providing better library services like CAS and SDI
- Cost sharing for technical and training support
- Electronic Journals demand neither library space nor shelving costs
- The DeLCON consortium has been offered better terms of licenses for use, archival access and preservation of subscribed electronic resources, which would not have been possible for any single institution; and
- Available 24 hours a day, 7 days a week

SELECTION PROCEDURES OF RESOURCES UNDER DeLCON CONSORTIUM

In order to understand the compilation base in DBT member Institutions, meetings of DBT Directors, & DeLCON Nodal Officers were held and their views and feedback are obtained. The print & online collection base available in DBT research institutions libraries and their needs are surveyed with the aim to recognize and determine e-resources to be subscribed under the DeLCON Consortium. Based on the feedback received from DBT Members, e-resources of various publishers are recognized and evaluated before negotiating licensing arrangements. Keeping in view the multiplicity of research programmes offered by DBT Institutions, every attempt was made to subscribe to e-resources that are multidisciplinary in nature with wide scope and coverage.

All e-resources were evaluated on the criteria as given below:

i) Qualitative and quantitative contents;

ii) Coverage;

iii) Their availability on different platforms and their comparative advantages / disadvantages;

iv) Rates applicable for these resources to individual institutions as well as to other consortia.

SUBJECT AREAS OF DeLCON CONSORTIUM

The DeLCON Consortium covers all the disciplines and subjects coming under Life Sciences i.e. Biotechnology, Bioinformatics, Biochemistry, Biology, Chemical Biology, Sciences, Immunology, Neuroscience, Plant Genome, Plant Biology, Microbiology, Physiology, Psychology, Physiotherapy, Psychotherapy, Genome, Gene, Genetics, Mathematics, Physics, Chemistry, Radiology, Medicines, Computational Biology, Cell Biology, Cell Sciences, Molecular Biology, Molecular and Cellular Biology, Computational Neuroscience, System Neuroscience etc.

OPERATIONAL FUNCTIONALITY OF DeLCON CONSORTIUM

The DeLCON is fully funded by DBT and has network connectivity among DBT Institutions. Individual Institutions have unique static IP address through which access is given by the publishers. However, the whole programme is administered, monitored and maintained by DeLCON Nodal Centre at NBRC and DeLCON National Steering Committee.

NODAL CENTRE & HEAD QUARTER OF DeLCON CONSORTIUM & ITS ACTIVITIES

The consortium headquarter functions under a National Steering Committee with the responsibilities of ensuring inter-institutional coordination; monitoring licenses for electronic resources, ordering and payment for subscribed services, establishing work groups on different subjects to improve the functioning of consortium as well as to identify new resources and evaluates the existing resources, and propagating the consortium to attract new members in it. The Department of Biotechnology has also setup a National Review Committee that have the overall responsibility of making policies, monitoring the progress, coordinating with Member Institutions for promoting the activities of DeLCON Consortium. The important functions of the consortium headquarter are : to act as nodal agency for increasing the cooperation amongst participating institutions; to coordinate all activities concerned with subscription of e-resources on behalf of consortium; to liaison with electronic publishers to provide training and technical help to participating member institutions to coordinate with DBT and participating institutions for subscription to resources; to organize the meeting of the National Steering Committee and to decide upon the policy issues to maintain a web site for the Consortium for the benefit of its members and to encourage sharing of resources in an online mode; to propagate the consortium with other institutions and enroll new members in the consortium; to organize annual meetings of the consortium members.

National Neuroimaging Facility (NNF)

National Neuroimaging facility, sponsored by the Department of Biotechnology, Govt. of India, came into existence in the year of 2006. The main purpose of this National Facility is to facilitate/support cutting edge brain imaging research undertaken by intramural and extramural laboratories. The facility is equipped with the following equipments:

1. 3 Tesla Magnetic Resonance Imaging (MRI): Philips Achieva 3.0 T scanner
2. Electroencephalography (EEG): Two systems in place
   A) 64-channel Synamps 2 EEG system, Compumedics Neuroscan, Inc
   B) 64 channel Brain products ActiChamp system
3. Transcranial magnetic stimulation (TMS): Magventure MagPro

All the instruments are available for research purposes for any user with necessary ethics approvals and paying of user charges.

Magnetic Resonance Imaging (MRI)

MRI provides much greater contrast between the different soft tissues of the body compared to computed tomography (CT), making it especially useful in neurological (brain), musculoskeletal, cardiovascular. Various imaging modalities also play important role providing crucial information which can aid to various diagnostic process. The various imaging modalities which are routinely used in National Neuroimaging facility are:

1. MR Spectroscopy (MRS) which provides non-invasive neurochemical level estimations and enables clinical correlation.
2. Functional MRI (fMRI) which, as the name suggests reveals the changes in brain metabolic activity over time.
3. Structural MRI (or simply MRI) can give us detailed high resolution pictures of brain structures as well as brain connectivity using diffusion weighted images.

The 3 Tesla Phillips whole body MRI scanner at our Facility is equipped with state-of-the-art hardware, software and data processing software required for each imaging modality. The facility is being used daily for performing structural and functional MRI (see Fig 1) and MRS. In addition to understanding brain function and clinical research, the center also is closely interacting with leading imaging centers within the country and across the globe.

Electroencephalography (EEG) is a test that measures and records the electrical activity of the brain. Special sensors are attached to the scalp (in a similar way as ECG) to detect brain electric activity and mV range and the signals are amplified via an amplifier that communicates and stores the information in a computer. Basic brain functions such as vision, auditory, somatosensory processing as well as higher order functions like memory, emotion, decision making and brain diseases such as epilepsy, dementia, and narcolepsy (sleeping disorder) can be studied by EEG.

Transcranial magnetic stimulation (TMS): TMS is a non-invasive neurostimulation technique by which researchers can induce a transient change in electric currents in a target brain area by applying very small amounts of external field magnetic field. This changes are completely reversible and the technique gives us a window to study brain information processing with profound insights.

Clinical studies on patients with Alzheimer's Disease, Parkinson's Disease, Autism and Brain Tumours, as well as monitoring of aging in normal healthy brain, are being performed extensively in the National Neuroimaging facility. Understanding the basic neurobiology

of various sensory and cognitive functions using non-invasive neuroimaging tools are also undertaken by several labs in NBRC.

The following are the publications having data collected at NNF between April 2021 - March 2022.

Publications

4. Sastry, N.C., Roy, D., & Banerjee, A. (2022): Stability of sensorimotor network sculpts the dynamic repertoire of resting state over lifespan. Cerebral Cortex, 1-22 https://doi.org/10.1093/cercor/bhac133

5. Thuwal, K, Banerjee, A. & Roy, D. (2021): Aperiodic and periodic components of ongoing oscillatory brain dynamics link distinct functional aspects of cognition across adult lifespan. eNeuro. 8 (5) ENEURO.0224-21.2021; DOI: https://doi.org/10.1523/ENEURO.0224-21.2021

6. Yazin, F., Das, M., Banerjee, A., & Roy, D. (2021) Contextual Prediction Errors Reorganize Episodic Memories in Time. Scientific Reports. 11(1). 12364. 1-17. https://www.nature.com/articles/s41598-021-90990-1

7. Naskar, A., Vattikonda, A., Deco, G., Roy, D., & Banerjee, A. (2021) Multiscale dynamic mean field model (MDMF) to relate resting-state brain dynamics with local cortical excitatory-inhibitory neurotransmitter homeostasis. Network Neuroscience 5 (3): 757–782. https://direct.mit.edu/netn/article/doi/10.1162/netn_a_00197/100794/Multi-scale-dynamic-mean-field-model-MDMF-relates

8. Ghosh, P., Roy, D., & Banerjee, A. (2021) Psychophysical data to study the brain network mechanisms involved in reorienting attention to salient events during goal directed visual discrimination and search tasks. Data in Brief , 107020. https://www.sciencedirect.com/science/article/pii/S2352340921003048#!

9. Mandal P. K, Roy GR, Samkaria A, "*Oxidative Stress: Glutathione and Its Potential to Protect Methionine-35 of Aß Peptide from Oxidation*", ACS Omega, 2022/07/02

10. Mandal P. K, Goel A, Bush A, Punjabi K, Joon S, Mishra R, Tripathi M, Garg A, Kuller N, Sharma P, Shukla D, Ayton S, Fazlollahi A, Maroon J, Dwivedi D, Samkaria A, Sandal K, Megha K, Shandilya S, Laalou F.-Z, "*Hippocampal Glutathione Depletion with Enhanced Iron Level in Patients with Mild Cognitive Impairment and Alzheimer's Disease Compared to Healthy Elderly Participants*", Brain Communications, 2022/06/29

11. Craven AR, Bhattacharyya PK, Clarke WT, Dydak U, Edden RA, Ersland L, Mandal PK, Mikkelsen M, Murdoch JB, Near J, Rideaux R *"Comparison of seven modelling algorithms for GABA-edited 1H-MRS. NMR in Biomedicine"* NMR in biomedicine DOI: 10.1002/nbm.4702(2022)

12. Handa P, Samkaria A, Sharma S, Arora Y, Mandal PK *"Comprehensive Account of Sodium Imaging and Spectroscopy for Brain Research"* ACS Chemical Neuroscience DOI: 10.1021/acschemneuro.2c00027, vol. 13, 859-875(2022)

13. Mandal P K*, Perry G* *"SWADESH: A Comprehensive Platform for Multimodal Data and Analytics for Advanced Research in Alzheimer's and other Brain Disorders"* Journal of Alzheimer's Disease 85 (1), 1-5(2022)

14. Mandal P.K, Dwivedi D, Shukla D, Samkaria A, Roy R G, Arora Y, Jindal K *"Interplay Between Hippocampal Glutathione Depletion and pH Increment in Alzheimer's Disease"* Journal of Alzheimer's disease 88 (1), 1-6(2022)

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Prepared by Dr. Arpan Banerjee

Translational & Clinical Neuroscience Unit

Since its inception, the National Brain Research Centre (NBRC) has strived to fulfil its commitment to reduce the burden of neurological disorders in our nation through basic and clinical research, services and awareness about brain disorders. As part of the social responsibility for services to the state of Haryana and to address the need of growing burden of neurological diseases in our country, the National Brain Research Centre offered neurology expertise to the Government General Hospital (GGH), Gurgaon more than a decade ago. This association was initiated with the Government General Hospital, as the hospital lacked the expertise of a neurologist and did not have a neurology department. This was causing extreme hardships for the patients coming from Gurgaon city as well as from neighboring districts and villages which had to be denied medical attention or referred to other private hospitals. Realizing the unmet need of medical care for patients suffering from neurological disorders, NBRC established the Translational and Clinical Neuroscience Unit and provided a neurology outpatient department (OPD) to the government hospital to augment their capabilities of medical care, and also assess the occurrence of neurological cases in Gurgaon and adjacent districts.

The Translational and Clinical Neuroscience Unit was started from room number 7 of the Government General Hospital, Gurgaon in heart of the city for easy access for the citizens. In 2019, when the GGH was shifted to Sector 10A in Gurgaon, the unit was also transferred with GCH from where NBRC continues to cater the neurology OPD service to the citizens of state of Haryana.

Investigation facilities

As the NBRC Unit is established at the hospital, the patients have access to several facilities listed below through the hospital or its associated clinics:

- MRI system: Siemens Magnetom 1.5 Tesla scanner with various study protocols
- CT (computed tomography) system
- Ultrasonography
- X-ray and Contrast imaging.

Laboratory facilities

- Biochemistry, Microbiology, Haematology, Pathology & Immunology.

The NBRC translational unit has highly qualified consultants and a support team of following personnel that works in association with clinicians at the Gurgaon General Hospital:

- *Consultant, Pediatric Neurology, Dr. Pooja Kapoor*
- *Clinic Assistant: Mr. Hanuman Singh*

Management of any disease and designing new therapeutic interventions necessitates the needs of understanding the pathways for disease pathogenesis. In this direction, a concerted effort of basic scientists and clinicians is critical. To facilitate this, attempts to bring the basic research scientists and clinicians has been one of the top priority of this institute. This Translational Research Unit has potential to fulfil this critical need for finding new therapies for ever increasing neurological disorders in the country. Prior to the establishment of the OPD services at GGH, the patients for brain disorders were seeking medical attention from unqualified practioners or following non-scientific superstitious practices, leading to worsening of their brain disorders. Following the establishment of the neurology OPD services at this unit, it has helped in better treatment, increased awareness about brain disorders and helping in reducing the sufferings of these patients. Furthermore as NBRC Unit

is housed within the Hospital, the patients have access to Neurology, Neuropsychology, Neuropsychiatry, Behavioral therapy, Psychology, and Psychometry services as well, which enhances the patient care.

The outpatient department of this unit at the Government General Hospital, is supported by highly qualified and accomplished consultants, including a Pediatric neurologist, Dr. Pooja Kapoor. We have noticed that the NBRC Unit has attracted an increase in number of pediatric patients, which were earlier left untreated. As the unit is part of the GGH, patients visit from Gurgaon and several nearby districts and as the word is spreading about the quality medical care the number of patients is gradually increasing. This clinical facility also maintains a good follow up rate of patients as significant number of the patients return to the clinics for follow-ups. Most of the patients seeking care at the neurology OPD are Geriatric patients that need care for Movement Disorders, dementia, and the adult patients mostly come with complaints of headache, depression, tremors, dementia and pediatric patients present with symptoms of mental retardation, ASD, seizure, epilepsy, this trend has been consistent as previous year. Patients requiring advanced specialist neurology in-patient care are referred to All-India Institute of Medical Sciences (AIIMS), Institute of Postgraduate Medical Education & Research – Rohtak, Institute of Human Behaviour & Allied Sciences (IHBAS), New Delhi or to other tertiary hospital as per the choice of the patient, if he/she so desires.

The NBRC Unit acknowledges the cooperation from the Ministry of Health - Government of Haryana, and the Deputy Commissioner - Gurgaon, and also from the Chief Medical Officer & Civil Surgeon and Principal Medical Officer of the Hospital. The translational and clinical research unit of NBRC provides the much needed neurological OPD services for the patients from Gurugram and adjoining districts.

Magnetoencephalography (MEG) Resource Facility

(Under DBT-SAHAJ Scheme, Funded by Department of Biotechnology, Ministry of Science &Technology, Govt of India)

Investigators from AIIMS: Prof. Manjari Tripathi
Prof.P.Sarat Chandra
Dr. Jyotirmoy Banerjee

Investigators from NBRC: Director-NBRC

Investigator from ACBR: Dr.Aparna Dixit

Magnetoencephalography (MEG) Resource Facility has been established in NBRC, it is a collaborative project between National Brain Research Centre (NBRC) and All India Institute of Medical Sciences (AIIMS) under the aegis of Department of Biotechnology (Government of India). The MEG facility has joined the prestigious DBT-SAHAJ infrastructure with the primary goal of creating a "National Service Facility" to provide access to resources.

Figure 1.MEG unit in MSR -NBRC

This is one of the few facilities in the world which brings together a premier medical science institute and a dedicated neuroscience research centre to study difficult-to-treat epilepsy. The main aim of the centre is to develop a cure for drug-resistant epilepsy by bridging the gap between clinical and basic research which is mediated by the close coordination between NBRC and AIIMS. For a comprehensive study the AIIMS component of the centre is using magnetic resonance imaging (MRI), electroencephalography (EEG), video EEG, as well as functional imaging techniques like positron emission tomography (PET) and single photon emission tomography (SPECT) to locate the epileptogenic area. The NBRC component of the centre is using non-invasive protocol of magnetoencephalography (MEG) for the localization of epileptogenic focus. We are presenting herewith our findings from the proposed objectives under this project conducted during this period (2021-2022) in brief report:

Establishing a diagnosis of drug resistant epilepsy (DRE) is an important milestone in the treatment of epilepsy as it marks the transition of a patient who is taking medications to control a condition and living a relatively normal life to someone who is at risk of worsening seizures, injuries or even death as well as social stigma and economic hardship associated with uncontrolled seizures. Identification of such patients and diagnosing drug refractory epilepsy (DRE) are very important steps in the management of these patients. MEG resource facility one of its kind facility in Northern India, proved very much fruitful in managing these kind of patients. Till March 2022, 2166 patients were evaluated using this facility from all over India (state-wise distribution of patients were shown in figure 2). Infact, International patients have been also benefitted, especially patients from SAARC countries.

INTERNATIONAL PATIENTS	NO.
SAUDI ARABIA	1
PAKISTAN	1
DUBAI	1
NEPAL	18
BANGLADESH	4
KENYA	1
AFGANISTAN	3
MUSCAT	1
NEW ZEALAND	1

STATE	NO OF PT.
UTTAR PRADESH	522
NEW DELHI	677
HARYANA	309
RAJASTHAN	148
BIHAR	130
GUJARAT	13
ASSAM	12
JHARKHAND	21
TELANGANA	10
ODISHA	19
PUNJAB	30
ANDHRA PRADESH	10
MADHYA PRADESH	76
UTTARAKHAND	50
WEST BENGAL	33
HIMACHAL PRADESH	13
JAMMU & KASHMIR	20
KERALA	8
MAHARASTRA	11
CHATTISHGARH	3
ARUNACHAL PRADESH	2
TAMIL NADU	3
MEGHALAYA	2
KARNATAKA	1

Figure 2. Showing the national and international distribution of total patients being evaluated at MEG, Resource facility.

Total Number of patients scanned till 31.03.2022 =2166

User Charges Revenue Generation under DBT SAHAJ scheme : (08.09.2021 to 31.03.2022): Rs.5,16,000

New Methods for MEG Analysis:

- Ictal High Frequency Oscillations (HFO) are an Indicator of seizure onset areas (80Hz-200Hz).
- Pre Spike Source Localisation (PSSL) are an indicator of seizure before inter-ictal spikes.
- Standardized Low Resolution Brain Electromagnetic Tomography Method (sLORETA).
- Inter-ictal high frequency oscillations (80Hz-500Hz) are an indicator seizure onset areas (Working).
- Exploring aberrant functional networks in persons with epilepsy using connectomics.

PATIENTS, WHO HAVE BEEN ANALYSED BY VARIOUS METHODS GIVEN BELOW: (01.04.2021-31.03.2022)

No. of patients Analysed in DANA	No. of patients Analysed in CURRY	No. of patients Analysed in sLORETA	No. of patients Analysed in PSSL	No. of patients Analysed in High Frequency Interictal Ripples	No. of patients Analysed in High Frequency Ictal Ripples	Total No. of Patients have been Analysed
210	223	217	49	175	06	223

One of the major advantages of this technique over the EEG is the lack of distortion of MEG signals by the skull and intervening soft tissue. In addition, the MEG preferentially records activity from tangential sources thus recording activity predominantly from sulci, which is not contaminated by activity from apical gyral (radial) sources. While the MEG is probably more sensitive than the EEG in detecting interictal spikes, especially in some locations such as the superficial frontal cortex and the lateral temporal neocortex, both techniques are usually complementary to each other. The diagnostic accuracy of MEG source localization is usually better as compared to scalp EEG localization. Functional localization of eloquent cortex is another major application of the MEG. The combination of high spatial and temporal resolution of this technique makes it an extremely helpful tool for accurate localization of visual, somatosensory and auditory cortices as well as complex cognitive functions like language.

Accurate localization of epileptogenic focus is of paramount importance for good seizure free outcome following surgery in patients with drug refractory epilepsy. It is also important to know the extent of overlap of epileptogenic focus with eloquent cortex to avoid post-operative morbidity and prognostication. Invasive EEG is of great help to identify epileptogenic focus and extent of overlap with eloquent cortex. SEEG implantation is usually done in MRI negative cases, when there is discordance between electro clinical and MRI, when there is overlap with eloquent cortex and dual pathology cases. Placement of SEEG electrodes is safe and effective technique to localize epileptogenic zone.

SEEG implantation is currently allowing us to localize the epileptogenic networks accurately and we have been able to develop a paradigm to provide accurately labelled tissues for better cellular electrophysiological and molecular characterization. Such a strategy would allow us to create better models to understand the cellular and molecular mechanisms of epileptogenesis.

We analysed data from our centre, of patients undergoing stereotactic electrode implantation. The following are the situations that required invasive intracranial monitoring in our patients:

1. Seizures that were lateralized but not localized; or seizures were localized but not lateralized.
2. Seizures were neither localized nor lateralized
3. Seizure localization was discordant with other data
4. Relationship of seizure onset to lesion to be determined (e.g., dual pathology or multiple intracranial lesions).
5. Eloquent motor cortex mapping comparison of FMRI and direct cortical stimulation and NEXSTIM was done in 78 PWE.

SEEG electrodes were implanted with the assistance of stereotactic robotic device. An image guided volumetric T1-weighted MRI with contrast along with FLAIR sequences was used for preoperative planning. DICOM format images were digitally transferred to the robot's native planning software. The proposed targets of SEEG electrodes were decided according to the working hypothesis derived from the non-invasive investigations of the patient. All the proposed trajectories were planned using the planning software. The trajectories were evaluated in all planes (axial, sagittal, and coronal), and also along the reconstructed "probe's eye view", to look for any compromise to the vascular structures. Trajectory was adjusted appropriately without affecting the proposed target area. The procedure was performed under general anesthesia to ensure the accuracy of registration. Stereotactic registration was carried out using predefined anatomical landmarks. Registration was validated and adjusted accordingly. The

desired trajectories were selected on the touch-screen interface. The robotic device used at our institute has an arm with six degrees of freedom, with an adaptor at one end for holding instruments. After trajectory confirmation, the arm movement was initiated using a foot pedal. The robotic arm automatically locks into position once the position of the selected trajectory was reached. A 2-mm diameter handheld drill (Synthes) was introduced through the adaptor and used to create a skull opening. The dura mater was then opened with a dural perforator after coagulating it with monopolar cautery at low settings. A tract for the electrode was made using a tracker, following which the depth electrode was inserted. The adaptor to target distance was provided by the robotic software. Depth electrodes were inserted using orthogonal or oblique orientation. A guiding bolt was screwed onto the insertion site to hold the electrode in place. The electrode length was decided after subtracting the length of the adaptor and the anchoring bolt. The number and position of the depth electrodes was decided according to the working hypothesis. All patients had post-operative CT scan of the head to insure proper position of the electrodes and to ensure no hemorrhage. Patients were monitored in the epilepsy monitoring unit. After adequate information was collected regarding the epileptogenic zone, the SEEG evaluations were discussed in patient management conferences for final decisions. The electrodes were then removed in the under local anesthesia and sedation.

Twenty-one patients underwent SEEG implantation during the study period at our center (AIIMS). Out of them 17 were males (80.9%). Mean age of patients is 21.7 years (Range- 1.5years to 44 years). Five patients were less than 18 years of age (35.7%). Two patients (Patient 5 and 17) were not operated in view low frequency of seizures and epileptogenic zone was involving eloquent cortex (visual areas). Two patients (Patient 18 and 20) are yet to be planned for definitive surgery. There were no SEEG implantation related complications in any of patients. Of the remaining seventeen patients, 13 patients (76.5%) are seizure-free (ILAE Class 1 outcome) at follow up. Mean follow up period is 16.1 moths (range-5months to 36 months). One patient had left hemiplegia in post period and improved to motor power to 3/5 both in upper and lower limbs. There were no other significant post-operative complications. One patient (case 08) continued to have drop attacks in post-operative period and succumbed to death due to head injury. Language showed intresting reorganisation patters to the other hemisphere/ ant and superior to pars triangularis. Motor function also shifted to more anterion in 1 and posterior in another.

MEG investigation helped to increase the accuracy of localization of epileptogenic zone as well as the eloquent cortex, thereby enhanced the outcome of surgery. Ictal-MEG source localization added information towards delineating the ictal-onset zone (IOZ) and helped final decision-making in epilepsy-surgery. The findings of the study are published in European Journal of Neurology &Clinical Neurophysiology. Tripathi M, Kaur K, Ramanujam B, Viswanathan V, Bharti K, Singh G, Singh V, Garg A, Bal CS, Tripathi M, Sharma MC, Pandey R, Dash D, Mandal P, Chandra PS. Diagnostic added value of interictal magnetic source imaging in presurgical evaluation of persons with epilepsy: A prospective blinded study. Eur J Neurol. (2021) 28(9):2940-2951.

We also compared the diagnostic value and accuracy of ictal SPECT and inter-ictal magnetoencephalography (MEG) in localizing the site for surgery in persons with drug resistant epilepsy. SPECT was found to be non-informative for most patients, but reported better diagnostic output than MEG. It was found that MEG may be a useful alternative for patients in whom SPECT cannot be done or was non-localizing. MEG was useful in indicating sites for SEEG implantation. SEEG implantation was performed in 21 patients with DRE for better surgical outcome. The findings

of the study is published in Seizure: European Journal of Epilepsy. Kaur K, Garg A, Tripathi M, Chandra SP, Singh G, Viswanathan V, Bharti K, Singh V, Ramanujam B, Bal CS, Sharma MC, Pandey R, Vibha D, Singh RK, Mandal PK, Tripathi M. Comparative contribution of magnetoencephalography (MEG) and single-photon emission computed tomography (SPECT) in pre-operative localization for epilepsy surgery: A prospective blinded study. Seizure. (2021) 86:181-188.

We invented a new "bloodless" technique for minimally invasive robotic thermocoagulativehemispherotomy (ROTCH). Such a method is being described in the literature for the first time. ROTCH seems to be a safe, feasible, and bloodless procedure, with a very low morbidity rate and promising outcomes. The details of the study is published in Journal of Neurosurgery: Pediatrics. Chandra PS, Doddamani R, Girishan S, Samala R, Agrawal M, Garg A, Ramanujam B, Tripathi M, Bal C, Nehra A, Tripathi M. Robotic thermocoagulativehemispherotomy: concept, feasibility, outcomes, and safety of a new "bloodless" technique. J NeurosurgPediatr. (2021) 2:1-12. doi: 10.3171/2020.10. PEDS20673. Due of its significance, this article has been placed on the Journal's cover page.

Reduced endogenous KYNA synthesis contributes to enhanced glutamatergic activity in MTLE-HS was demonstrated. Reduced endogenous KYNA synthesis was due to altered levels of KAT II and PLP. This study provides evidence that application of KYNA may have therapeutic potential. The findings of the study is published in British Journal of Pharmacology: Dey S, Banerjee Dixit A, Tripathi M, Doddamani RS, Sharma MC, Lalwani S, Chandra PS, Banerjee J. Altered hippocampal kynurenine pathway metabolism contributes to hyperexcitability in human mesial temporal lobe epilepsy-hippocampal sclerosis. Br J Pharmacol. 2021;178(19):3959-3976.

FCD is a diffuse lesion with poorly defined epileptogenic zones, and poor surgical outcome in FCD is associated with inaccurate localization of the EZ. Hence, identifying novel epileptogenic markers to aid in the localization of EZ in patients with FCD is very much needed.For this purpose,we, for the first time performed RNA sequencing of surgically resected paired tissue samples obtained from electrocorticographically graded high (MAX) and low spiking (MIN) regions of FCD type II patients and autopsy controls. We identified significant changes in the MAX samples of the FCD type II patients when compared to non-epileptic controls, but not in the case of MIN samples. We found significant enrichment for myelination, oligodendrocyte development and differentiation, neuronal and axon ensheathment, phospholipid metabolism, cell adhesion and cytoskeleton, semaphorins, and ion channels in the MAX region. Through the integration of both MAX vs non-epileptic control and MAX vs MIN RNA sequencing (RNA Seq) data, PLP1, PLLP, UGT8, KLK6, SOX10, MOG, MAG, MOBP, ANLN, ERMN, SPP1, CLDN11, TNC, GPR37, SLC12A2, ABCA2, ABCA8, ASPA, P2RX7, CERS2, MAP4K4, TF, CTGF, Semaphorins, Opalin, FGFs, CALB2, and TNC were identified as potential key regulators of multiple pathways related to FCD type II pathology. We have identified novel epileptogenic marker elements that may contribute to epileptogenicity in patients with FCD and could be possible markers for the localization of EZ. This study has been published in Molecular Brain. Srivastava A, Kumar K, Banerjee J, Tripathi M, Dubey V, Sharma D, Yadav N, Sharma MC, Lalwani S, Doddamani R, Chandra PS, Dixit AB. Transcriptomic profiling of high- and low-spiking regions reveals novel epileptogenic mechanisms in focal cortical dysplasia type II patients. Mol Brain. 2021;14(1):120. doi: 10.1186/s13041-021-00832-4.

Role of HDACs and its sub-cellular distribution was studied in MTLE patients with hippocampal sclerosis. Knowledge regarding expression pattern and sub-cellular distribution of HDACs may help to devise specific HDACi therapy for epilepsy.

Proteomic studies on MTLE patients have been conducted. The findings of the present study is published in Cellular & Molecular Neurobiology. o Srivastava A, Banerjee J, Dubey V, Tripathi M, Chandra PS, Sharma MC, Lalwani S, Siraj F, Doddamani R, Dixit AB. Role of Altered Expression, Activity and Sub-cellular Distribution of Various Histone Deacetylases (HDACs) in Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis. Cell Mol Neurobiol. 2022;42(4):1049-1064.

Alteration in the TGFβ signalling, CK2, Cdk5, cPLA2 enzyme, Fibronectin-integrin-Src pathway and MMPs were demonstrated in MTLE-HS patients. These molecules may represent new potential therapeutic target for treatment of MTLE. Bera A, Srivastava A, Dubey V, Dixit AB, Tripathi M, Sharma MC, Lalwani S, Chandra PS, Banerjee J. Altered hippocampal expression and function of cytosolic phospholipase A2 (cPLA2) in temporal lobe epilepsy (TLE). Neurol Res. 2022;44(8):748-753.Paul D, Dixit AB, Srivastava A, Banerjee J, Tripathi M, Suman P, Doddamani R, Lalwani S, Siraj F, Sharma MC, Chandra PS, Singh RK. Altered expression of activating transcription factor 3 in the hippocampus of patients with mesial temporal lobe epilepsy-hippocampal sclerosis (MTLE-HS). Int J Neurosci. 2022;21:1-7. Paul D, Dixit AB, Srivastava A, Banerjee J, Tripathi M, Suman P, Doddamani R, Lalwani S, Siraj F, Sharma MC, Chandra PS, Singh RK. Altered expression of activating transcription factor 3 in the hippocampus of patients with mesial temporal lobe epilepsy-hippocampal sclerosis (MTLE-HS). Int J Neurosci. 2022;21:1-7.

Our studies demonstrated that Cdk5 differentially regulates excitatory synaptic activity in the hippocampal and ATL region of patients with MTLE-HS. We also demonstrated that it might have a potential role in increasing the stability of gephyrin-dependent γ2 subunitcontaining GABAA receptor clusters in FCD. Part of this study has been published in Neuroscience Letters. Banerjee J, Srivastava A, Sharma D, Dey S, Manjari Tripathi, Sharma MC, Sarat Chandra P, Banerjee Dixit A. Differential regulation of excitatory synaptic transmission in the hippocampus and anterior temporal lobe by cyclin dependent kinase 5 (Cdk5) in mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS). NeurosciLett. (2021):136096. doi: 10.1016/j.neulet.2021.136096

We utilize liquid chromatography and tandem mass spectrometry to identify altered lipids in resected brain specimens from FCD patients compared to non-epileptic controls. Based on these results, we propose that a similar approach utilizing unique lipid mass spectra can be used for defining the EZs in FCD. The observed distinct lipid mass spectra of cortical tissues from FCD patients could be used for real-time guidance during surgery as well as for ex vivo examination of resected tissues for diagnostic purposes. This study has been published in Epilepsy Research: Kumar K, Yadav N, Banerjee J, Tripathi M, Sharma MC, Lalwani S, Siraj F, Chandra PS, Sengupta S, Dixit AB. Mass spectrometry-based lipidomic analysis reveals altered lipid profile in brain tissues resected from patients with focal cortical dysplasia (FCD). Epilepsy Res. 2021;177:106773.

The current findings show association of altered TAG synthesis/metabolism with FCD pathology. Downregulation of DAGs, phosphatidylcholine, and phosphatidylethanolamine in FCD further suggests that degradation and/or decreased synthesis of these structural glycophospholipids and DAGs may contribute to increased TAGs. We propose that increased TAG levels could serve as potential biomarker of FD and the lipid mass spectra, if validated on a greater number of FCD patients, can aid in real time identification of resection margins akin to intelligent knife (iKnife) approach.

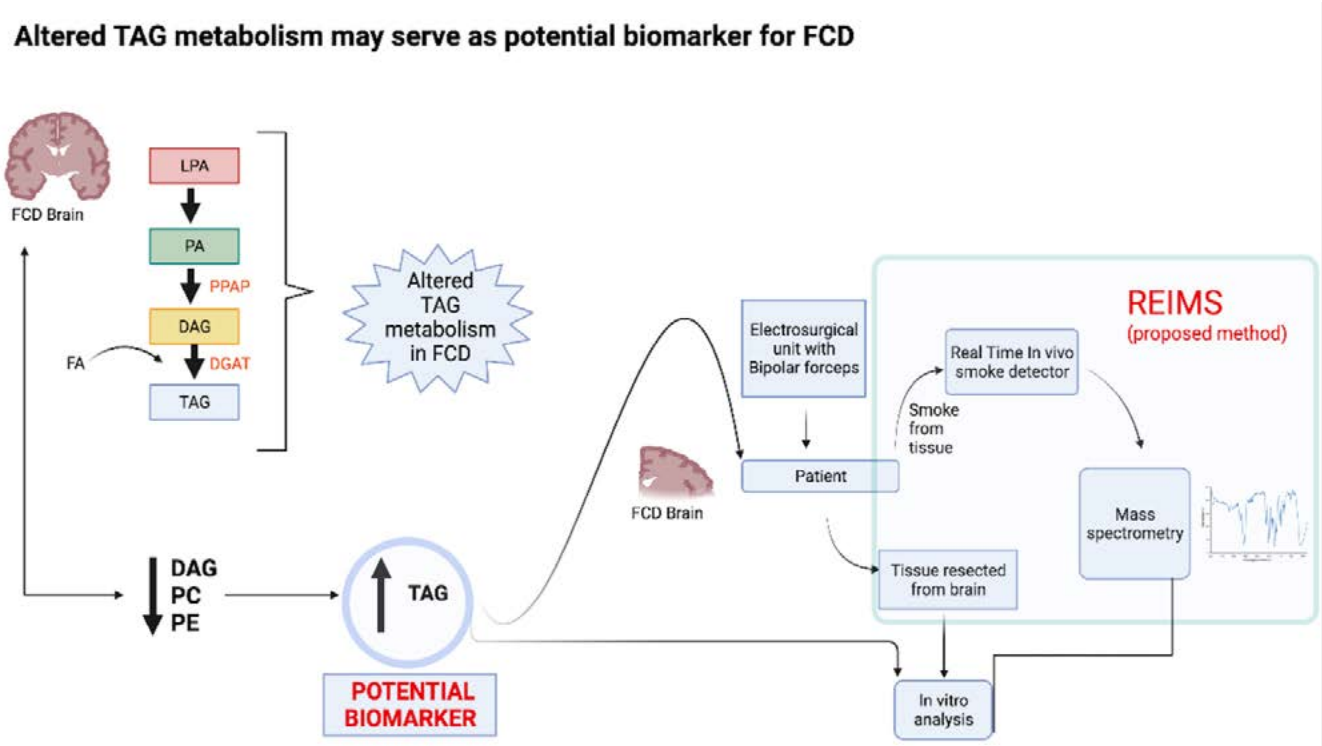

Fig: The current findings show association of altered TAG synthesis/metabolism with FCD pathology. Downregulation of DAGs, phosphatidylcholine, and phosphatidylethanolamine in FCD further suggests that degradation and/or decreased synthesis of these structural glycerophospholipids and DAGs may contribute to increased TAGs. we propose that increased TAG levels could serve as potential biomarker of FCD and the lipid mass spectra, if validated on a greater number of FCD patients, can aid in real-time identification of resection margins akin to intelligent knife (iKnife) approach

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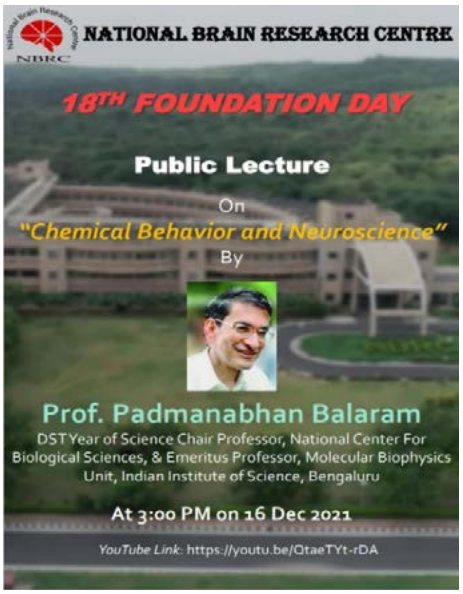
Lecture, Meetings and Workshops

NBRC 18th Foundation Day



National Brain Research Centre celebrated its 18th Foundation Day of NBRC on 16th December 2021 which was held virtually due to the Covid-19 pandemic. A grand lecture was delivered virtually to all the scientists and students by Prof. Padmanabhan Balaram, DST Year of Science Chair Professor, National Centre for Biological Sciences, & Emeritus Professor, Molecular Biophysics Unit, Indian Institute of Science, Bengaluru. The talk entitled "Chemical Behavior and Neuroscience". By Prof. Balaram is highly informative highlighting the chemical diversity in biology and neuroscience. Everyone joined in the auditorium and the lecture was also streamed live on YouTube. The foundation day celebrations ended with the prize distribution ceremony in the auditorium.

16th Ramamurthi Memorial Lecture

The 16th B. Ramamurthi Memorial Lecture was delivered by Dr. Vedantam Rajshekhar, M.B.B.S., M.Ch. (Neuro), Professor of Neurosurgery, Head, Department of Neurological Sciences, Christian Medical College Hospital, Vellore on 23rd November 2021 in the NBRC auditorium. Prof. Rajsekhar is a renowned neurosurgeon with international repute. Dr. Rajsekhar was introduced to the audience by the Prof. Pravat K Mandal, (Director I/C). Dr. Rajsekhar delivered his lecture entitled "Changing landscapes in publishing and measuring research". He emphasized on the pattern of publications, different journals being cited, and evaluation of the research with a motive to increase the threshold of journals. His talk was well received by the audience. The program was ended with vote of thanks to Dr. Rajsekhar.

General & Academic Administration

General & Academic Administration – A Profile

The Administration of the Institute consists of the following major wings:

1. General Administration is headed by the Chief Administrative Officer, who is responsible for overall Management of Establishment, Personnel & Administration Wing, Stores & Purchase Wing, Import & Project Cell, Finance & Accounts Wing, Estate Management & Engineering Maintenance Wing – Civil, Electrical & Mechanical.
2. Academic Administration is headed by the Registrar, who is responsible for the students' administration, project co-ordination, new students' admissions, course co-ordination etc. The officer is also responsible for administration of all the projects.

During the year under review, the Administration of NBRC observed all the important days as directed by the Government of India such as Anti-terrorism day, Sadbhavana Diwas, Independence Day, Vigilance Awareness week, International Yoga Day etc. The Administration achieved excellence in execution of the following activities at NBRC:

- Made major imports from different countries in terms of equipment and other consumables with meticulous planning and adhered to a precise schedule.
- The annual cultural festival of NBRC, 'TANTRIKA 2022' was organized within the campus which included a variety of cultural and sports events. Students, officers, and staff of NBRC participated in the event.
- A street play by Meraki on 19th March, 2022 as Tantrika Event was organized.
- A talk by Dr. Bittu Kaveri Rajaraman, Prof. Ganesh Bagler, Dr. P. Venkatakrishnan, were organized on 22nd March, 2022.
- On 23rd March a talk of Dr. Rudrani Chhetri was organized.
- Provided necessary logistics in conducting international and national conferences/ seminars organized in the campus as well outside the campus.
- Made major imports from different countries in terms of equipment and other consumables with meticulous planning and adhered to a precise schedule.
- The 18th Foundation Day of NBRC was held on 16th day of December, 2021. On this occasion, due to COVID-19 pandemic virtual program was performed.
- On this august occasion, Prof. Padmanabhan Balaram, DST Year of Science Chair Professor, National Center for Biological Sciences, & Emeritus Professor, Molecular Biophysics Unit, Indian Institute of Science, Bengaluru delivered the lecture virtually to the students and scientific community.

Implementation of Official Language

NBRC Administration has given due importance for the implementation of Hindi as the Official Language at this centre and has made full efforts to implement the use of Official Language in all the administrative jobs such as internal official meetings, interviews, debates, general applications etc.

RTI Act

The provisions of RTI Act are being followed at NBRC in letter and spirit. All RTI applications received during 2021-22 seeking information on various matters concerning NBRC were provided the requisite information within the prescribed time limit. The quarterly reports containing number of requests received with

date, details of compliance, amount of charges etc., were sent to CIC and updated on NBRC website.

Women Empowerment

NBRC has a distinct feature of giving equal opportunity to women. The Committees, constituted to do various work of Administration, Academics and scientific activities, have women members on them which ensure fair participation and protection of women. There is a committee for redressal of complaints relating to any sexual harassment of women at NBRC and grievances, if any, from aggrieved girl students/ women employees of NBRC. Any lady/ woman of NBRC, among the Students/ Employees who is subjected to sexual harassment may approach any of the committee members.

Reservations and concessions in Employment & Admissions of Students

NBRC follows reservations & concessions as per rules of Government of India in employment, as applicable.

Vigilance

The Institute has a Chief Vigilance Officer. As per the guidelines of DBT, one of the scientists of NBRC has been nominated as Part time Chief Vigilance Officer of the Centre.

Institutional Governance

Structure & People at NBRC

Members of Governing Body

Dr. Rajesh S. Gokhale, Chairperson
Secretary
Department of Biotechnology,
C.G.O Complex,
New Delhi – 110 003

Shri Chaitanya Murthy, (Ex-Officio)
Joint Secretary (Admin),
Department of Biotechnology, Lodhi Road,
CGO Complex, New Delhi – 110 003

Shri Viswajit Sahay, (Ex-Officio)
Additional Secretary & Financial Advisor,
Department of Biotechnology,
New Delhi – 110003

Dr. Sanjay Kr. Mishra, (Ex-Officio)
Scientist - H
Department of Biotechnology,
New Delhi-110003

Prof. Pravat Kr. Mandal, (Ex-Officio)
Director-in- Charge
National Brain Research Centre,
Manesar – 122 052, Haryana

Prof. Pankaj Seth, (Ex-Officio)
Scientist-VII
National Brain Research Centre,
Manesar – 122 052, Haryana

Dr. Suraksha S. Diwan,
Nodal Officer of NBRC (Ex-Officio)
Scientist 'F',
Department of Biotechnology,
Ministry of Science & Technology,
Government of India,
BLOCK-3, Room No.517, C.G.O. Complex,
Lodhi Road, New Delhi -110 003

Shri Tanmoy Bhattacharya,
Member Secretary
Chief Administrative Officer (Ex-Officio)
National Brain Research Centre,
Manesar – 122 052, Haryana

Prof. Vidita Vaidya,
Professor,
Department of Biological Science,
Tata Institute of Fundamental Research
(TIFR), Mumbai.

Prof. Jayasri Das Sarma,
Department of Biological Sciences,
Indian Institute of Science Education and
Research (IISER),
Kolkata.

Prof. M. R. Satyanarayana Rao,
Honorary Professor,
Chromatin Biology
Laboratory, Neuroscience Unit (NSU),
Jawaharlal Nehru Centre for Advanced
Scientific Research (JNCASR),
Bengaluru.

Prof. Kameshwar Prasad,
Former Professor,
Department of Neurology,
All India Institute of Medical Sciences
(AIIMS), and
Director, RIMS, Ranchi
New Delhi

Members of Finance Committee

Shri Viswajit Sahay, Chairperson
Additional Secretary & Financial Advisor,
Department of Biotechnology,
New Delhi – 110003

Dr. Sanjay Kr. Mishra, (Ex-Officio)
Scientist - H
Department of Biotechnology,
New Delhi-110003

Prof. Pravat Kr. Mandal, (Ex-Officio)
Director -in-Charge
National Brain Research Centre,
Manesar – 122 052, Haryana

Shri. Tanmoy Bhattacharya, (Ex-Officio)
Chief Administrative Officer
National Brain Research Centre,
Manesar – 122 052, Haryana

Mrs. Shiwani Tanwar, Member Secretary
In-Charge F&AO (Ex-Officio)
National Brain Research Centre,
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Prof. Pramod Kr. Garg
Executive Director
Translational Health Science and
Technology Institute (THSTI)
NCR Biotech Science Cluster
3rd Miolestone, Faridabad-121001 (Haryana)

Shri Praveen Kumar Bansal
Former Vice President,
Income Tax Appellate Tribunal,
Government of India

Shri M. Satish Kumar Reddy
IRS, Former Commissioner of Central
Goods and Services Tax (CGST) and
Customs, Government of India

Members of Building Committee

Prof. Dinakar M. Salunke
Chairperson
Director
International Centre for Genetic Engineering and Biotechnology
New Delhi – 110 067

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Director,
National Institute of Immunology (NII),
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Engineer-In-Charge (Civil)
IUAC
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Prof. Sidhartha Satpathy
HOD Hospital Administration
AIIMS
New Delhi

Prof. Pravat Kumar Mandal
Director (I/C) (Ex-Officio)
National Brain Research Centre
Manesar - 122052

Members of NBRC Society

Dr. Jitendra Singh, President
Hon'ble Minister of State (IC) of the Ministry of S&T, Govt. of India

Shri. Anil Vij, (Ex-Officio)
Hon'ble Minister in-charge of the Department handling Science and Technology matters in the State of Haryana

Dr. Rajesh S. Gokhale, (Ex-Officio)
Secretary,
Department of Biotechnology
Ministry of Science & Technology
Government of India
New Delhi

Dr. Balram Bhargava, (Ex-Officio)
Secretary,
Department of Health Research and
Director General,
Indian Council of Medical Research,
New Delhi

Dr. Srivari Chandrasekhar, (Ex-Officio)
Secretary,
Department of Science and Technology
Government of India

Shri. Ashok Khemka, (Ex-Officio)
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Prof. Ashok Panagariya,
Former IMA President,
Jaipur

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Indian Institute of
Science (IISc), Bengaluru.

Prof. Prabhu Nath Pandey,
Professor & Head,
Department of Neurosurgery,
Lok Nayak Jai Prakash Narayan Hospital,
New Delhi.

Prof. M. V. Padma Shrivastava,
Professor & Head,
Department of Neurology,
Chief Neurosciences Centre,
AIIMS, New Delhi.

Prof. B. N. Gangadhar,
Former Director,
National Institute of Mental Health and
Neuro-Sciences (NIMHANS), Bengaluru.

Dr. Senapathy 'Kris' Gopalakrishnan,
Co-Founder,
Infosys Ltd., Bengaluru.

Members of NBRC Scientific Advisory Committee (SAC)

Prof. Siddharta Roy, Chairperson
J.C. Bose Fellow,
Department of Biophysics Centenary Campus,
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Prof. Kameshwar Prasad
Director
Rajendra Institute of Medical Sciences,
An Autonomous Institute under the Govt. of
Jharkhand, Ranchi, Jharkhand

Prof. Venkatasubramanian Ganesan
Officer In-Charge
Translational Psychiatry Laboratory
Cognitive Neurobiology Division, Neurobiology
Research Centre, National Institute of Mental
Health and Neuro-Sciences (NIMHANS),
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Prof. Ashalatha Radhakrishnan
Professor
Department of Neurology,
Sree Chitra Tirunal Institute of Medical
Sciences and Technology (SCTIMST),
Trivandrum

Prof. Rama Jayasundar
Professor & Head
Department of Nuclear Magnetic Resonance
(NMR),
AIIMS, New Delhi

Prof. Vijay Kumar Kuchroo
Samuel L. Wasserstrom Professor of Neurology,
Harvard Medical School, Boston, USA

Members of Academic Council

Prof. Pravat K. Mandal Director I/C, National Brain Research Centre Manesar, Haryana	Prof. Soumya Iyengar National Brain Research Centre Manesar, Haryana
Prof. Sudha Bhattacharya School of Environmental Sciences Jawaharlal Nehru University, New Delhi	Prof. Anirban Basu National Brain Research Centre Manesar, Haryana
Prof. Ishan Patro School of Studies in Zoology / Neuroscience Jiwaji University, Gwalior	Prof. Ellora Sen National Brain Research Centre Manesar, Haryana
Prof. Gurcharan Kaur Department of Biotechnology Guru Nanak Dev University, Amritsar	Prof. Ranjit K. Giri National Brain Research Centre Manesar, Haryana
Prof. Pankaj Seth National Brain Research Centre Manesar, Haryana	Dr. Sourav Banerjee National Brain Research Centre Manesar, Haryana
Prof. Shiv K. Sharma National Brain Research Centre Manesar, Haryana	Dr. Arpan Banerjee National Brain Research Centre Manesar, Haryana
Prof. Nandini C. Singh Professor (on deputation to UNESCO, New Delhi)	Dr. Anindya Ghosh Roy National Brain Research Centre Manesar, Haryana

Members of Board of Studies

Prof. Pravat K Mandal Director I/C, National Brain Research Centre Manesar, Haryana	Prof. Ranjit K. Giri National Brain Research Centre Manesar, Haryana
Prof. Kunzang Chosdol Department of Biochemistry, All India Institute of Medical Sciences, New Delhi	Dr. Anindya Ghosh Roy National Brain Research Centre Manesar, Haryana
Dr. Sushil Kumar Jha Associate Professor, Jawaharlal Nehru University, New Delhi	Dr. Arpan Banerjee National Brain Research Centre Manesar, Haryana
Prof. Soumya Iyengar National Brain Research Centre Manesar, Haryana	Dr. Dipanjan Roy National Brain Research Centre Manesar, Haryana
Prof. Ellora Sen National Brain Research Centre Manesar, Haryana	Dr. Sourav Banerjee National Brain Research Centre Manesar, Haryana

List of Students

Wellcome Trust India Alliance / DBT India Alliance Early Career Fellow

S/No	Faculty
1	Dr. Nivethida Thirugnanasambandam
2	Dr. Swagata Dey

Ph.D. Degrees Awarded

S/No	Name of the Student
1	Dr. John Thomas
2	Dr. Shankhamala Sen
3	Dr. Priyanka
4	Dr. Dharmendra Puri
5	Dr. Atrayee Basu
6	Dr. Utkarsha A Singh

M.Sc. Degrees Awarded

S/No	Name of the Student
1	Ms. Aamna Jain
2	Mr. Ankit Kumar Shah
3	Ms. Anwesha Das
4	Ms. Bhanumita Agrawal
5	Ms. Debapriya Roy
6	Ms. Bapat Ojasee Ajinkya
7	Ms. Pooja Kri Gupta
8	Mr. Rudradeep Mukherjee
9	Mr. Akshay Kumar Tiwari

Ph.D. Students

S/No	Name of the Student
1	Mr. Biswaranjan Sahoo
2	Mr. Tushar Arora
3	Mr. S Balakumar
4	Ms. Arti Kumari
5	Mr. Dharmendra Puri
6	Ms. Mukta Kumari
7	Mr. Raghav Shankar (Till 15/03/2022)
8	Md. Tipu Khan
9	Ms. Priyanka Ghosh
10	Ms. Sarbani Samaddar
11	Ms. Shruti Patrick
12	Mr. Surajit Chakraborty
13	Ms. Bindu
14	Mr. Sibaram Behera
15	Mr. Abhishek Singh Narvaria
16	Ms. Deepti Dama
17	Mr. Karthick R
18	Ms. Nisha Chetana Sastry
19	Ms. Shivangi Sharma
20	Ms. Sunanda Sharma
21	Ms. Dipanjana Banerjee
22	Ms. Gargi Majumdar
23	Ms. Kamakshi Garg
24	Ms. Khushboo Vinod Punjabi (Till 02/08/2021)
25	Ms. Partika
26	Ms. Shalini Sharma
27	Ms. Stuti Mohapatra
28	Ms. Anjali
29	Mr. Ankit Yadav
30	Ms. Archana Mehta
31	Mr. Chandramouli Mukherjee
32	Ms. Sonia Balahun Umdor
33	Mr. Arkaprovo Sarkar
34	Ms. P. V. Vinitha
35	Ms. Athira M Sarath
36	Mr. Anirudh S
37	Mr. Dhyey Vyas
38	Mr. Shashank Saxena
39	Ms. Archana Panwar
40	Ms. Deepti Thapliyal
41	Ms. Krittika Biswas
42	Ms. Sania Sultana

Integrated Ph.D. Students

S/No	Name of the Student
1	Ms. Uzma Din
2	Ms. Chitra Mohinder Singh Singal
3	Ms. Pooja Parishar
4	Mr. Apurva Agrawal (Till 16/01/2022)

S/No	Name of the Student
5	Mr. Atanu Datta
6	Ms. Atrayee Basu (Till 14/01/2022)
7	Ms. Priyanka (Till 03/08/2021)
8	Mr. Gourav Sharma
9	Ms. Harjot Kaur Brar
10	Mr. Shubham Krishna

M.Sc. Students

S/No	Name of the Student
1	Ms. Aamna Jain (Till 30/07/2021)
2	Mr. Ankit Kumar Shah (Till 30/07/2021)
3	Ms. Anwesha Das (Till 30/07/2021)
4	Ms. Bhanumita Agrawal (Till 30/07/2021)
5	Ms. Debapriya Roy (Till 30/07/2021)
6	Ms. Bapat Ojasee Ajinkya (Till 30/07/2021)
7	Ms. Pooja Kri Gupta (Till 30/07/2021)
8	Mr. Rudradeep Mukherjee (Till 30/07/2021)
9	Mr. Akshay Kumar Tiwari (Till 30/07/2021)
10	Ms. Dyutika Banerjee
11	Ms. Janhvi Mahesh Dhongdi
12	Ms. Mohima Mukherjee
13	Ms. Mrittika Dey
14	Ms. Muskaan Verma
15	Ms. R. Madhumita
16	Mr. Rajat Joshi
17	Mr. Shuvrangshu Guha
18	Ms. Debadrita Mondal
19	Mr. Mihir Prafulla Pradhan
20	Mr. Rishabh Vikram Bapat
21	Ms. Sreyashi Bhattacharjee
22	Mr. Aninda Sundar Modak
23	Mr. Shivam Malviya
24	Ms. Soumi Sen
25	Ms. Tulika Khargonkar
26	Mr. Tanmay Singhal
27	Mr. Sudipto Chaki
28	Ms. Triparna Chakraborty
29	Ms. Ayisha Mariyam P M

M.Sc.-Ph.D. Integrated Students

S/No	Name of the Student
1	Ms. Himali Arora
2	Ms. Meenakshi Bhaskar
3	Mr. Neeraj Kumar
4	Mr. Anagh Pathak
5	Ms. Kirti
6	Ms. Ritu Moni Borah
7	Mr. Azman Akhter
8	Ms. Guneet Kaur
9	Ms. Kirti Saluja
10	Ms. Pallavi Singh
11	Ms. S Indira Priya
12	Ms. Shashwati Tripathi
13	Ms. Vinsea AV Singh

Project Assistant

S/No	Name
1	Dr. Fahd M Yasin (Till 12/04/2021)
2	Ms. Sigar Priyanka Jaipal (Till 01/07/2021)
3	Mr. Shubham Singhal
4	Mr. Arun EVR
5	Ms. Dimpi (Till 06/08/2021)
6	Mr. Vinayak Ghosh
7	Mr. Santhosh Kumar S (Till 06/01/2022)
8	Ms. Avantika Samkaria
9	Ms. Rimil Guha Roy
10	Ms. Kavinila S
11	Mr. Souren Sadhukhan
12	Ms. Bhavya Gohil
13	Ms. Kusum Thuwal (Till 05/11/2021)
14	Ms. Sanchi Ahuja
15	Mr. Mukaram Hafiz Bhat
16	Ms. Saumya Rastogi
17	Ms. Tuhina Sanwal
18	Ms. Mydhily Vasudevan
19	Mr. Samuel Bekins S
20	Mr. Kameev Sharma

Research Associates

S/No	Name
1	Dr. Sonika
2	Dr. Priyanka Chakraborty (Till 17/12/2021)
3	Ms. Nidhi Sharma
4	Dr. Sushma Dagar
5	Ms. Km Nisha
6	Dr. Atreye Majumdar
7	Dr. Shubhi Kansal (Till 01/11/2021)
8	Dr. Dimpi

ICMR Research Associate

S/No	Name
1	Dr. Deepali Singh

SERB-National Post-Doctoral Fellowship

S/No	Name
1	Dr. Soibam Shyamchand Singh
2	Dr. Suman Saha

Research Fellows

S/No	Name
1	Mr. Dharmendra Puri (From 13/08/2021 till 12/02/2022)
2	Ms. Tripti Joshi (From 12/02/2022 till 10/05/2022)
3	Mr. Hriday Shankar Pandey (From 10/02/2022 till 30/08/2022)
4	Ms. Chitra Mohinder Singh Singal (From 19/02/2022 till 26/07/2022)

Project Employees

S/No	Name
1	Mr. Manjit, Lab attendant (MEG Project)
2	Mr. Rakesh Yadav, Nursing Orderly (MEG Project)
3	Mr. Ashok Kumar, Nurse (MEG Project)
4	Mr. Om Prakash Jakhar, Nurse (MEG Project)
5	Ms. Shalini, Technical Assistant (Project)
6	Mr. Neeraj Kasana, Technical Assistant (Project)
7	Mr. Sukhvir Singh Pundir, Technical Associate (Computer / IT)
8	Mr. Prem Chand, Manager (MEG Project)
9	Ms. Priya Shrivastav, Nurse (MEG Project)
10	Ms. Shallu, Neuropsychologist (Project) (Till 13-12-2021)
11	Dr. Swagata Dey, DST INSPIRE Faculty
12	Mr. Gaurav Singh, Technologist (MEG Project)
13	Mr. Dharmendra Jakhar, Technical Assistant (Project) (MEG Project)
14	Mr. Kuldeep Singh, R&D Engineer (Project) (Till 19-11-2021)
15	Ms. Sunita Kumawat, Nursing Orderly (MEG Project)
16	Ms. Srimathi P, Technician (MEG Project) (Till 25-03-2022)
17	Mr. Sachin Kumar, Lab Attendant (MEG Project)
18	Ms. Kirandeep Kaur, Technologist (MEG Project) (Till 26-08-2021)
19	Mr. Deepak Kumar, Nursing Orderly (MEG Project)
20	Ms. Meenu Yadav, Technician (MEG Project)
21	Mr. Anupam Das, Junior Research Fellow (Project) (Till 21-01-2022)
22	Mr. Saurav Roy, R&D Engineer (Project) (Till 18-05-2021)
23	Ms. Shallu, Research Scientist (Project)

S/No	Name
24	Dr. Rini Dhawan, Project Coordinator-I (Project) (Till-24-03-2022)
25	Dr. Nivethida Thirugnanasambandam, India Alliance CPH Fellow (Intermediate)
26	Krishan Kant, Technical Assistant (Project) (Till 18-10-2021)
27	Ms. Komal Jindal, Senior R&D Engineer (Project) (Till-17-02-2022)
28	Ms. Sruthy Ravivarma, Project Assistant (Project)
29	Ms. Kusum Thuwal, Project Assistant (Project) (Till-25-05-2021)
30	Ms. Pallavi Pant, Junior Research Fellow (Project) (Till 11-03-2022)
31	Dr. Jasleen Gund, Project Scientist I (Till 18-10-2021)
32	Mr. Rishabh Kapoor, Project Assistant (Project) (Till 23-04-2021)
33	Ms. Divya Dwivedi, Clinical Coordinator (Project) (Till 03-11-2021)
34	Ms. Shallu, Scientist (Project)
35	Dr. Shah Zinkal Atul, Project Scientist-III (Project)
36	Mr. Amit Kumar Srivastva, Nursing Orderly (MEG Project)
37	Dr. P. Prarthana Chandra, Casaulty Medical Officer (MEG Project)
38	Ms. Divyasree V.M, Nurse (MEG Project)
39	Ms. Anshika Goel, Research Scientist (Project) (Till 03-02-2022)

S/No	Name
40	Mr. Gaurav Rawat, Technician (Project) (MEG Project)
41	Ms. Risna K. R., Junior Research Fellow (Project)
42	Dr. Yashika Arora, Project Scientist I (Project)
43	Ms. Dhurgadevi K.R, Project Assistant (Project)
44	Dr. Suman Saha, Project Scientist I (Till 09-03-2022)
45	Mr. Zohab Ahasan, R&D Engineer (Project) (Till 13-01-2022)
46	Mr. Ritwick Mishra, Neuro Imaging Analyst (Project) (Till 23-08-2021)
47	Mr. Ritwick Mishra, Scientist (B) (Till 18-11-2021)
48	Ms. Kundnani Jigna Jagdishbhai, Junior Research Fellow (Project) (Till 25-01-2022)
49	Ms. Ritika Mahajan, Neuro Imaging Analyst (Project) (Till 15-02-2022)
50	Dr. Priyanka Chakraborty, Project Scientist - I
51	Ms. Anshika Goel, Research Scientist (Project)
52	Mr. Kuldeep Singh, Senior R&D Engineer (Project) (Till 25-02-2022)
53	Ms. Shardha Gaur, Neuropsychologist (Project)
54	Ms. Komal Jindal, Project Scientist-II (Project)
55	Mr. Ajay Pal, Project Assistant (Project)
56	Dr. Suman Saha, National Post-Doctoral Fellowship (Till 09-03-2022)

Scientists

S. No.	Name	Designation
1.	Prof. Pravat Kumar Mandal	Director-in-Charge/ Scientist – VII
2.	Prof. Pankaj Seth	Scientist – VII
3.	Prof. Anirban Basu	Scientist – VII
4.	Prof. Shiv Kumar Sharma	Scientist-VII
5.	Prof. Soumya Iyengar	Scientist – VII
6.	Prof. Nandini C. Singh	Scientist-VI (Working at UNESCO, New Delhi on deputation basis)
7.	Dr. Ellora Sen	Scientist – VI
8.	Dr. Ranjit Kumar Giri	Scientist – VI
9.	Dr. Sourav Banerjee	Scientist - V
10.	Dr. Arpan Banerjee	Scientist – V
11.	Dr. Anindya Roy Ghosh	Scientist – V
12.	Dr. Dipanjay Roy	Scientist-IV
13.	Dr. Mayanglambam Dhruba Singh	Scientist-III
14.	Dr. Bhavani Shankar Sahu	Scientist-III
15.	Mr. Mahender Kumar Singh	Information Scientist

Administrative Staff

S.No.	Name	Designation
1.	Mr. Tanmoy Bhattacharyya	Chief Administrative Officer
2.	Mr. Santosh Kumar Choudhary	Deputy Finance Officer
3.	Mrs. Pooja Gosain	Administrative Officer
4.	Ms. Shiwani Tanwar	Administrative Officer (Acad.)
5.	Mr. Ravinder Pal	Stores & Purchase Officer
6.	Mr. Sanjay Kumar Gupta	Office Assistant
7.	Mr. Suraj Bhan	Office Assistant
8.	Mr. Himanshu Mal	Office Assistant (Working at ICSSR, New Delhi on deputation basis)
9.	Mr. Ajay Kumar Dehariya	Office Assistant
10.	Mr. Rakesh Kumar Yadav	Office Assistant
11.	Mr. Parmander Singh Rawat	Office Assistant
12.	Mr. Jitendra Kumar Meena	Office Assistant
13.	Mr. Bhupender Pal Sharma	Driver Grade-I
14.	Mr. Satish Kumar	Driver Grade-II

Technical Staff

S. No.	Name	Designation
1.	Mr. Sanjeev Kumar Choudhary	Assistant Engineer
2.	Dr. D.D. Lal	Technical Officer
3.	Dr. Inderjeet Yadav	Veterinarian
4.	Mr. Jitender Ahlawat	Technical Officer – B
5.	Mr. Arvind Singh Pundir	Technical Officer – B
6.	Mr. Kedar Singh Bajetha	Computer Operator
7.	Ms. Seepika	Computer Operator
8.	Mr. Sachin Kumar	Computer Operator
9.	Ms. Tarnnum Mansoori	Computer Operator
10.	Mr. Sanjeev Bhardwaj	Computer Operator
11.	Dr. Kanhaiya Lal Kumawat	Technician-C
12.	Mr. Shankar Datt Joshi	Technician-C
13.	Mr. Sumit Kumar Sinha Mahapatra	Technician-C
14.	Mr. D. Narender	Technician-C
15.	Mr. Mithlesh Kumar Singh	Technician-B
16.	Mr. Ankit Sharma	Technician-B
17.	Mr. Sanjay Kumar	Technician-B
18.	Mr. Yunis Khan	Technician-B
19.	Md. Irshad Alam	Technician-B
20.	Mr. Durga Lal Meena	Technician-B
21.	Mr. Manish Kumar	Technician-B
22.	Mr. P. Manish	Technician-B
23.	Mr. Dil Bahadur Karki	Technician-A
24.	Mr. Rammehar	Technician-A
25.	Mr. Hari Shankar	Technician-A
26.	Mr. Mahendra Singh	Technician-A
27.	Mr. Sanjay Kumar Singh	Technician-A

Annual Financial Statements

KUMAR KHARE & CO.
CHARTERED ACCOUNTANTS
S-160, L.G.F. GREATER KAILASH PART-I
NEW DELHI-110048
Phone – 41733110, 9811133110
E-mail alok@kumarkhareca.com website: kumarkhareca.com

INDEPENDENT AUDITOR'S REPORT

To the Members
NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURUGRAM, HARYANA-122052

REPORT ON THE FINANCIAL STATEMENTS

Opinion

We have audited the accompanying financial statements of **National Brain Research Centre** ("the Society"), which comprise the Balance Sheet as of March 31, 2022, Receipts & Payments Account and the Income & Expenditures Account for the year ended on that date, and a summary of significant accounting policies and other explanatory information (hereinafter referred to as "the Financial Statement").

Basis for Opinion

We conducted our audit of the Financial Statements in accordance with the Standards on Auditing. Our responsibilities under those Standards are further described in the Auditor's Responsibilities for the Audit of the Financial Statements section of our report. We are independent of the society in accordance with the Code of Ethics issued by the Institute of Chartered Accountants of India (ICAI) together with the independence requirements that are relevant to our audit of the financial statements under the provisions of the Act and the Rules made thereunder, and we have fulfilled our other ethical responsibilities in accordance with these requirements and the ICAI's Code of Ethics. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion on the Financial Statements.

Responsibilities of Management for the Financial Statements

The Society's Board of members are responsible for the preparation and presentation of these financial statements that give a true and fair view of the financial position, financial performance and cash flows of the society in accordance with the AS and other accounting principles generally accepted in India. This responsibility also includes the maintenance of adequate accounting records in accordance with the provisions of the bye laws for safeguarding the assets of the Society and for preventing and detecting the frauds and other irregularities; selection and application of appropriate accounting

KUMAR KHARE & CO. FRN-006740C NEW DELHI CHARTERED ACCOUNTANTS

KUMAR KHARE & CO.
CHARTERED ACCOUNTANTS
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NEW DELHI-110048
Phone – 41733110, 9811133110
E-mail alok@kumarkhareca.com website: kumarkhareca.com

policies; making judgments and estimates that are reasonable and prudent; and design, implementation and maintenance of adequate internal financial control, that were operating effectively for ensuring the accuracy and completeness of the accounting records, relevant to the preparation and presentation of the financial statements that give a true and fair view and are free from material misstatement, whether due to fraud or error.

In preparing the financial statements, management is responsible for assessing the society 's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless management either intends to liquidate the society or to cease operations, or has no realistic alternative but to do so.

Auditor's Responsibility for the Audit of the Financial Statements

1.) Our objectives are to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditor's report that includes our opinion. Reasonable assurance is a high level of assurance but is not a guarantee that an audit conducted in accordance with SAs will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements.

2.) We believe that our audit provides a reasonable basis for our opinion:

a) we have sought and obtained all the information and explanations which to the best of our knowledge and belief were necessary for the purpose of our audit.

b) in our opinion proper books of account as required by law have been kept by the society so far as it appears from our examination of those books.

c) the Balance Sheet, the Receipts & Payment Account and the Income & Expenditures Account dealt with by this Report are in agreement with the books of account.

3.) In our opinion and to the best of our information and according to the explanations given to us, the financial statements give a true and fair view in conformity with the accounting principles generally accepted in India.

KUMAR KHARE & CO. FRN-006740C NEW DELHI CHARTERED ACCOUNTANTS

KUMAR KHARE & CO.
CHARTERED ACCOUNTANTS
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E-mail alok@kumarkhareca.com website: kumarkhareca.com

a) As it relates to Balance sheet, of the state of affairs of the society as at 31st March, 2022;

b) As it related to Income and Expenditures Account, of the Deficit over Income for the year ended on that date;

For Kumar Khare & Co.
Chartered Accountants
Firm Regn. No.: 006740C

Sunil Kumar
Partner
Membership No. 546026

Place: New Delhi
Date: 13/09/2022

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGRAM, HARYANA
Balance Sheet as at 31st March 2022

(Amounts in Rs)

		Particulars	Schedule	31-03-2022	31-03-2021
I		**EQUITY AND LIABILITIES**			
1		**Owners' Funds**			
	a	Owners' Capital Account	1	1,44,50,02,000	1,40,35,02,000
	b	Reserves and surplus	2	-34,84,43,882	-23,80,89,863
	c	Earmarked/Endowment Funds	3	40,88,26,614	63,86,15,715
2		**Current liabilities**			
	a	Trade payables			
		-Dues of MSME	4	-	-
	b	-Dues of others	4	42,58,739	11,52,789
	c	Other current liabilities	5	5,33,92,018	3,30,29,243
	d	Short-term provisions	6	78,68,296	80,57,551
			Total	**1,57,09,03,785**	**1,84,62,67,435**
II		**ASSETS**			
1		**Non-current assets**			
	a	Property, Plant and Equipment and Intangible Assets			
		i.Property, Plant and Equipment	7(a)	91,24,51,063	98,28,02,590
		ii. Intangible assets	7(b)	4,97,639	6,63,518
		iii. Capital work in progress	7(c)	-	-
		iv. Intangible asset under development	7(d)	-	-
	b	Non-current investments	8	1,33,98,826	1,35,63,572
2		**Current assets**			
	a	Cash and bank balances	9	42,78,38,530	82,53,57,206
	b	Short Term Loans and Advances	10	21,67,17,726	2,38,80,548
			Total	**1,57,09,03,785**	**1,84,62,67,435**
		Summary of significant accounting policies			
		The accompanying notes are an integral part of the financial statements			

As per our separate report of even date attached

For Kumar Khare & Co.
Chartered Accountants
FRN-006740C

KUMAR KHARE & CO. FRN-006740C NEW DELHI CHARTERED ACCOUNTANTS

Sunil Kumar
Partner
Membership No. 546026
Date: 13-09-2022
Place: New Delhi

SHIWANI TANWAR
FINANCE & ACCOUNTS OFFICER (I/C)
NBRC

वित्त एवं लेखा अधिकारी
Finance & Account Officer
राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
National Brain Research Centre
मानेसर / Manesar-122050
हरियाणा / Haryana

PROF. PRAMOD KUMAR GARG
DIRECTOR
NBRC

Prof. Pramod Kumar Garg
प्रो. प्रमोद कुमार गर्ग
निदेशक (अतिरिक्त प्रभार) / Director (Addl. Charge)
राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
National Brain Research Centre
मानेसर–122052 / Manesar-122052
हरियाणा / Haryana

NATIONAL BRAIN RESEARCH CENTRE

NH-8, NAINWAL MORE, MANESAR, GURGRAM, HARYANA

Statement of Profit and Loss for the year ended March 31, 2022

(Amounts in Rs)

	Particulars	Note	31-03-2022	31-03-2021
I	Revenue from operations	11	25,67,74,368	25,87,69,268
II	Other Income	12	1,48,54,968	2,89,24,669
III	**Total Income (I+II)**		**27,16,29,336**	**28,76,93,937**
IV	**Expenses:**			
a	Employee benefits expense	13	10,75,16,921	9,35,43,820
b	Depreciation and amortization expense	14	8,61,52,411	9,15,93,133
c	Other expenses	15	18,61,22,345	17,80,60,339
	Total Expenses		37,97,91,677	36,31,97,292
V	**Profit/(loss) before exceptional and extraordinary items and tax (III-IV)**		-10,81,62,341	-7,55,03,355
VI	Exceptional items (specify nature & provide note/delete if none)			
VII	**Profit/(loss) before extraordinary items and tax (V-VI)**		-10,81,62,341	-7,55,03,355
VIII	Extraordinary Items (specify nature & provide note/delete if none)		-	-
IX	**Profit before tax (VII-VIII)**		-10,81,62,341	-7,55,03,355
X	Tax expense:			
a	Current tax			
b	Excess/Short provision of tax relating to earlier years			
c	Deferred tax charge/ (benefit)			
XI	**Profit/(Loss) for the period from continuing operations (VII-VIII)**		(10,81,62,341)	(7,55,03,355)
XII	Profit/(loss) from discontinuing operations		-	-
XIII	Tax expense of discontinuing operations		-	-
XIV	**Profit/(loss) from discontinuing operations (after tax) (XII-XIII)**			
XV	**Profit/(Loss) for the year (XI+XIV)**		(10,81,62,341)	(7,55,03,355)
	The accompanying notes are an integral part of the financial statements			

As per our separate report of even date attached

For Kumar Khare & Co.
Chartered Accountants
FRN-006740C

KUMAR KHARE & CO. FRN-006740C NEW DELHI CHARTERED ACCOUNTANTS

Sunil Kumar
Partner
Membership No. 546026
Date: 13-09-2022
Place: New Delhi

SHIWANI TANWAR
FINANCE & ACCOUNTS OFFICEER (I/C)
NBRC

13/9/22

वित्त एवं लेखा अधिकारी
O/ Finance & Account Officer
राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
National Brain Research Centre
मानेसर / Manesar-122050
हरियाणा / Haryana

PROF. PRAMOD KUMAR GARG
DIRECTOR
NBRC

Prof. Pramod Kumar Garg
प्रो. प्रमोद कुमार गर्ग
निदेशक (अतिरिक्त प्रभार) / Director (Addl. Charge)
राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
National Brain Research Centre
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हरियाणा / Haryana

NATIONAL BRAIN RESEARCH CENTRE, MANESAR

NH-8, NAINWAL MORE, MANESAR, GURGAON, HARYANA

RECEIPTS AND PAYMENTS FOR THE YEAR ENDED March 31, 2022

	RECEIPTS	CURRENT YEAR	PREVIOUS YEAR		PAYMENTS	CURRENT YEAR	PREVIOUS YEAR
		Amount in (Rs.)				Amount in (Rs.)	
I.	**Opening Balances**			I.	**Expenses**		
a)	Cash in Hand	39,098.00	262,526.00	i)	Establishment Expenses	14,110,120.00	8,472,715.00
b)	Bank Balances			ii)	Administrative Expenses	2,448,451.17	2,949,240.14
i)	In Deposit Accounts		-	II.	**Payment Made Against Funds For Various Projects**		
ii)	Saving Accounts	497,109,024.36	198,080,018.04	i)	Recurring /Capital expenditure	12,587,481.46	23,592,665.03
iii)	CPF Investments	8,778,018.19	231,321.99	ii)	Capital Grant Refunded to DBT		-
II.	**Grants Received**			iii)	Refund to RCGB		-
a)	From Government of India			iv)	Refund of Interest	2,191,677.00	50,745,938.00
	Plan			v)	Bank Deposits		210,000,000.00
i)	Recurring Income	251,000,000.00	254,500,000.00	III.	**Maintenance Cost**		
ii)	Non-Recurring Income	41,500,000.00	30,000,000.00	i)	Lab Maintenance Expenses	3,646,909.22	1,686,923.24
	Plan (Recurring)			ii)	Office Maintenance	38,901,031.00	34,513,748.00
b)	Fellowship Grant	853,865.00	466,170.00	iii)	Vehicle Running & Maintenance	802,547.00	560,581.00
c)	Delcon Projects (Including Interest)	420,540,321.00	241,779,366.00	IV.	**Investment and Deposit Made**		
III.	**Receipt made against funds for various projects**			i)	Out of Earkmarked/Endowment funds	1,559,688.00	3,244,000.00
i)	Recurring Receipt/ Capital Grant	29,317,861.88	63,882,011.50	V.	**Expenditure of Fixed Assets & Capital Work-in-progress**		
	(Including Interest)			i)	Purchase of Fixed Assets	22,819,506.14	4,693,298.11
ii)	Bank Deposits	151,637,535.00	690,000,777.00	VI.	**Training Expenses**	3,305,874.78	1,620,957.00
IV.	**Interest Received**			VII.	**Other Payments(Specify)**		
i)	On Bank Deposits			i)	Advances to Supplier	167,137,976.61	12,453,768.53
ii)	Savings Account	5,033,880.00	9,115,353.99	ii)	Advances to Staff	2,148,164.00	1,386,771.00
iii)	On CPF Fund		11,518,624.00	iii)	Leave Encashment/ LTC/ Bonus	453,360.00	733,167.00
iv)	Other Interest			iv)	Security Deposit Paid	1,202,328.00	946,232.00
V.	**Any Other Receipt**			v)	EMD Refunded	1,340,700.00	812,500.00
	Indirect Income			vi)	TDS Paid	43,952,571.00	42,296,949.00
i)	Advance to Supplier Received	5,369.00	113,076.00	vii)	Imprest	228,000.00	163,578.00
ii)	Advance to Staff Received	656,953.00	846,472.89	viii)	Payment of Current Liabilities	842,470,441.18	619,156,292.48
iii)	Sale of Tender Documents	12,500.00	499,620.00	ix)	Prepaid Insurance	-	-
iv)	Fees received	255,680.00					
v)	Misc. Receipts.	2,385.00	393,693.67	VIII.	**Closing balances**		
vi)	Earnest Money Deposit Received	3,333,766.00	1,031,300.00	a)	Cash in Hand	93,695.00	39,098.00
vii)	Sale of Scrap	3,900.00	-	b)	Bank Balance		
viii)	Guest House Charges	119,050.00	65,369.00	i)	In Deposit Accounts		-
ix)	Hostel Deposit	343,000.00	300,000.00	ii)	Saving Accounts	242,577,995.48	497,109,024.36
x)	CPF Fund Received	-	21,582,528.00	iii)	CPF Investments	8,369,470.39	8,778,018.19
xi)	Library Deposit	102,000.00	108,000.00				
xii)	Current Liabilities Rec.	605,072.00	995,298.00				
xiii)	Other Receipts	1,098,709.00	183,938.00				
	TOTAL	1,412,347,987.43	1,525,955,464.08		TOTAL	1,412,347,987.43	1,525,955,464.08

SHIWANI TANWAR
FINANCE & ACCOUNTS OFFICER (I/C)
NBRC

13/9/22

वित्त एवं लेखा अधिकारी
Finance & Account Officer
राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
National Brain Research Centre
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PROF. PRAMOD KUMAR GARG
DIRECTOR
NBRC

Prof. Pramod Kumar Garg
प्रो. प्रमोद कुमार गर्ग
निदेशक (अतिरिक्त प्रभार) / Director (Addl. Charge)
राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
National Brain Research Centre
मानेसर–122052 / Manesar-122052
हरियाणा / Haryana

As per our separate report of even date attached

For Kumar Khare & Co.
Chartered Accountants
FRN-006740C

Sunil Kumar
Partner
Membership No. 546026
Date:13/09/2022
Place: New Delhi

KUMAR KHARE & CO. FRN-006740C NEW DELHI CHARTERED ACCOUNTANTS

NATIONAL BRAIN RESEARCH CENTRE

NH-8, NAINWAL MORE, MANESAR, GURGRAM, HARYANA

Notes forming part of the Financial Statements for the year ended, 31 March 2022

SCHEDULE 1-CORPUS/CAPITAL FUND:					
		31st March 2022		31st March 2021	
1	Grant-in-Aid - Balance as at the beginning of the year		1,403,502,000		1,373,502,000
	Add: Contribution towards Corpus/Capital Fund	41,500,000		30,000,000	
	Add/(Deduct): Balance of net income/(expenditure) transferred from		41,500,000		30,000,000
	the Income and Expenditure Account				
	Balance as at the year end		**1,445,002,000**		**1,403,502,000**

SHIWANI TANWAR
FINANCE & ACCOUNTS OFFICEER (I/C)
NBRC

वित्त एवं लेखा अधिकारी
Finance & Account Officer
राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
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मानेसर / Manesar-122050
हरियाणा / Haryana

PROF. PRAMOD KUMAR GARG
DIRECTOR
NBRC

Prof. Pramod Kumar Garg
निदेशक (अतिरिक्त प्रभार) / Director (Addl. Charge)
राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
National Brain Research Centre
मानेसर–122052 / Manesar-122052
हरियाणा / Haryana

As per our separate report of even date attached

For Kumar Khare & Co.
Chartered Accountants
FRN-006740C

KUMAR KHARE & CO. ★ FRN-006740C NEW DELHI ★ CHARTERED ACCOUNTANTS

Sunil Kumar
Partner
Membership No. 546026
Date:13/09/2022
Place: New Delhi

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGRAM
SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2022

Amount in (Rs.)

FUND-WISE BREAK UP SCHEDULE 3 - EARMARKED/ENDOWMENT FUNDS				TOTALS			
Endowment Fund for Building		Donation		Current Year		Previous Year	
	-		2,631,788		638,615,715		836,824,080
-		-		459,906,918		319,578,988	
-		-		-		-	
-	-	-	-	3,892,647	463,799,565	7,267,312	326,846,300
	-		**2,631,788**		**1,102,415,281**		**1,163,670,380**
-		-		14,034,404		12,110,217	
-		-		-		-	
	-		-		**14,034,404**		**12,110,217**
-		-		18,957,007		17,904,677	
-		-		-		-	
-		-		620,643,778		433,943,141	
-		-		38,806,623		42,536,309	
	-		-		**678,407,408**		**494,384,127**
	-		-		**692,441,813**		**506,494,344**
				1,146,854		18,560,321	
					1,146,854		**18,560,321**
	-		**2,631,788**		**408,826,614**		**638,615,715**

SHIWANI TANWAR
FINANCE & ACCOUNTS OFFICEER (I/C)
NBRC

वित्त एवं लेखा अधिकारी
Finance & Account Officer
राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
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Sunil Kumar
Partner
Membership No. 546026
Date:12/09/2022
Place: New Delhi

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGRAM
SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2022

Amount in (Rs.)

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-		-		459,906,918		319,578,988	
-		-		-		-	
-	-	-	-	3,892,647	463,799,565	7,267,312	326,846,300
	-		**2,631,788**		**1,102,415,281**		**1,163,670,380**
-		-		14,034,404		12,110,217	
-		-		-		-	
	-		-		**14,034,404**		**12,110,217**
-		-		18,957,007		17,904,677	
-		-		-		-	
-		-		620,643,778		433,943,141	
-		-		38,806,623		42,536,309	
	-		-		**678,407,408**		**494,384,127**
	-		-		**692,441,813**		**506,494,344**
				1,146,854		18,560,321	
					1,146,854		**18,560,321**
	-		**2,631,788**		**408,826,614**		**638,615,715**

SHIWANI TANWAR
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FRN-006740C

KUMAR KHARE & CO. ★ FRN-006740C ★ NEW DELHI CHARTERED ACCOUNTANTS

Sunil Kumar
Partner
Membership No. 546026
Date:12/09/2022
Place: New Delhi

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURUGRAM
Notes forming part of the Financial Statements for the year ended 31st March, 2022

(Amounts in Rs)

2 Reserves and surplus	31/03/2022	31/03/2021
a General Reserve	-	-
As per last Account	-238,089,863	-111,840,570
Addition during the Year	-	
Surplus during the yar (as per I&E A/c)	-108,162,341	-75,503,355
Less : Deductions during the year (deficit)	2,191,677	50,745,938
Total Reserves and surplus	**-348,443,882**	**-238,089,863**

4 Trade payables	31/03/2022	31/03/2021
a Total outstanding dues of micro, small and medium enterprises	-	-
b Total outstanding dues of creditors other than micro, small and medium enterprises	4,258,739	1,152,789
Total Trade payables	**4,258,739**	**1,152,789**

Disclosure relating to suppliers registered under MSMED Act based on the information available with the entity Company:

Particulars	31/03/2022	31/03/2021
a Unpaid amount to any supplier at the end of each accounting year:		
i Principal	-	-
ii Interest	-	-
Total	**-**	**-**
b The amount of interest paid by the buyer in terms of section 16 of the MSMED Act, along with the amount of the payment made to the supplier beyond the appointed day during each accounting year.	-	-
c The amount of interest due and payable for the period of delay in making payment (which have been paid but beyond the appointed day during the year) but without adding the interest specified under the MSMED Act.	-	-
d The amount of interest accrued and remaining unpaid at the end of each accounting year.	-	-
e The amount of further interest remaining due and payable even in the succeeding years, until such date when the interest dues above are actually paid to the small enterprise, for the purpose of disallowance of a deductible expenditure under section 23 of the MSMED Act.	-	-

5 Other current liabilities	31/03/2022	31/03/2021
a Advance Received	4,178,780	4,194,866
b TDS payable	15,513,402	394,317
c Other payables (specify nature)	33,699,835	28,440,060
Total Other current liabilities	**53,392,018**	**33,029,243**

6 Provisions	Long Term		Short Term	
	31/03/2022	31/03/2021	31/03/2022	31/03/2021
Provision for employee benefits				
a Provision for gratuity	-	-	6,162,367	6,137,980
b Provision for leave Encashment	-	-	1,705,929	1,919,571
Total Provisions	-	-	**7,868,296**	**8,057,551**

Continue Page: 1-2

KUMAR KHARE & CO. CHARTERED ACCOUNTANTS FRN-006740C NEW DELHI

Continue from pre- Page: 2-2

13/9/22

SHIWANI TANWAR
FINANCE & ACCOUNTS OFFICER (I/C)
NBRC

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Chartered Accountants
FRN-006740C

KUMAR KHARE & CO. ★ FRN-006740C NEW DELHI ★ CHARTERED ACCOUNTANTS

PROF. PRAMOD KUMAR GARG
DIRECTOR
NBRC

Prof. Pramod Kumar Garg
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हरियाणा / Haryana

Sunil Kumar
Partner
Membership No. 546026
Date:13/09/2022
Place: New Delhi

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESR, GURUGRAM
Notes forming part of the Financial Statements for the year ended 31st March, 2022

7 Property, Plant and Equipment and Intangible Assets (owned assets)

a Property, Plant and Equipments

(Amounts in Rs)

Particulars /Assets	Freehold land	Buildings	Plant and Equipment	Office equipment	Furniture & Fixtures	Library Books	Project Equipments	Vehicles	Computer/Peripherals	Total
Gross carrying amount										
At 1 April 2021	-	753,965,742	370,671,670	48,502,071	41,123,751	561,784	819,569,976	4,145,034	12,980,107	2,051,520,135
Additions		-	32,792,632	529,928	805,006	20,040	14,034,404	-	6,259,617	54,441,628
Deductions/Adjustments		-	-	-	-	-	-	-	-	-
At 31 March 2022	**-**	**753,965,742**	**403,464,303**	**49,031,999**	**41,928,757**	**581,824**	**833,604,381**	**4,145,034**	**19,239,724**	**2,105,961,763**
At 1 April 2020	-	753,965,742	358,723,303	47,868,754	40,988,269	554,544	807,459,759	4,145,034	12,377,215	2,026,082,619
Additions	-	-	11,948,368	633,317	135,482	7,240	12,110,217	-	602,892	25,437,516
Deductions/Adjustments	-	-	-	-	-	-	-	-	-	-
At 31 March 2021	**-**	**753,965,742**	**370,671,670**	**48,502,071**	**41,123,751**	**561,784**	**819,569,976**	**4,145,034**	**12,980,107**	**2,051,520,135**
Depreciation/Adjustments										
At 1 April 2021		172,380,994	249,790,682	31,828,751	27,106,378	359,595	573,989,509	2,580,243	10,681,393	1,068,717,545
Additions		58,158,475	20,779,548	2,569,673	1,461,055	86,753	38,806,623	234,719	2,696,309	124,793,155
Deductions/Adjustments	-	-	-	-	-	-		-	-	-
At 31 March 2022	**-**	**230,539,469**	**270,570,231**	**34,398,423**	**28,567,433**	**446,348**	**612,796,132**	**2,814,962**	**13,377,702**	**1,193,510,700**
At 1 April 2020	-	107,760,467	229,379,697	28,940,437	25,551,580	225,802	531,453,200	2,304,104	9,193,991	934,809,276
Additions	-	64,620,528	20,410,986	2,888,314	1,554,799	133,793	42,536,309	276,140	1,487,402	133,908,269
Deductions/Adjustments	-	-	-	-	-	-	-	-	-	-
At 31 March 2021	**-**	**172,380,994**	**249,790,682**	**31,828,751**	**27,106,378**	**359,595**	**573,989,509**	**2,580,243**	**10,681,393**	**1,068,717,545**
Net carrying value										
At 31 March 2022	-	523,426,273	132,894,072	14,633,575	13,361,324	135,476	220,808,249	1,330,072	5,862,022	912,451,063
At 31 March 2021	**-**	**581,584,748**	**120,880,988**	**16,673,320**	**14,017,373**	**202,189**	**245,580,467**	**1,564,791**	**2,298,714**	**982,802,590**

b Intangible assets

Particulars /Assets	Patents & Copyright	Liscense and franchise	Others (specify nature)	Total
Gross carrying amount				
At 1 April 2021	5,355,643	-	-	5,355,643
Additions				-
Deductions/Adjustments				-
At 31 March 2022	**5,355,643**	-	-	**5,355,643**
At 1 April 2020	5,355,643			5,355,643
Additions				-
Deductions/Adjustments				-
At 31 March 2021	5,355,643	-	-	5,355,643
Amortization/Adjustment				
At 1 April 2021	4,692,125	-	-	4,692,125
Additions	165,880			165,880
Deductions/Adjustments				-

KUMAR KHARE & CO. ★ FRN-006740C NEW DELHI ★ CHARTERED ACCOUNTANTS

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESR, GURUGRAM
Notes forming part of the Financial Statements for the year ended 31st March, 2022

At 31 March 2022	**4,858,004**	-	-	**4,858,004**
At 1 April 2020	4,470,952			4,470,952
Additions	221,173			221,173
Deductions/Adjustments	-			-
At 31 March 2021	**4,692,125**	-	-	**4,692,125**
Net carrying value				
At 31 March 2022	497,639	-	-	497,639
At 31 March 2021	**663,518**	-	-	663,518

SHIWANI TANWAR
FINANCE & ACCOUNTS OFFICER (I/C)
NBRC

वित्त एवं लेखा अधिकारी
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राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
National Brain Research Centre
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As per our separate report of even date attached

For Kumar Khare & Co.
Chartered Accountants
FRN-006740C

KUMAR KHARE & CO. CHARTERED ACCOUNTANTS FRN-006740C NEW DELHI

Sunil Kumar
Partner
Membership No. 546026
Date:13/09/2022
Place: New Delhi

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURUGRAM

Notes forming part of the Financial Statements for the year ended 31st March, 2022

(Amounts in Rs)

8 Investments - Non Current & Current

A Non-Current Investments

(valued at historical cost unless stated otherwise)

	As at 31 March 2022			As at 31 March 2021		
	Face Value	Numbers/ Units/ Shares	Book Value	Face Value	Numbers/ Units/ Shares	Book Value
Other Investments						
Other non-current investments (CPF Fund)			13,398,826			13,563,572
Total Non-current investment			**13,398,826**			**13,563,572**

9 Cash and Bank Balances	**31/03/2022**	**31/03/2021**
A Cash and cash equivalents		
a On current accounts	-	-
b On Deposit Accounts (includes margin money)	185,166,840	328,209,084
c On Savings Accounts	242,577,995	497,109,024
f Cash on hand	93,695	39,098
Total cash and cash equivalents	**427,838,530**	**825,357,206**

10 Loans and advances	Long Term		Short Term	
	#########	#########	**31/03/2022**	**31/03/2021**
a Other loans and advances (specify nature)				
Prepaid expenses	-	-	2,209,686	1,101,173
Advance to parties	-	-	192,212,200	992,025
Other Advance	-	-	5,762,502	5,762,502
Balance with government authorities	-	-	11,773,959	10,761,831
Total (a+b+c)= A	-	-	**211,958,348**	**18,617,531**

B Unsecured	Long Term		Short Term	
	#########	#########	**31/03/2022**	**31/03/2021**
a Other loans and advances (specify nature)	-	-	-	-
Staff	-	-	4,725,405	5,214,242
Others (Imprest)	-	-	33,973	48,775
Total	-	-	4,759,378	5,263,017
Total Loans and advances (A+B)	-	-	**216,717,726**	**23,880,548**

SHIWANI TANWAR
FINANCE & ACCOUNTS OFFICER/वित्त एवं लेखा अधिकारी
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FRN-006740C

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Sunil Kumar
Partner
Membership No. 546026
Date:13/09/2022
Place: New Delhi

NATIONAL BRAIN RESEARCH CENTRE					
NH-8, NAINWAL MORE, MANESAR, GURUGRAM					
Notes forming part of the Financial Statements for the year ended 31st March, 2022					*(Amounts in Rs)*
11	**Revenue from operations**			**31/03/2022**	**31/03/2021**
	a	Grants or donations received		251,000,000	254,500,000
	b	Fees/Subscriptions		461,205	1,064,771
		Income from Investments (Income on Invest. from earmarked)		1,269,504	1,267,054
	c	Other operating revenue		4,043,659	1,937,443
		Revenue from operations (Gross)		256,774,368	258,769,268
		Less: GST/Excise duty		-	-
		Revenue from operations (Net)		**256,774,368**	**258,769,268**
12	**Other income**			**31/03/2022**	**31/03/2021**
	a	Interest income		14,854,968	28,924,669
	Total other income			**14,854,968**	**28,924,669**
13	**Employee benefits expense**			**31/03/2022**	**31/03/2021**
	(Including contract labour)				
	a	Salaries, wages, bonus and other allowances		66,915,925	62,116,648
	b	Contribution to pension funds		211,489	602,870
	c	Gratuity expenses		-	-
	d	Staff welfare expenses		104,998	41,963
	e	Children education reimbursement		1,377,000	1,566,000
	f	Leave encashment		270,156	294,790
	g	LTC expenses		754,433	788,571
	h	NPS(employer subscription)		10,888,180	4,661,052
	i	overtime allowance		19,175	3,077
	j	Skilled manpower		26,637,058	21,747,667
	k	Medical insurance (Staff)		338,507	1,721,182
	Total Employee benefits expense			107,516,921	93,543,820
14	**Depreciation and amortization expense**			**31/03/2022**	**31/03/2021**
	a	on tangible assets (Refer note 11)		85,986,532	91,371,960
	b	on intangible assets (Refer note 11)		165,880	221,173
	Total Depreciation and amortization expense			**86,152,411**	91,593,133

KUMAR KHARE & CO. CHARTERED ACCOUNTANTS FRN 006740C NEW DELHI

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Notes forming part of the Financial Statements for the year ended 31st March, 2022				*(Amounts in Rs)*
15	**Other Expenses**		**31/03/2022**	**31/03/2021**
	Electricity and Power		38,892,783	36,407,260
	Insurance		38,207	494,310
	Repairs and maintenance		47,420,657	42,632,885
	Rent (Lease Rent), Rates and Taxes		1,405,777	1,405,777
	Vechicles Running and Maintenance		185,211	52,719
	Postage, Telephone and Communication Charges		536,598	538,013
	Printing and Stationary		1,287,592	734,727
	Travelling and Conveyance Expenses		1,104,992	2,010,200
	Expenses on Seminar/Workshops		484,864	150,114
	Subscription Expenses		3,111,444	1,805,152
	Expenses on Fees		90,211	-
	Auditor Remuneraion			24,000
	Tax Audit fee	70,000		
	Other Compliance & Certification Fee	65,000	135,000	
	Hospitality Expenses		110,357	195,930
	Professional Charges		692,011	667,067
	Medical Expenses (Students)		580,814	-
	Trainining (Salaries)		34,728,031	-
	Bandwidth charges-Core		247,800	-
	Advertisement and Publicity		1,442,738	3,980,177
	Prior Period Expenses		-	1,111,292
	Others - Bank charges		6,195	9,367
	Misc. expenses		288,020	307,772
	Books and Periodicals		83,365	90,912
	Honorarium (others)		431,250	386,500
	Petrol, Diesel & CNG etc.		888,447	623,480
	Manpower		17,781,520	20,275,107
	Horticulture		2,029,273	2,476,425
	Training and networking expense		734,822	38,870,367
	Laboratory & Animal Consumables		28,958,878	20,833,662
	Accreditation Fee		730,981	250,774
	Medical reimbursement		1,219,668	1,343,800
	Office expenses		474,839	382,551
	Total other expenses		**186,122,345**	**178,060,339**

SHIWANI TANWAR
FINANCE & ACCOUNTS OFFICEER (I/C)
NBRC

13/9/22

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National Brain Research Centre
मानेसर / Manesar-122050
हरियाणा / Haryana

PROF. PRAMOD KUMAR GARG
DIRECTOR
NBRC

Prof. Pramod Kumar Garg
प्रो. प्रमोद कुमार गर्ग
निदेशक (अतिरिक्त प्रभार) / Director (Addl. Charge)
राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
National Brain Research Centre
मानेसर–122052 / Manesar-122052
हरियाणा / Haryana

As per our separate report of even date attached

For Kumar Khare & Co.
Chartered Accountants
FRN-006740C

KUMAR KHARE & CO. ★ CHARTERED ACCOUNTANTS ★ FRN-006740C NEW DELHI

Sunil Kumar
Partner
Membership No. 546026
Date:13/09/2022
Place: New Delhi

NATIONAL BRAIN RESEARCH CENTRE, MANESAR, GURGAON

- **SIGNIFICANT ACCOUNTING POLICIES & NOTES ON ACCOUNTS FORMING PART OF THE BALANCE SHEET AS AT 31ST MARCH, 2022 AND INCOME & EXPENDITURE ACCOUNT FOR THE YEAR ENDED 31STMARCH,2022.**

• SIGNIFICANT ACCOUNTING POLICIES & NOTES ON ACCOUNTS

1. Accounting Convention:

1.1 The financial statements of National Brain Research Centre (***NBRC***) are prepared on the basis of historical cost convention and on the accrual basis of accounting, unless otherwise stated.

1.2 The NBRC is prepared based on the 'Uniform Format of Accounting' prescribed for the Central Autonomous Bodies by the Ministry of Finance, Govt. of India for preparing the Income & Expenditure Account, Receipts & Payments Account, Balance Sheet & other Schedules thereto

2. Inventory Valuation:

2.1 All purchases of chemicals, glassware, consumables and printing & stationery have been booked/charged to consumption/expenditure at the time of purchases. Inventories had been so booked, based on their purchase cost & other costs incurred in bringing the inventories to their present location & condition.

3. Property Plant & Equipment's & Intangible Assets:

3.1 Property Plant & Equipment's & Intangible Assets are stated at written down value. i.e., at their cost of acquisition inclusive of inward freight, duties and taxes & incidental & direct expenses related to the acquisition.

3.2 In respect of projects involving construction, related pre-operational expenses (including interest on loans for specific project prior to its completion), form part of the value of the assets capitalized.

3.3 Property Plant & Equipment's & Intangible Assets received by way of non-monetary grants, (other than towards the corpus Fund), are capitalized at values stated, by corresponding credit to Capital Reserve

3.4 Property Plant & Equipment's & Intangible Assets have been created mainly out of grants received from the Department of Biotechnology, Ministry of Science and Technology, Government of India.

4. Depreciation:

4.1 Depreciation provided for current year on the fixed assets of Project for Rs. 3,88,06,623.00 (previous year Rs. 4,25,36,309.00) and which has been directly debited to the fixed assets funds account. These assets were created through the non-Recurring and project-based grant from the funding agencies. Depreciation for other than project assets amounting to Rs. 8,61,51,849.46 for current financial year (Rs. 9,15,93,133.03 for previous year) had been debited to Income & Expenditure Account. Depreciation is being charged as per Income Tax Act 1961 on W.D.V basis.

5. Investments:

5.1 Investments classified as "long term investments" are carried at cost, provision for decline, other than temporary, is made in carrying cost of such investments.

5.2 Investments classified as "Current" are carried at lower of cost and fair value. Provision for shortfall on the value of such investments is made for each investment considered individually and not on a global basis.

5.3 Cost included acquisition expenses like brokerage, transfer stamps.

5.4 Investments in term deposits with banks are valued on cost.

5.5 Interest received on term deposits are accounted for on accrual basis.

6. Government Grants / Subsidies:

6.1 Government grants of the nature of contribution towards capital cost of setting up projects are treated as Capital Reserve/Fund.

6.2 Government grants are accounted for in accordance with the sanctioned terms & on realization basis.

6.3 Interest on Government Grant has been considered under the respective projects in view of the project sanctioned terms, as in the past.

6.4 Grants in respect of specific fixed assets acquired are shown as the deduction from the cost of the related assets

KUMAR KHARE & CO. ★ FRN-006740C NEW DELHI ★ CHARTERED ACCOUNTANTS

7. Foreign Currency Transactions/ Grants:

7.1 Transactions denominated in foreign currency are accounted at the exchange rate prevailing at the date of the transaction.

7.2 Current assets, foreign currency current liabilities are converted at the exchange rate prevailing as at the year end.

8. Lease:

The NBRC is located on the leasehold land at Manesar taken from Indian Vaccine Corporation Ltd. for Rs. 14, 05,777/- per annum lease amount. The annual lease rental being charged against revenue for respective year.

9. Retirement Benefits:

9.1 The NBRC is not registered with the Provident Fund authorities and it maintains a separate Contributory Provident Fund (CPF), which is yet to be recognized and the CPF fund required the separate accounting. At present all the employees have been joined under New Pension Scheme (NPS).

9.2 The NBRC has not made any provision for gratuity and leave encashment during financial year 2021-2022 as against the requirement of AS-15 issued by ICAI. However, the amount of gratuity and leave encashment to the extent of Rs. 61,62,367.00 and Rs. 17,05,929.00 respectively already exists on 31st March, 2022, (Rs. 61,37,980.00 and Rs. 19,19,570.80 respectively as on 31st March, 2021) against provision made earlier.

10. Taxation:

In view of the tax exemption status of the National Brain Research Centre, has been registered society registration Act-1860 at Autonomous bodies.

11. Current Assets, Loans & Advances:

In the opinion of the Management, the current assets, loans and advances have a value on realization in the ordinary course of business, equal at least to the aggregate amount shown in the Balance Sheet. However, advances appearing under the head Current assets, Loans & Advances under Schedule-11 are subject to confirmation from respective parties. Further an amount is showing under head **Advance to Parties** amounting to **Rs. 19,22,12,200.48** against which no bills are received till date.

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12. Bank Balance:

All Banks accounts have been reconciled till 31st March, 2022.

14. Fraud/Manipulation of funds encountered by NBRC:

No Fraud was detected during the year.

15. Outstanding Balances of Closed Projects:

As on 31st March, 2022, 3 Projects have already been closed which amounting of Rs. 6.92 Lakh transferred to DBT & reaming other project of Rs.19.68 (Debit balance) is still pending.

16. Contingent Liabilities

1.1 Claims against the Entity not acknowledged as debt. Rs. NIL (Previous year Rs. NIL).

1.2 In respect of:

- Bank guarantees given by/on behalf of the entity Rs. NIL (Previous year Rs. NIL).
- Letters of Credit opened by Bank on behalf of the Entity Rs. NIL (Previous year Rs. NIL).
- Bills discounted with banks Rs. NIL (Previous year Rs. NIL).

1.3 Disputed demands in respects of Income tax (TDS) Rs. 78,03,805.00 (Previous year Rs. 56,77,370.00) which is under representation before the concerned authorities. Further, TDS deducted and to be received as refund amounts to Rs. 57,78,690.28 out of which Rs. 40,30,217.52 is pending since 2008-09. The appeal has already been made to Income tax Authority (CIT - Chandigarh) in the previous year.

17. Capital Commitments

Estimated value of contract remaining to be executed on capital account and not provided for (net of advances) Rs. –Nil (Previous year Rs. NIL). However, reference is drawn to para 3.5 above.

18. Lease Obligations

Future obligations for rentals under finance lease arrangements for plant and machinery amount to Rs. NIL (Previous year Rs. NIL).

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19. Foreign Currency Transactions

20.1 Value of Imports Calculated on C.I.F Basis:

- Purchase of finished Goods Rs. NIL.
- Raw Materials & Components (Including in transit) Rs. NIL.
- Capital Goods Rs. NIL.
- Purchased Consumables /Non-Consumables for Rs. 2,87,62,009.05/-

20.2 Expenditure in foreign currency:

a) Travelling charges Rs. 1,71,593/-
b) Remittances and Interest payment to Financial Institutions/ Banks in Foreign Currency Rs. NIL.
c) Other expenditure
   -Commission on Sales Rs. NIL.
   -Legal and Professional Expenses Rs. NIL.
   -Miscellaneous Expenses Rs. NIL.

20.3 Earnings:

Value of Exports of FOB basis Rs. NIL.

20. Remuneration to auditors:

- As Auditors Rs. 1,35,000/-
  Tax Audit fee 70000, Other Compliance & Certification Fee 65,000/-)
  (Previous year Rs. 24,000.00).

21. Others

22.1 The Balance in the name of various parties under the head Current Liabilities are subject to confirmation/ reconciliation by respective parties. The total amount payable to Sundry Creditors is Rs. 42,58,739.00 (previous year Rs. 11,52,789.00).

22.2 Schedules 1 to 15 along with Annexures 1 to 20 are annexed to and form an integral part of the Balance Sheet as at 31st March, 2022 and the Income and Expenditure Account for the year ended on that date.

22.3 Corresponding figures for the previous year have been regrouped/ rearranged, wherever necessary.

KUMAR KHARE & CO. CHARTERED ACCOUNTANTS FRN-006740C NEW DELHI

22.4 Accounting polices not referred to otherwise be consistent with Generally Accepted Accounting Principles (GAAP).

22.5 There is outstanding balance of Expenses Payable of Rs. 2,43,54,039.76 out of which most of the expenses is related to next financial year but the same are booked in current financial year. Further no voucher has been received for the verification of the same.

22.6 There is an outstanding Income Tax Demand for A.Y. 2017-18 amounting to Rs. 2,35,76,571.00 and A.Y. 2018-19 amounting to Rs. 1,36,03,15,740.00 respectively against which appeals to CIT- Chandigarh has already been filed in previous year.

22.7 The institute is not complied for filling returns which are required as per FCRA rule and regulations.

SHIWANI TANWAR 13/9/22

(FINANCE & ACCOUNTS OFFICER (I/C)

वित्त एवं लेखा अधिकारी
Finance & Account Officer
राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
National Brain Research Centre
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PRAMOD KUMAR GARG

(DIRECTOR I/C)

Prof. Pramod Kumar Garg
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National Brain Research Centre
मानेसर–122052 / Manesar-122052
हरियाणा / Haryana

Place: New Delhi
Date: 13/09/2022

As per our separate report of even date attached

For Kumar Khare & Co,
(Chartered Accountants)
(FRN-006740C)

KUMAR KHARE & CO. ★ FRN-006740C NEW DELHI ★ CHARTERED ACCOUNTANTS

(CA SUNIL KUMAR)
PARTNER
M.NO. 546026

NATIONAL BRAIN RESEARCH CENTRE, NH-8, NAINWAL MORE, MANESAR GURGAON
ANNEXURE OF PROJECT GRANTS AND EXPENDITURE FOR THE YEAR ENDED 31.03.2022

S. No./ Annx. No.	NAME OF PROJECT	Opening Balance as on 01.04.2021	Grants received during the year 2021-22	Interest earned during the year 2021-22	Capital Exp. during the year 2021-22	Revenue Expenditure during the year 2021-22			Refund of Unspent Balance	Closing Balance as on 31.03.2022
						Manpower	Others	Total Expenditure		
2	Wellcom Trust/DBT Indian Alliance -Dr. Anindya Ghosh Roy	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3	CSIR Japanese Enccephalities - Dr. Anirban Basu	106,867.00	376,040.00	3,163.00	0.00	0.00	308,361.04	308,361.04	0.00	177,708.96
4	Elucidating the role of long non coding RNAs (lnCRNAs) (Dr. Anirban Basu)	50,702.00	0.00	0.00	0.00	0.00	80,938.00	80,938.00	0.00	-30,236.00
5	MicroRNA mediated Reg. of Neural stem(Dr. Anirban Basu)	1,140,610.62	0.00	0.00	0.00	0.00	1,079,352.00	1,079,352.00	47,204.00	14,054.62
6	Tata innovation fellowship award- Dr. Anirban Basu	-5,775.53	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-5,775.53
7	Therapeutic Role DBT(Dr. Anirban Basu)	838,132.96	0.00	13,707.00	0.00		788,108.96	788,108.96	0.00	63,731.00
8	J C BOSE FELLOWSHIP (Dr. Anirban Basu)	0.00	1,900,000.00	0.00	0.00	0.00	200,000.00	200,000.00	0.00	1,700,000.00
9	Mapping of Common Mental Disorders Over Lifespan- Dr Arpan Banerjee	24,750,681.00	0.00	270,107.00	5,219,743.00	3,061,312.00	0.00	3,061,312.00	0.00	16,739,733.00
10	Early Dignostics of structural and functional- Dr Arpan Banerjee	1,442,723.00	0.00	36,151.00	0.00	52,258.00	735,078.00	787,336.00	0.00	691,538.00
11	Dementia Tissue MRI studies(Dr. Dipanjan Roy)	1,726,831.00	0.00	25,635.00	0.00			0.00	17,831.00	1,734,635.00
12	Oscillatory network dynamics DST(Dr. Dipanjan Roy)	81,783.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	81,783.00
13	Ramalinga Swamy - Dr. Dipanjan Roy	245,459.47	0.00	0.00	0.00	84,933.00	142,412.00	227,345.00	0.00	18,114.47
14	Implications in tumor progression- Dr. Ellora Sen	1,045,345.49	0.00	0.00	0.00	0.00	424,529.49	424,529.49	0.00	620,816.00
15	National Bioscience Award- Dr. Ellora Sen	26,403.29	0.00	0.00	0.00			0.00	0.00	26,403.29
16	NON CANONICAL FUNCTION(SERB)- Dr. ELLORA SEN	0.00	1,270,000.00	0.00	0.00	0.00	90,000.00	90,000.00	0.00	1,180,000.00
17	Neurobiology of Dyslexia Brain & Behavior-Dr.Nandini C.Singh	614,968.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	614,968.00
18	Fetal neural stem cells to oligodendrocytes (Dr. Pankaj seth)	0.00	558,000.00	0.00	0.00	0.00	0.00	0.00	0.00	558,000.00
19	Dyslexia Linked RNA(Dr. Pankaj Seth)	797,811.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	797,811.05
20	Effect of Hypoxia on different Neural-Dr Pankaj Seth	736,580.30	0.00	11,632.00	0.00	264,194.00	557,312.17	821,506.17	16,922.00	-90,215.87
21	Hypoxia Ind. Change in Blood Brain- Dr Pankaj Seth	1,034,526.92	0.00	0.00	0.00	347,194.00	629,097.00	976,291.00	15,358.00	42,877.92
22	A CROSS-CULTURE PERSPECTIVE(DBT-NETHERLANDS) -Dr. PRAVAT MANDAL	-449,027.00	1,540,000.00	0.00	0.00	730,539.00	39,287.00	769,826.00	0.00	321,147.00
23	Characterizing biomarkers of Alzheimer's disease Dr. Pravat Mandal	-10,011.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-10,011.50
24	Dementia Imaging studies(Dr. Pravat Kumar Mandal)	823,440.00	0.00	7,643.00	0.00	357,264.00	0.00	357,264.00	16,966.00	456,853.00
25	Novel Imaging Dignostics Indo-Aus grant(Dr. Pravat Kumar Mandal)	1,179,085.00	2,290,000.00	5,870.00	0.00	2,004,111.00	1,014,512.00	3,018,623.00	5,870.00	450,462.00
26	SPECIFIC BRAIN TEMPLATE DST Dr. PRAVAT K MANDAL	-367,110.50	0.00	0.00	0.00	0.00		0.00	0.00	-367,110.50
27	Tata innovation fellowship Award - Dr. Pravat Mandal	-5,212.00	0.00	0.00	0.00	0.00		0.00	0.00	-5,212.00
28	Crspri System - Dr. Sourav Banarjee	-725,783.32	0.00		0.00	22,000.00	0.00	22,000.00	0.00	-747,783.32
29	DBT Mirna Meditate Control - Dr. Sourav Banarjee	189,009.97	0.00	0.00	0.00			0.00	0.00	189,009.97
30	Mechanism of Combinational Control(SERB)- Dr Sourav	470,621.00	1,400,000.00	10,499.00	0.00	322,000.00	1,351,558.00	1,673,558.00	0.00	207,562.00
31	Innovation In Science Pursuit For Inspired Research(INSPIRE)- Dr. Yogita	222,009.18	0.00	0.00	0.00	0.00		0.00	0.00	222,009.18
32	DST-CSRI (Dr. Prem Chand)	28,916.16	0.00	0.00	0.00			0.00	0.00	28,916.16
33	Centre for Excellence for Epilepsy(Phase-II)	72,752,455.00	0.00	1,141,884.00	529,216.00	6,937,649.00	24,964,982.00	31,902,631.00	746,223.00	40,716,269.00
34	Dementia Science Programme	8,956,266.32	0.00	83,191.00	3,189,464.83	726,398.00	154,596.00	880,994.00	112,611.00	4,856,387.49
35	Dementia Basic Biology(Dr. Shiv Kumar Sharma)	4,007,933.50	0.00	50,535.00	1,302,113.67	0.00	62,451.00	62,451.00	42,706.00	2,651,197.83
36	Distributed Information Centre	-247,800.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-247,800.00
37	Epilepsy Project of NBRC	5,382,067.30	0.00	0.00	0.00			0.00	0.00	5,382,067.30
38	PDF-SERB-Dr Sandeep Kumar	140,015.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	140,015.00
39	PDF-SERB(Soibam Shyamchand)	-58,472.00	0.00	0.00	0.00			0.00	0.00	-58,472.00
40	DST- Inspired Fellow (Sriparna Mukherjee)	4,288.00	0.00	0.00	0.00			0.00	0.00	4,288.00
41	TWAS-DBT (Saliu Ibrahim)	11,045.00	0.00	0.00	0.00			0.00	0.00	11,045.00
42	Workshop & Conference(NBRC)	-520,940.31	0.00		0.00		0.00	0.00	0.00	-520,940.31
43	IBRO RETURNED HOME START-UP GRANT-DR BHAVANI SHANKAR SAHU	1,339,062.00	0.00	0.00	0.00		358,246.00	358,246.00	0.00	980,816.00
44	UNDERSTANDING THE REGULATED SECRETORY PATHWAY AND ITS ROLE REGUATING PHYSIO-METABOLIC FUNCTION- Dr BHAVANI SHANKAR SAHU	1,232,511.47	1,869,448.00	7,158.00	0.00	0.00	1,792,502.87	1,792,502.87	25,967.00	1,290,647.60
45	ROLE OF EPHRINS/EPH RECEPTORS IN HIV MEDIATED NEUROPATHOGENSIS- DR PANKAJ SETH	555,614.57	1,302,000.00	1,288.00	0.00	54,767.00	754,396.00	809,163.00	41,150.00	1,008,589.57
46	ARTIFICIAL INTELLIGENCE - DR PRAVAT K. MANDAL	731,918.00	1,444,800.00	10,441.00	895,686.00	845,045.00	314,303.00	1,159,348.00	0.00	132,125.00
47	NEUROANATOMICAL STUDY- DR SOUMYA IYENGAR	834,640.63	0.00	0.00	0.00	0.00	505,904.24	505,904.24	0.00	328,736.39
48	CRISPR-CAS13- DR SOURAV BANERJEE	2,247,724.00	1,346,523.00		0.00	1,651,161.21	205,833.00	323,748.00	529,581.00	58,046.00	1,325,458.79

S. No./ Annx. No.	NAME OF PROJECT	Opening Balance as on 01.04.2021	Grants received during the year 2021-22	Interest earned during the year 2021-22	Capital Exp. during the year 2021-22	Revenue Expenditure during the year 2021-22			Refund of Unspent Balance	Closing Balance as on 31.03.2022
						Manpower	Others	Total Expenditure		
49	EMOTIONAL PRIMING- DR SHUBHAM KUMAR	658,747.00	0.00	0.00	0.00			0.00	0.00	658,747.00
50	WELLCOME TRUST/DBT INDIA ALLIANCE FELLOW- DR SWAGATA DEY	3,141,239.00	79,897.00	49,009.00	27,801.00	0.00	1,531,960.00	1,531,960.00	0.00	1,710,384.00
51	INSPIRED FELLOW- DR SWAGATA DEY	0.00	0.00	0.00	0.00	0.00	32,795.00	32,795.00	0.00	-32,795.00
52	WELLCOME TRUST/DBT INDIA ALLIANCE FELLOW- DR NIVETHIDA T.	611,983.00	5,075,730.00	61,778.00	0.00	372,000.00	2,786,615.67	3,158,615.67	0.00	2,590,875.33
53	THE WELLCOME TRUST/DBT INDIA ALLIANCE EARLY CAREER FELLOW- DR NIVETHIDA T.	0.00	2,661,280.00	0.00	0.00	69,355.00	323,170.96	392,525.96	0.00	2,268,754.04
54	C V Raman Interest Income Fellow(Dr. Rolland Kipre)	26,543.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	26,543.00
55	Neuro -Cognitive Networks Underlying Dr. Arpan Banerjee	18,438.00	0.00	0.00	0.00			0.00	0.00	18,438.00
56	Vision Guide Speech Percention- Dr. Arpan Banerjee	585,272.00	0.00	0.00	0.00			0.00	0.00	585,272.00
57	Autism Behavior and Diffusion Tensor Imaging - Dr. Nandini C. Singh	60,474.00	0.00	0.00	0.00			0.00	0.00	60,474.00
58	DBT ITPAR Grant-Dr.Nandini C. Singh	556,234.89	0.00	0.00	0.00			0.00	0.00	556,234.89
59	CSIR -Project Dr. Nihar Ranjan Jana	73,089.50	0.00	0.00	0.00			0.00	0.00	73,089.50
60	Tata Innovation Fellowship- Dr. Nihar Ranjan Jana	309,758.91	0.00	0.00	0.00			0.00	0.00	309,758.91
61	INDO-US & NIH RO1 - Dr. Pankaj Seth	-631,828.42	0.00	0.00	0.00			0.00	0.00	-631,828.42
62	National Initiative On Glia Cell Research Project - Dr. Pankaj Seth	92,588.71	0.00	0.00	0.00			0.00	0.00	92,588.71
63	PDF-SERB(AMIT NASKAR)	-128,935.00	0.00	0.00	0.00			0.00	0.00	-128,935.00
64	PDF-SERB(Ashok Datusalia)	45,920.00	0.00	0.00	0.00			0.00	0.00	45,920.00
65	DBT Tata Innovation Fellowship -Dr P.K.Roy	667,424.60	0.00	0.00	0.00			0.00	0.00	667,424.60
66	Study of Neuronal Regeneration after Injury using Caenorhabditis Elegans- Dr. Anindya Ghosh Roy	1,146,191.81	0.00	8,410.00	442,743.60	365,800.00	249,491.00	615,291.00	0.00	96,567.21
67	International Centre for Gentic Engineering and Biotechnology(ICGEB)- Dr BHAVANI SHANKAR SAHU	1,179,370.58	0.00	0.00	751,800.00	0.00	332,093.29	332,093.29	0.00	95,477.29
68	Austin Spectrum Disorders, Genes and the Gut Microbiome: Utilizing Song Birds(Zebra Finches) as a Model System- DR SOUMYA IYENGAR	1,250,120.00	0.00	18,163.00	0.00	122,133.00	500,800.28	622,933.28	0.00	645,349.72
69	Exploring Auditory Perception in House Crows using functional Magnetic Resonance Imaging and Neuroanatomical Techniques- DR SOUMYA	591,592.56	800,000.00	8,702.00	24,675.00	265,567.00	246,157.00	511,724.00	0.00	863,895.56
70	DST INSPIRE FACULTY AWARD -Dr. XYZ(2020-21)	1,524,000.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1,524,000.00
71	NPDF-DR. SUMAN SAHA	0.00	960,000.00	0.00	0.00	0.00	0.00	0.00	0.00	960,000.00
72	LABORATORY ANIMALS LTD (DR. INDERJEET)	0.00	437,866.88	0.00	0.00	0.00	0.00	0.00	0.00	437,866.88
73	ICMR-Deepali Singh	-314,900.00	1,070,667.00	0.00	0.00	654,867.00	5,099.00	659,966.00	0.00	95,801.00
74	ICMR-NEW PROJEC(2021-22)	0.00	624,644.00			0.00	0.00	0.00	0.00	624,644.00
	Total (A)	**144,821,239.18**	**26,976,895.88**	**1,824,966.00**	**14,034,404.31**	**17,865,219.00**	**42,679,856.97**	**60,545,075.97**	**1,146,854.00**	**97,896,766.78**
1	DELCON E-LIBRARY CONSORTIUM (B)*	238,851,744.84	418,472,640.00	2,067,681.00	0.00	1,091,788.00	575,226,425.39	576,318,213.39	0.00	83,073,852.45
	Grand Total (A+B)	**383,672,984.02**	**445,449,535.88**	**3,892,647.00**	**14,034,404.31**	**18,957,007.00**	**617,906,282.36**	**636,863,289.36**	**1,146,854.00**	**180,970,619.23**

Ms. Shiwani Tanwar
F& AO(Incharge)
वित्त एवं लेखा अधिकारी
Finance & Account Officer
राष्ट्रीय मस्तिष्क अनुसंधान केंद्र
National Brain Research Centre
मानेसर / Manesar-122050
हरियाणा / Haryana

PROF. Pramod kumar Garg
DIRECTOR (I/C)

Prof. Pramod Kumar Garg
प्रो. प्रमोद कुमार गर्ग
निदेशक (अतिरिक्त प्रभार) / Director (Addl. Charge)
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National Brain Research Centre
मानेसर–122052 / Manesar-122052
हरियाणा / Haryana

For Kumar Khare & Co.
Chartered Accountants
FRN-006740C

As per our separate report
of even date attached

Membership No. 546026
Date:13/09/2022
Place: New Delhi

KUMAR KHARE & CO. FRN-006740C NEW DELHI CHARTERED ACCOUNTANTS

Compiled and Edited by Kedar Singh Bajetha

Front cover:

Green: Syntaxin 6 staining in DIV (Days in vitro) 14 neurons, Purple: Synaptophysin staining in DIV (Days in vitro) 14 neurons

Image credit : Sushma Dagar from BSS lab.

Back cover

Image 1:

1. The main theme of the illustration is temporal "stability" of brain network patterns. The three brains are different configurations of brain networks at different instances of time. There are some brain network patterns that are "similar" for extended duration of time indicating "stability" of those patterns. I have stuck to the red/yellow color scheme because it connects with our color scheme in the Main figures - yellow indicating brain network patterns that are closer (connects with less angular/mahal distance).
2. The arrow indicates the 'arrow of time', hence a tiny clock at the left hand corner.

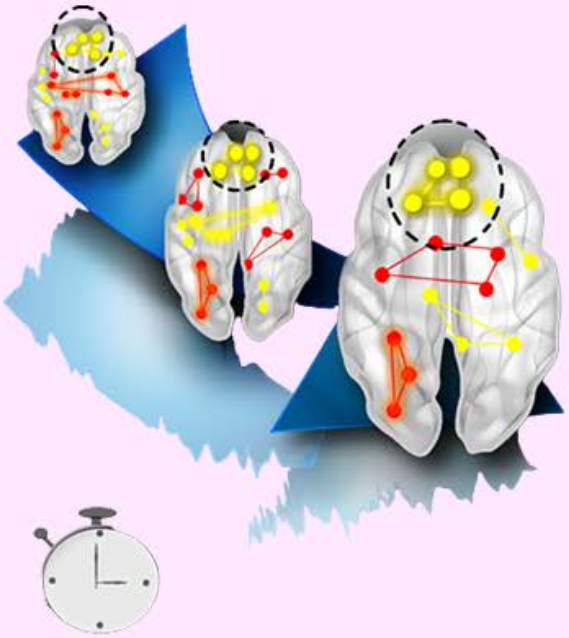
The art is developed by Nisha Chetna Sastry based on the "story" presented in publication 1. Sastry, N.C., Roy, D., & **Banerjee, A**. (2022): Stability of sensorimotor network sculpts the dynamic repertoire of resting state over lifespan. ***Cerebral Cortex,*** 1-22 https://doi.org/10.1093/cercor/bhac133

Back cover

Image 2:

"Drosophila third instar larva expressing GFP in the Vesicular Glutamate transporter (vGlut) expressing neurons. VGlut is highly expressed in the ventral nerve cord as compared to the Central brain region."

Image credit: Bhavya gohil from MDS lab.



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