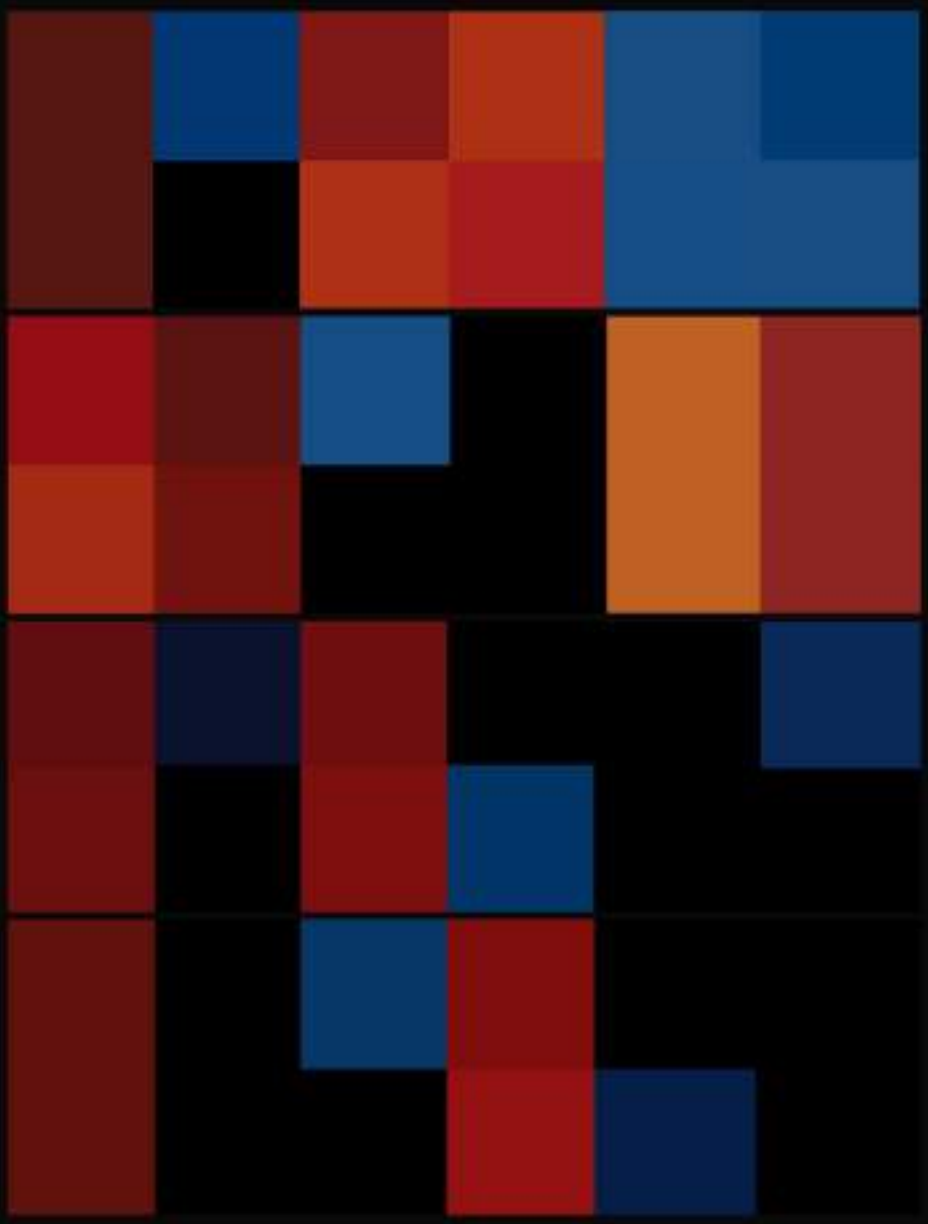
ANNUAL REPORT
2019-2020

National Brain Research Centre
NBRC

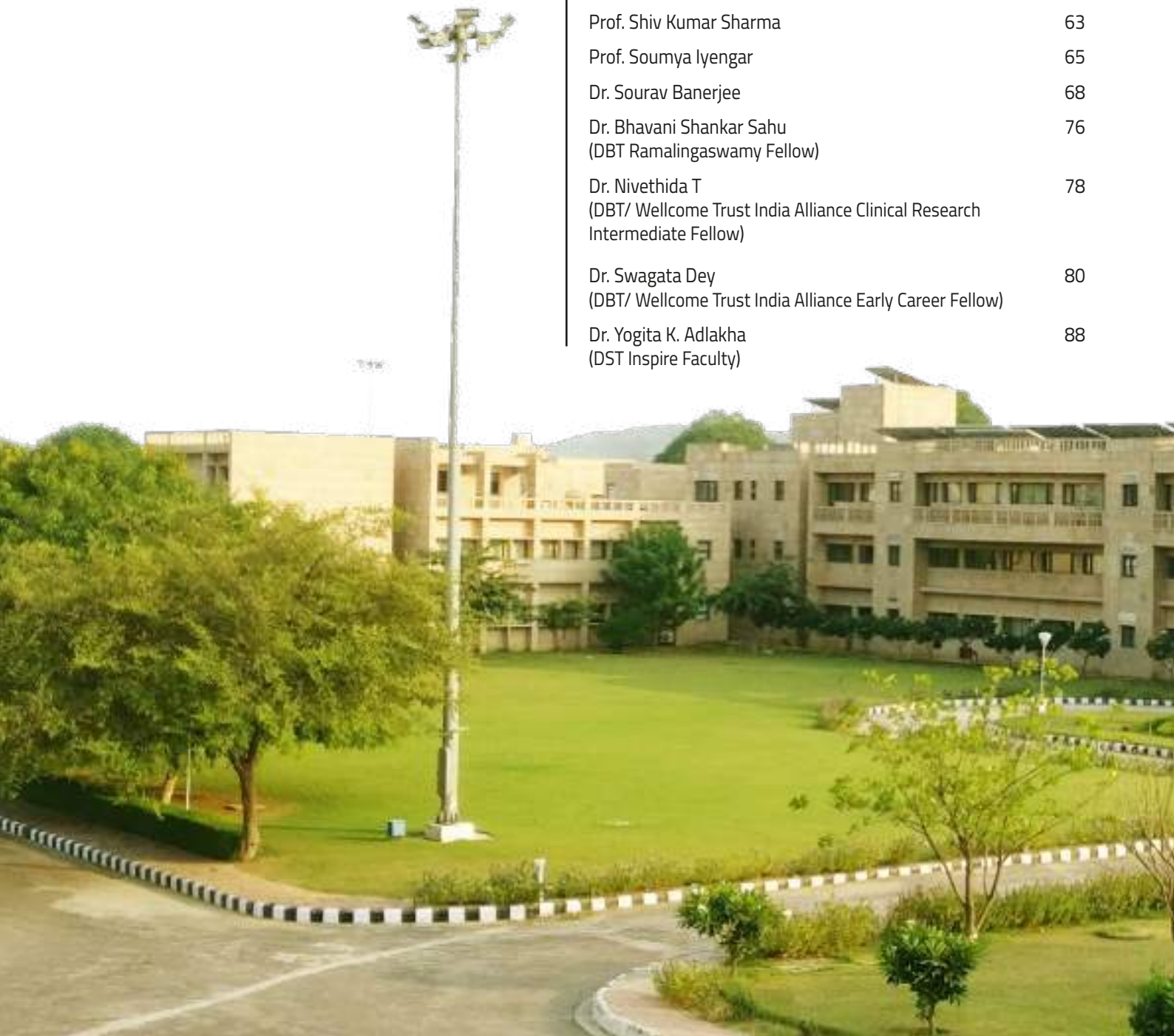


NATIONAL BRAIN RESEARH CENTER
MANESAR, INDIA

Annual Report 2019-20

National Brain Research Centre

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

OBJECTIVES

- To undertake, aid, promote, guide and coordinate research of high caliber in basic and clinical neuroscience related to diseases and disorders of the nervous system.
- To develop NBRC as the national apex centre for neuroscience research and promote neuroscience research at different centres in the country and to provide consulting services to other institutions, agencies and industries.
- To promote, encourage and augment effective linkages, alliances and affiliations between the centre and national and international scientific and research institutions, bodies, agencies/laboratories and other organizations working in the field of brain and neurosciences research.
- To establish one or more satellite centers to serve different regions of the country for efficient achievement of the objectives of the Center.
- To collect, assimilate, publish and disseminate data and information on relevant aspects of neuroscience to the scientific community.
- To establish, operate and maintain state-of-the-art facilities as well as databases for carrying research and development activities and make such facilities and databases available to scientists and researchers from all over the country and abroad.
- To provide for instructions and training in such other branches of learning as the Centre may deem fit.
- To provide facilities for the advancement of research and development to facilitate learning and dissemination of knowledge.
- To undertake extramural studies, extension programmes and field outreach activities to contribute to the development of society.
- To promote, develop, collaborate or otherwise assist in providing services of research, training, consulting or guidance related to neurosciences activities comprising biological, psychological, sociological and clinical aspects; and
- To do all such other acts and things as may be necessary or desirable to further the objectives of the Centre.

From the Director's Desk

National Brain Research Centre (NBRC) was established with a mandate to understand brain function in health and disease, and to generate trained human resources capable of taking up the future challenges of neuroscience research. In the two last decades it has emerged as an advanced Centre for neuroscience research with international recognition. NBRC is a deemed university. We conduct M.Sc. and Ph.D. programs to impart specialized knowledge and skills for conducting interdisciplinary research in neurosciences. NBRC is organized into five divisions - Cellular and Molecular, Systems, Cognitive, Computational, and Translational Research. However, faculty collaborate across divisions, and with scientists in other institutions to address their research questions. It is my pleasure to present the Annual Report for 2019-20, which summarizes our major research achievements and other activities during the year.

A major area of research at NBRC is on viral diseases that affect the brain. Dr Anirban Basu's work showed that JEV infection induces classical activation (M1) of microglia that drive the production of pro-inflammatory cytokines, while suppressing alternative activation (M2) that could serve to dampen the inflammatory response. Furthermore, their work suggests that the JEV-induced expression of miR-301 supresses expression of NKRF thereby resulting in increasing inflammation. This suggests that supressing miR301 can be a strategy to manage viral-induced neuro-inflammation.

Dr Pankaj Seth's laboratory works to understand how HIV-1 and Zika viral proteins modulate properties and function of human brain cells at the cellular and molecular levels to understand disease pathogenesis and neurodegeneration, which is a pre-requisite for designing therapeutic strategies. They have identified how astrocytes cause neuronal damage by altering mitochondrial dynamics in neuroAIDS.

Prof. Pravat Mandal has developed the first Indian brain template named as BRAHMA using T1/T2/Flair 3D MRI images from participants from different parts of the country. Brahma template is now publicly available for any fMRI studies. Another software package, KALPANA has been developed for multimodal brain signals analysis that include brain pH, antioxidant and GABA levels.

Dr Dipanjan Roy's lab works on understanding how information processing networks in the brain are affected during aging. They have uncovered how peak theta frequency remains invariant with age, while the peak gamma frequency decreases with age. This leads to fewer gamma cycles to integrate and couple to the phase of the ongoing theta oscillation/cycle that might be leading to decline in the capacity for visual short-term working memory with age.

Studies on glioma biology in Dr. Ellora Sen's lab highlights the involvement of p53 in TLR4 mediated regulation of tumor suppressor SOCS1 in glioma. This has important ramifications from a clinical perspective as classification of gliomas based on p53 mutational status could determine responsiveness to anti-TLR4 therapy aimed at limiting inflammatory responses. Dr Ranjit Giri's lab has established differentiation of neuroblastoma to investigate the expression profile of CPEB transcript splice variants. They show alteration of CPEB transcript variant in pure neuronal lineage that will pave a way to identify specific splice variants which can be novel molecular markers for neuroblastoma.

In my own lab we have looked at brain-wide changes in the resting-state connectivity of the somatomotor cortex after spinal cord injuries. Data show that accompanying large-scale plasticity that follows spinal cord injuries, there is also a decrease in connectivity of the primary motor cortex with other regions. This suggests that even small spinal

cord injuries have brain-wide repercussions for information processing.

Dr. Anindya's and Dr Swagata Dey's labs use the worm *C. elegans* as a model system to understand cytoskeletal determinants of neuronal polarity during development and understand dendritic remodeling following injuries. They demonstrate that Kinesin-13 family microtubule catastrophe factor is a critical determinant of neuronal microtubule dynamics and polarity. This work provides a mechanistic link between Wnt signaling and Kinesin-13 in establishing microtubule polarity and directional axonal transport in touch neurons of C. elegans. They established the polymodal PVD neuron in C. elegans as a model for dendrite regeneration. They found that dendrite regeneration pathways are independent of the major signaling pathways that control axon regeneration. The microtubule depolymerizing Kinesin-13, KLP-7, actin dynamics regulator TIAM-1, and actin-microtubule regulator PAK-1 regulate the formation of the higher-order dendrites.

In November this year, we held a series of mid-year thematic Scientific Advisory Committee meetings. This was apart from the regular statutory SAC meeting that is held every year. Faculty were divided according their broad area of research and the domain experts were invited to spend extended period of time with faculty and their lab members to review their research programs. This in-depth discussion was found to be particularly useful by the faculty. The Committees reported that overall research work at was of high quality, and that the students were highly motivated.

NBRC continues to contribute to the neurological outpatient services at the Civil Hospital, Gurgaon as part of our research program on brain related disorders. Besides contributing to the community welfare, this provides us a valuable resource of patients for our research.

In order to provide a platform for exchange of knowledge and learning NBRC organizes meetings and workshops. One such major event was the meeting 'Molecular motors, transport and trafficking (M2T2)' organized in association with IISER, Mohali, in which cell biologists from India, USA and UK gathered to discuss recent developments in the field. The meeting received overwhelming response from young participants all over the country.

NBRC faculty is acutely aware of its responsibility of taking science to the schools. We organize 'open days' and other events where students from the nearby schools are invited to visit our laboratories and freely interact with the students and faculty to learn about our research and to satisfy their curiosity about how scientific research is done. This year we organized three open days and participated in India International Science Fair (IISF) 2019 organized in Kolkata. One of the open days was organized to coincide with our Foundation Day celebrations, the day our then President of India Dr. A P J Abdul Kalam dedicated NBRC to the Nation. We also organized a public lecture on this occasion. This year public lecture 'Seven Myths of Memory' was delivered by Prof Nicola Clayton, FRS, of University of Cambridge, and Prof Clive Wilkins Artist in Residence, University of Cambridge and a Member of the Magic Circle.

Our own students are our most valuable assets. With their increasing numbers a need was felt to expand the current hostel facility. Foundation Stone of the upcoming hostel building was kindly laid by Dr Renu Swarup, Chairperson of our Governing Council and Secretary DBT in the month of March.

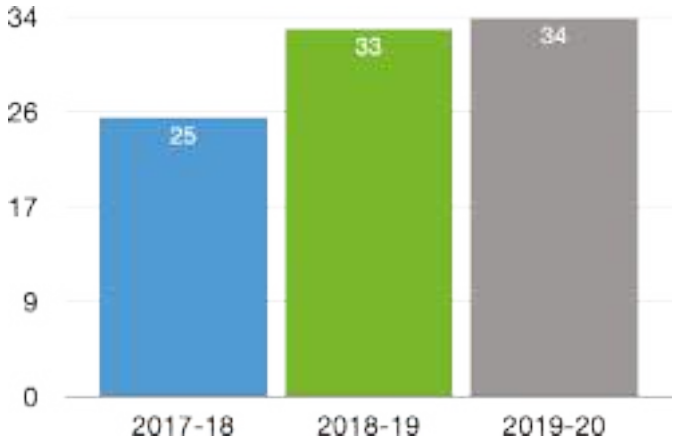
The year ended with an unprecedented threat to the health of peoples the Nation in the form of COVID-19. In order to deal with the threat effectively Hon'ble Prime Minister of India put the country under a lockdown. While the NBRC was shut down as directed, as a research institute it is also a repository of resources developed over decades that need to be maintained so that the efforts and resources invested remain safe. The support staff of NBRC rose to the challenge to ensure that cell lines and animal colonies were maintained, campus remained secure, needs of the remaining students in the hostel were taken care of, and the salaries paid. I would like to recognize and commend Mr Sanjeev Choudhury, in-charge of the Engineering, Dr Inderjeet Yadav, in-charge of the Animal Facility, Ms Pooja Gosain, Administrative Officer, Mr Ravinder Pal, Stores and Purchase Officer, Mr Santhosh Choudhury, Deputy Finance and Accounts Officer, their staffs and our IT personnel, who worked from home, traveled to NBRC as required, and some of who even stayed on the campus away from their families for the duration of the lock-down to ensure that none of the essential services were affected. These support staff are the strength and backbone of NBRC.

I end by expressing my sincere gratitude to Department of Biotechnology for its generous and continued support to NBRC. A special thanks to the members of all the statutory committees of NBRC, and other members of the Indian scientific community who served on various committees, acted as thesis examiners, and advised or collaborated with us, adding enormously to the continued growth and progress of NBRC. I look forward to this continued support to help NBRC achieve the goals it has set for itself.

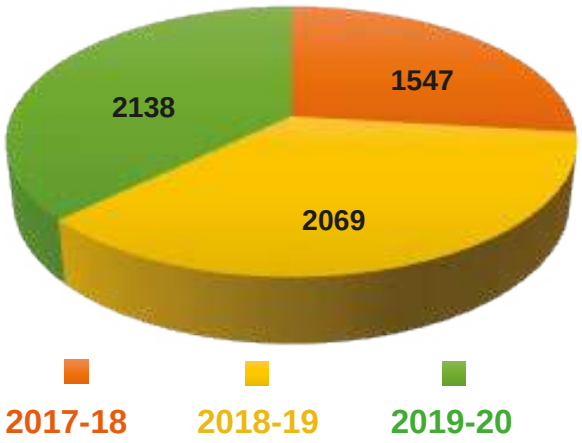
Prof. Neeraj Jain
Director

2019-20 at a glance .....

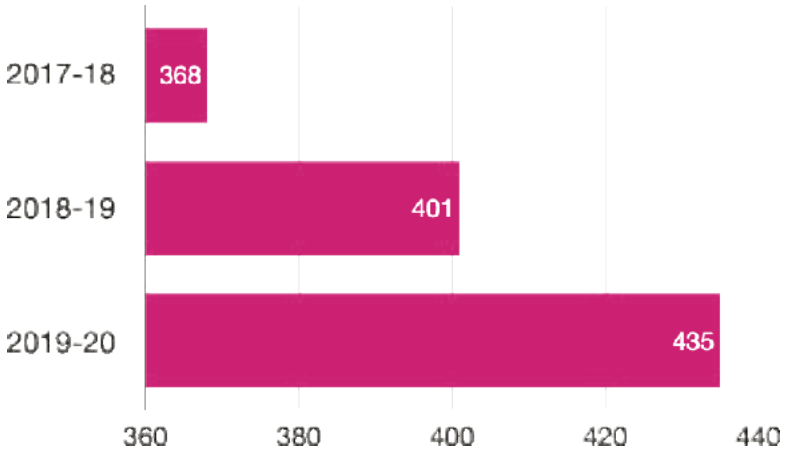
Number of Papers in the year



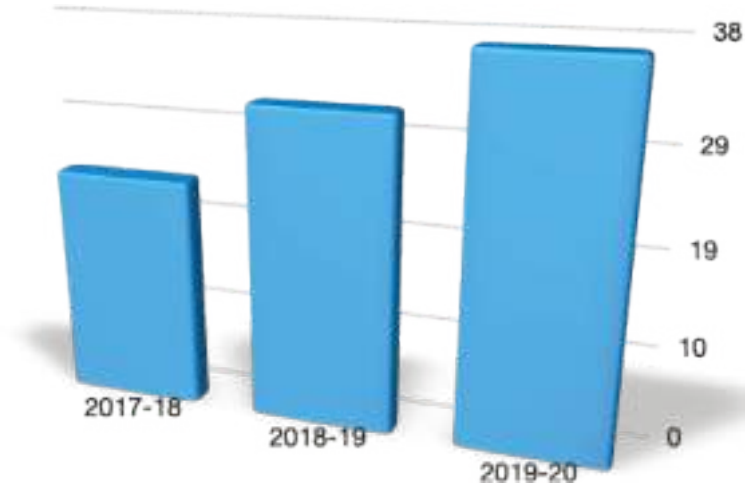
Number of Citations



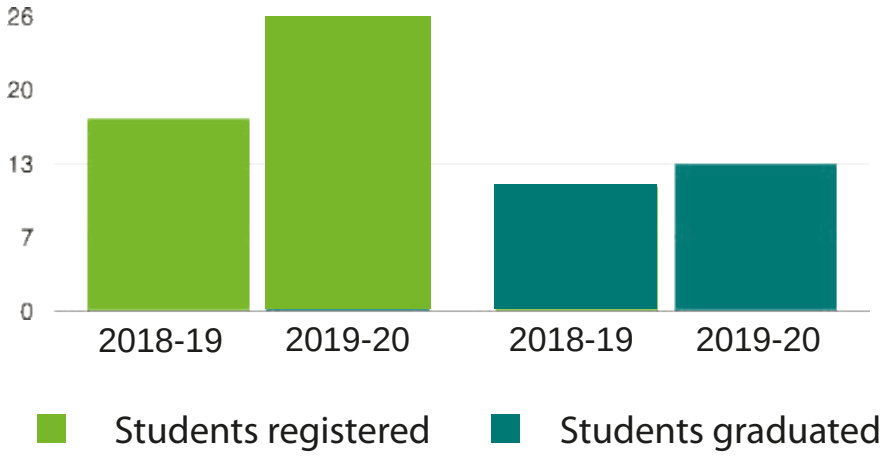
Number of papers upto



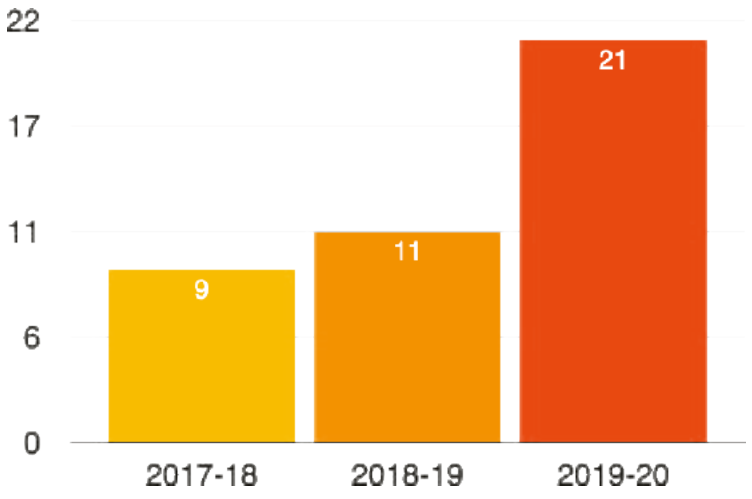
Number of Active Grants



Human Resource Development



Number of Schools that Visted NBRC



Dementia Science Programme

National Brain Research Centre
NBRC

THE INCLEN TRUST

NEIGRIHMS

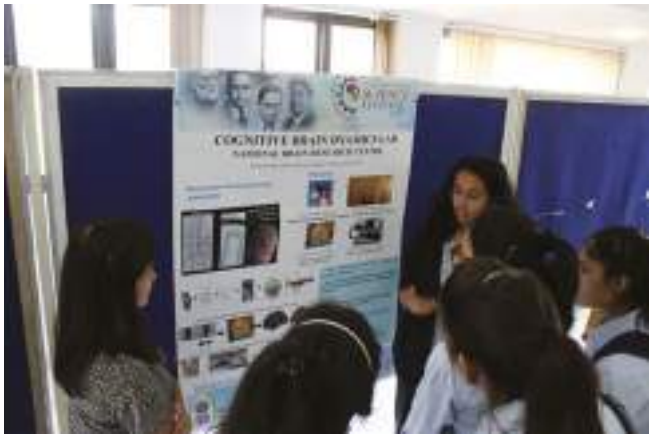
BANGUR

Please see page 95

Foundation Day-2019

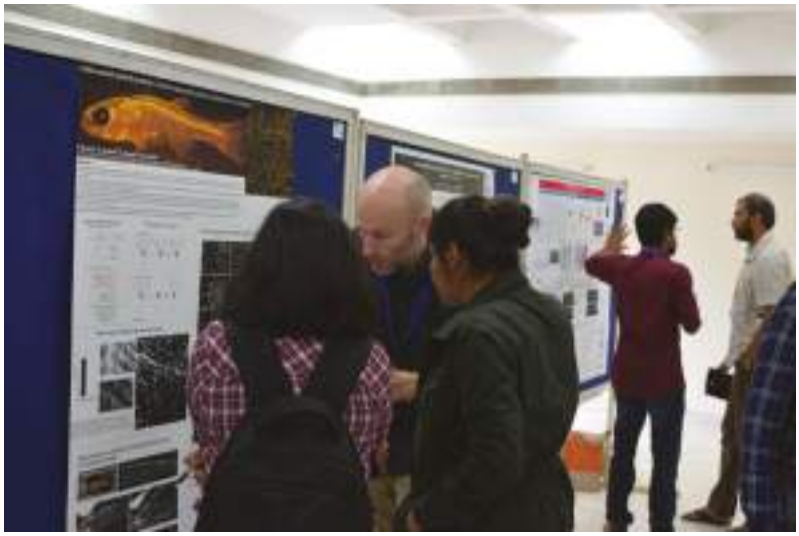
Dr Renu Swarup, Secretory DBT, Chairperson Governing Council Laid Foundation Stone of the New Hostel Building

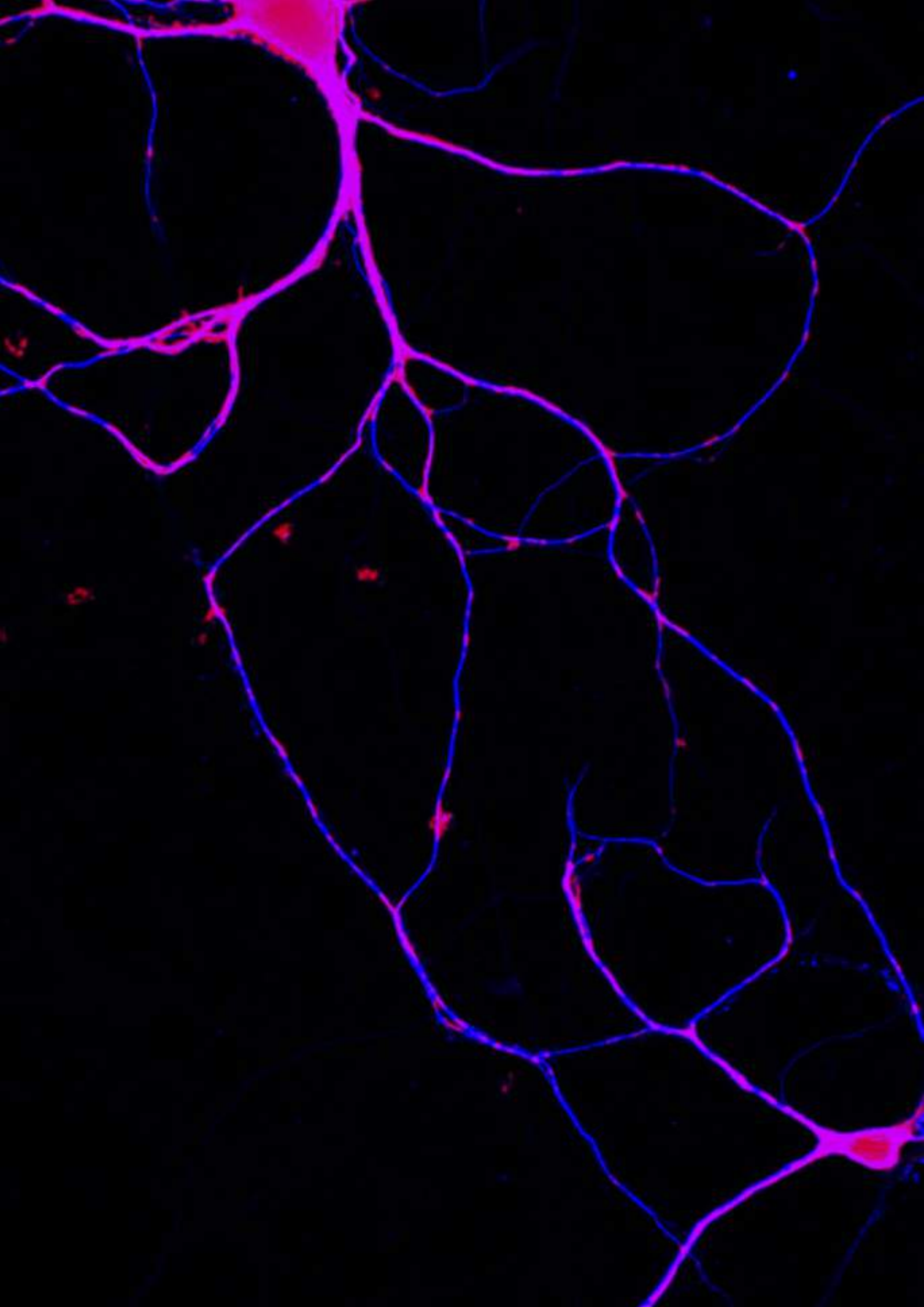
IISF-NBRC Open Day: From Neurons to Knowledge



NBRC Stall at IISF 2019

The Molecular Motors, Transport and Trafficking Meeting 2019 (18th to 20th October)





Scientific Reports

Anindya Ghosh Roy

Department of Cellular & Molecular Neuroscience,

System Neuroscience

Post Doctoral Fellows

Sandeep Kumar, Swagata Dey (India Alliance Early career fellow)

PhD Students

Dharmendra Puri
Atrayee Basu
Harjot Kaur
Sibaram Behera
Sunanda Sharma
Pallavi Singh Rajput

MSc. Student

Akanksha Goyel

Project Assistants

Devashish Pande
Keerthana P
Smriti Bharadwaj

Technical Assistants

Sumit mahapatra
Yunis Khan

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

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 polarity:

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 leads to ectopic extension of axon-like processes from PLM cell body. Live imaging of microtubules and axonal transport with EBP-2::GFP and GFP::RAB-3 reporters, respectively revealed mixed polarity of MTs in the short posterior process suggesting its dendrite like nature. KLP-7 is positively regulated in the posterior process by Planar Cell Polarity components of Wnt involving RHO-1/ROCK to induce mixed polarity of MTs. Whereas KLP-7 is negatively regulated in the anterior process by the UNC-73/CED-10 cascade to establish uniform MT polarity. Our work elucidated how evolutionary conserved Wnt signaling establishes MT polarity in a neuron through Kinesin-13. (Figure 1, Manuscript under review; http://dx.doi.org/10.2139/ssrn.3456296).

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.

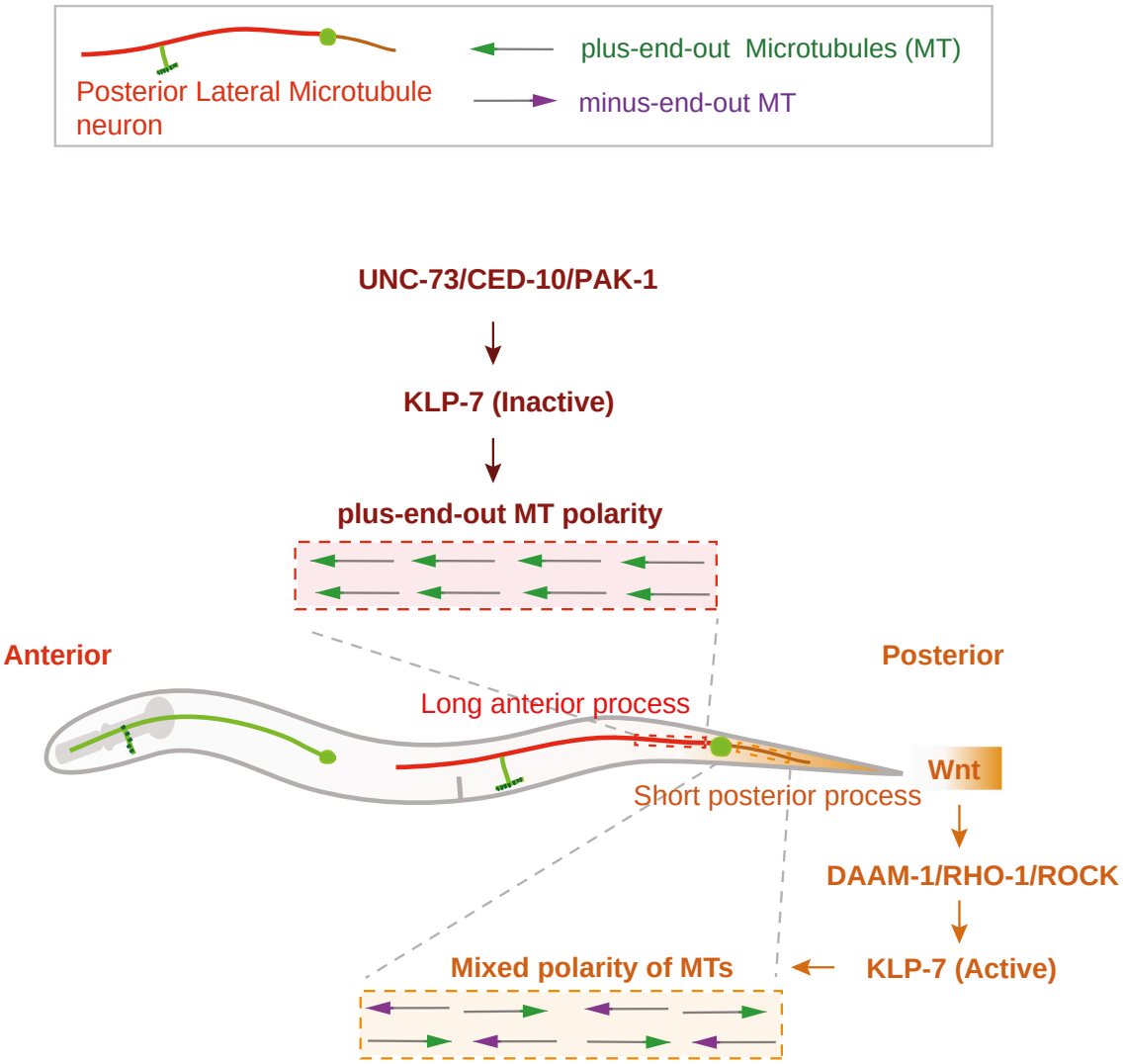


Figure 1: A model describing the mechanism by which Kinesin-13 is regulated in PLM neuron In the posterior process of PLM neuron, KLP-7 is positively regulated by the planar cell polarity components of Wnt signaling. An active version of KLP-7 induces instability and mixed polarity in MTs present in the posterior process. Whereas in the anterior process, KLP-7 is negatively regulated by UNC-73/CED-10 cascade in order to stabilize and polarize the MTs in plus-end-out manner.

RNA binding protein Muscleblind-1(MBL-1) is required for axon growth

One of 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 and improper synapse formation. MBL-1 tagged with GFP is present both in nucleus and axon. To identify the possible targets of MBL-1 in axon development, we performed an interaction analysis between *mbl-1* and genes required for axon development. We found that *mbl-1* is epistatic to genes encoding MEC-7 (β-tubulin), VAB-8 (Kinesin-11 family motor), and UNC-76 (adaptor for Kinesin-1 mediated transport). We hypothesize that MBL-1 is required for proper splicing of *mec-7*, *vab-8* and *unc-76* mRNA to optimize microtubule growth and transport during axonal growth. Alternatively, MBL-1 might act as an adaptor for these mRNA for their transport (Figure 2, Manuscript under preparation).

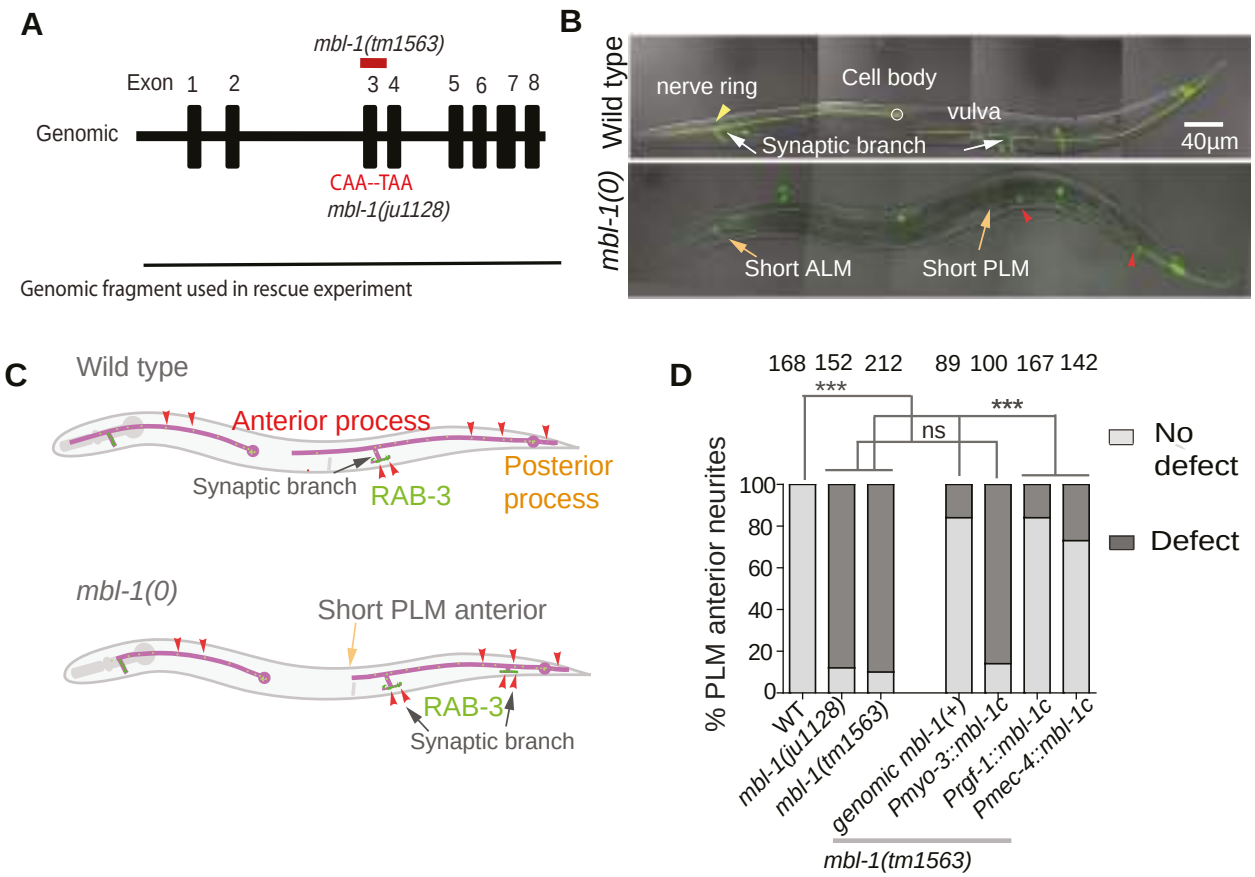


Figure-2: (A) Genomic organization of mbl-1. (B-D) Confocal images, schematics and quantitative representation of the developmental defects due to loss of mbl-1

2) Nerve regeneration study:

Adult nervous system has limited capacity to regenerate after accidental damages. Post injury functional restoration requires proper targeting of the injured axon to its postsynaptic cell. Although initial regenerative response to axonal injury has been studied in great extent, it is rather less clear what controls re-establishment of functional connection.

We showed that axotomy of posterior touch neurons on both sides of a worm leads to a dramatic loss of posterior touch sensation. Using this paradigm, we have shown that initial response to injury is a local raise in axonal Ca2+/cAMP level which activates the a signalling cascade involving dual leucine zipper MAPKKK DLK-1. Several screening using candidate approaches identified the essential, permissive and the inhibitory components of axon regeneration. Rather less is explored whether the axon regeneration of PLM neuron would give rise to functional recovery. We have recently addressed this question and showed that the regrowing axon which could fused to its distal fragment leads to speedy functional recovery [Basu et al 2017, https://www.pnas.org/content/114/47/E10206]. We also showed that functional recovery declines with age and loss of *let-7* miRNA overcomes the age-related decline in functional recovery [Basu et al 2017].

Neuron and muscle-specific activities of DAF-16 cooperate to promote functional rewiring of injured axon

We have seen that the injured axons which regrows without fusing to its distal end also leads to functional recovery in later time points. Particularly, the axons which reaches the original target area in the ventral nerve cord are likely to give functional recovery. We have seen that presynaptic machinery also gets accumulated along the ventral cord. Ventral targeting and functional restoration decline with age. We found that loss of either Insulin signaling (IIs) receptor DAF-2 or downstream kinase AKT-1 promotes ventral targeting in a DAF-16 dependent manner irrespective of age. We further

showed that coordinated activities of DAF-16 in neuron as well as muscle promote ventral targeting during axon regrowth. In response to axotomy, DAF-16 upregulates the expression and localization of the netrin/unc-6 receptor UNC-40/DCC in the growth cone of proximal stump. Neuronal activity of DAF-16 synergizes with that in muscle. Our study reveals that Insulin signaling helps the cross-talk between injured nervous system and adult environment to fine-tune functional rewiring process (Figure 3, Manuscript under preparation).

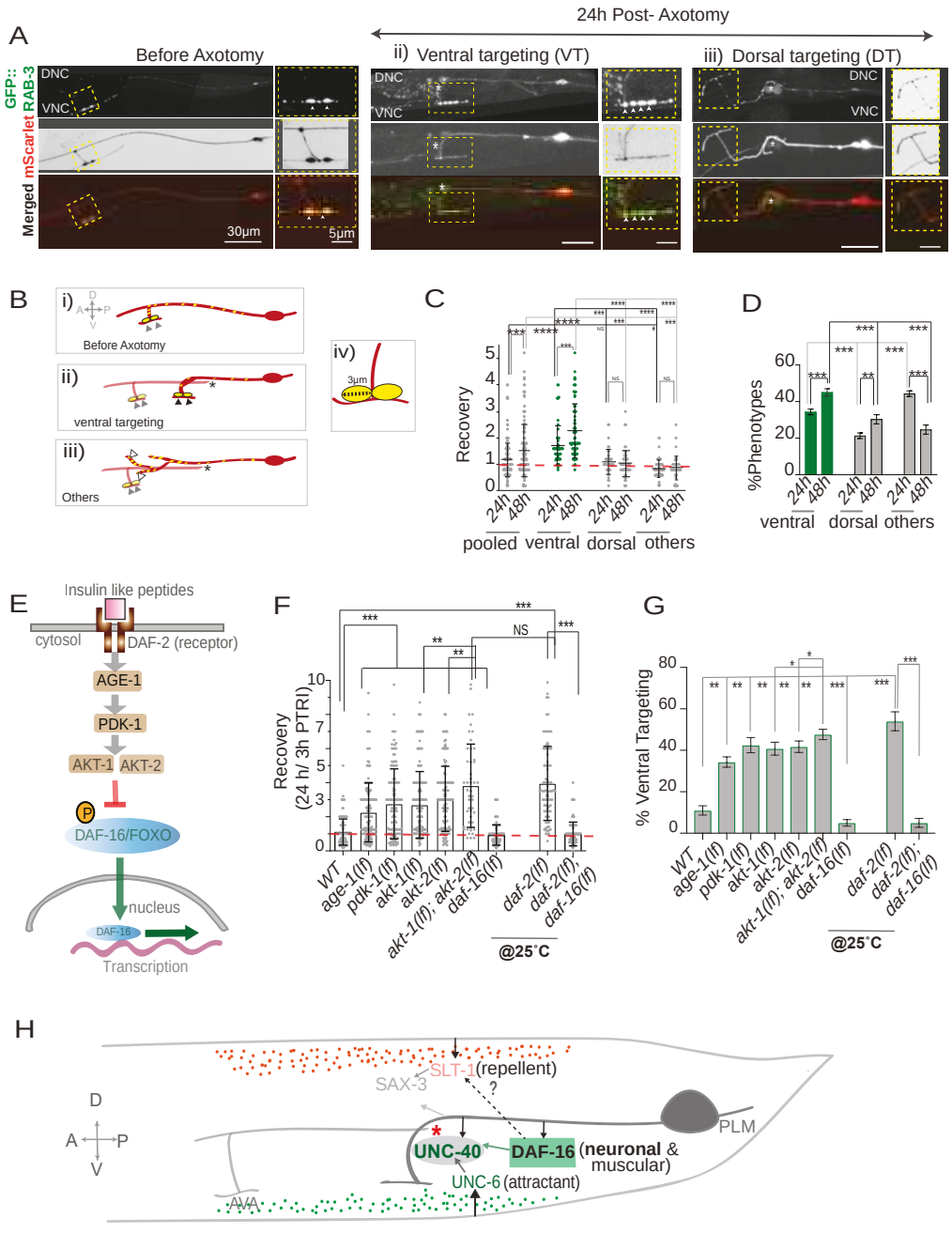


Figure 3: (A-B) The panel represents the anatomical features of PLM axon and its synapse before and after axotomy. Presynaptic protein RAB-3 is enriched at the developmental synapse (i, arrowheads in yellow dotted box) and at the tip of the regrowing axon, which gets targeted towards ventral nerve cord (ii). (C) The dot plot represents the recovery values for different regeneration patterns after 24h and 48h of axotomy. Only those ventrally targeted events show significant recovery. (D) The bar plot represents the percentage of "ventral targeted", "dorsal targeted" and "others" events at 24 and 48h post-axotomy. (E-G) Functional recovery and guidance parameters in mutants lacking the componenets of insulin (IIS) signaling. (H) Model describing how activities of DAF-16 in injured PLM neuron and muscle cooperate to regulate axon-guidance cues. Staitsics, ANOVA, * $p<0.05$, ** $p<0.01$, ***$p<0.001$.

Study of Dendrite Regeneration using PVD neuron as Model

Both dendrites and axons are vulnerable to physical insults during the life span of an individual. Several studies recently have focused on understanding the regenerative capacity of an injured axon. The p38 MAP kinase signaling cascade involving Dual Leucine zipper kinase DLK-1 is essential for axon regeneration. The cyclic AMP and mTOR signaling are limiting factors in axon regeneration. But less is known about dendrite regeneration.

To understand the mechanisms of dendrite regeneration, we used PVD neuron in C. elegans, which has branched dendrites (Figure 5A). The PVD neurons are responsible for harsh touch sensation. Using femtosecond laser, we severed the major and minor primary dendrites and axons of this neuron. After the primary dendrite was severed near the cell body, we observed sprouting of new branches from the cut site within 3 hours. By 24 hours the primary dendrite regrew, following similar trajectory with more complex branching patterns unlike the original menorah in uninjured PVD. We quantified the regeneration pattern in two aspects - length of primary dendrite and number of branches. Axon injury causes a retraction of the severed end followed by a DLK-1 dependent regrowth from the severed end or conversion of neighboring dendrite to axon. To test whether the dendrite regeneration shares the mechanism that of axon, we tested the major signaling hubs such as Dual leucine zipper kinase-1-RPM-1, cAMP elevation, *let-7* miRNA, Akt-1, Phosphatidyl serine (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 downstream kinase Max-2 is essential for dendrite regeneration. Our work provides a framework for understanding the cellular mechanism of dendrite regeneration using PVD model (Figure 4, Manuscript under preparation).

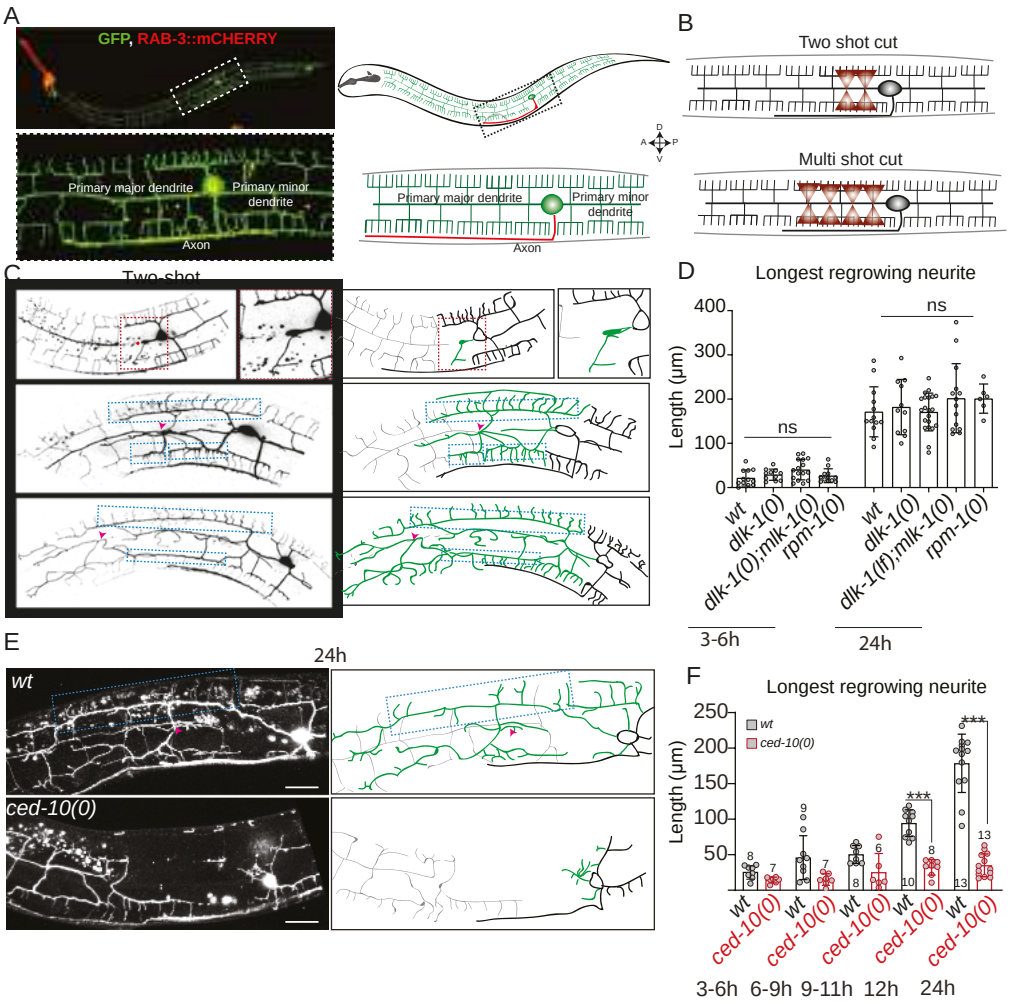


Figure-4: (A) Confocal image and schematics of PVD neuron with branched dendrites. (B) Strategy for dendrotomy. (C) Primary dendrite regrows new processes from the cut dendrite tip. (D) Quantification and dendrite regeneration. (E-F) In ced-10(0) mutant, dendrite fails to regrow efficiently.

Overall our research on neuronal regeneration has been stimulated by many leads in past few years. We are actively pursuing these discoveries for submission to peer reviewed journals.

Presentations

1. Restoration Hardware, Workshop on Molecular Neurobiology: From Genes, Neurons to behavior in health and disease at RCB, Faridabad, February 2020

2. Wnt signaling establishes microtubule polarity in neuron through the regulation of Kinesin-13, Symposium on Chromaffin Cell Biology, ISCCB-20 at the Indian Institute of Technology, Chennai, January 2020

3. Regulation of functional restoration after neuronal injury by miRNA pathway, 1st International, Molecular Medicine Conference "From Bench to Bedside and Beyond" at the Amity University, Gurgaon, August 2019

Funding

SERB

Wellcome Trust-DBT

NBRC Core

Collaborators

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

Award from Students and fellows

1. Atrayee Basu: Travel Award for attending 22nd International *C. elegans* conference, UCLA, CA from SERB and Genetics Society of America (GSA)

2. Post-doctotral fellow Swagata Dey received India Alliance Early Career Felllowship

Conference organized:

Molecular Motors, Transport and Trafficking Meeting 2019 (18th to 20th October). Highlighted in a report in Journal of Cell Scince (https://jcs.biologists.org/content/133/8/jcs245928)

Anirban Basu

Department of Cellular & Molecular Neuroscience,

Translational Neuroscience

Research Associate

Sriparna Mukherjee

PhD Students

Surojit Chakrabarty
Meenakshi Bhaskar
Shivangi Sharma
Stuti Mohapatra

MSc student

Indira S Priya

Technician C

Kanhaiya Lal Kumawat

Technician B

Manish Dogra

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

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. 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.

Microglia being the resident macrophage of brain provides neuroprotection following diverse microbial infection. JEV invades the central nervous system (CNS) resulting in neuro-inflammation, which turns the neuroprotective role of microglia detrimental as characterized by increased microglial activation and neuronal death. Several host factors, including microRNAs (miRNAs), play vital roles in regulating virus-induced inflammation. We have demonstrated that the expression of miR-301a- is increased in JEV-infected microglial cells and human brain. Overexpression of miR-301a augments the JEV-induced inflammatory response, whereas inhibition of miR-301a completely reverses the effects. Mechanistically, NF-κB repressing factor (NKRF), functioning as inhibitor of NF-κB activation is identified as a potential target of miR-301a in JEV infection. Consequently, miR-301a mediated inhibition of NKRF enhances nuclear translocation of NF-κB, which in turn resulted in amplified inflammatory response. Conversely, NKRF overexpression in miR-301a inhibited condition restored nuclear accumulation of NF-κB to a basal level. We also observed that JEV infection induces classical activation (M1) of microglia that drive the production of pro-inflammatory cytokines, while suppressing alternative activation (M2) that could serve to dampen the inflammatory response. Furthermore, in vivo neutralization of miR-301a in mouse brain restores NKRF expression, thereby reducing inflammatory response, microglial activation and neuronal apoptosis. This study suggests that the JEV-induced expression of miR-301a positively regulates inflammatory response by suppressing NKRF production, which might be targeted to manage viral-induced neuro-inflammation.

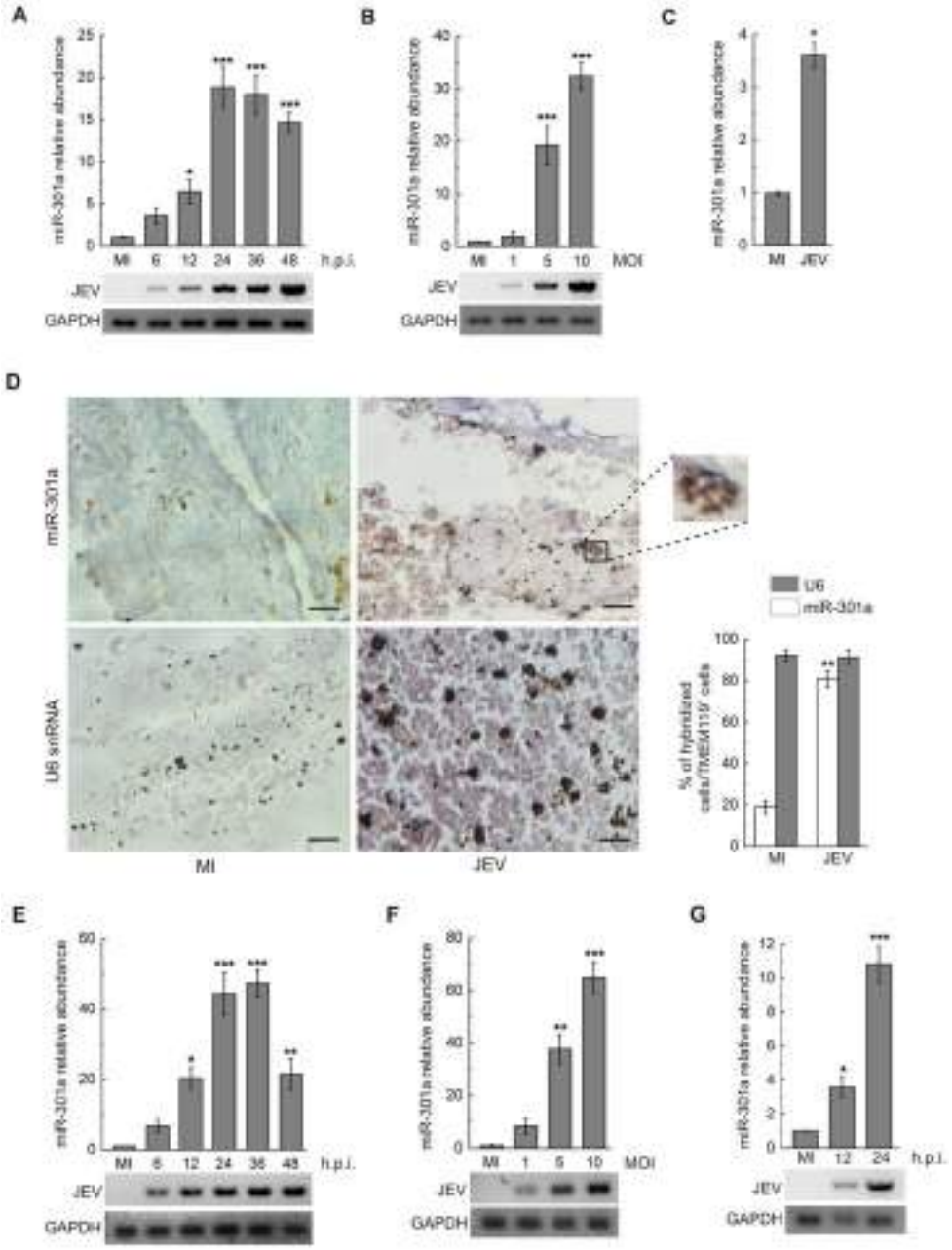


Figure: miR-301a expression is induced in JEV-infected microglia. (A and B) CHME3 cells were infected with JEV at an MOI of 5 for the indicated times (A) or infected with indicated MOIs for 24 hours (B). The relative abundances of miR-301a compared to uninfected (MI) were determined by qRT-PCR analysis and normalized to that of SNORD68 snRNA. RT-PCR was performed to determine JEV infection (lower panels). GAPDH expression was verified as loading control. *P < 0.05, ***P < 0.001. (C) miRNA was isolated from uninfected (MI) and JEV-infected human brain sections and miR-301a expression was determined by qRT-PCR. Data are representative of two different brains per group. *P < 0.05 (Student's t test) compared to uninfected human brain. (D) ISH of miR-301a (purple chromogen) in microglial cells (gray black chromogen) from human brain. Uninfected (MI) and JEV-infected brain sections were hybridized with the miRCURY LNA miR-301a probe or the LNA U6 snRNA probe, which was followed by IHC analysis of microglia with DAB (3,3′-diaminobenzidine). Scale bars, 20 μm; magnification, ×40. The ubiquitously expressed U6 snRNA (purple chromogen) was used as a positive control. Quantification was performed by calculating the percentage of ISH+ to total TMEM119+ (microglial marker) cells (Right panel). Data are mean ± SD from 5 fields per section (2 sections/human brain of each group). **P < 0.01 (Student's t test) compared to uninfected human brain (MI). (E and F) BV2 cells were exposed to JEV for the indicated times (E) or were infected with indicated MOIs of JEV for 24 hours (F) and the abundance of miR-301a was evaluated by qRT-PCR analysis. JEV infection was assessed by RT-PCR (lower panels) and GAPDH was used as internal control. *P <0.05, **P < 0.01, ***P < 0.001 compared to uninfected cells (MI). (G) Primary microglial cells were isolated from postnatal day 0 (P0) to P2 BALB/c mouse pups, cultured for 12-14 days, and infected with JEV for the indicated times. miR-301a abundance was quantified by qRT-PCR analysis, and the results are expressed as the fold change compared to that in uninfected cells (MI). *P <0.05, ***P < 0.001. h.p.i., hours post infection. All data in bar graphs are means ± SD of three biological replicates. P values are calculated by analysis of variance (ANOVA) followed by Bonferroni's post hoc test. (Hazra et al; Journal of Immunology 5;203(8):2222-2238)

It is evident from our previous work that JEV damages the neural stem/progenitor cell population of the mammalian brain. However, JEV-induced alteration in the miRNA expression pattern of the cell population remains an open question, hence warranting our present study. Recently we have shown that the downregulation of four miRNAs, and we prepared a protein-protein interaction (PPI) network of miRNA target genes. We have identified two types of hub genes in the PPI network, namely, connector hubs and provincial hubs. These two types of miRNA target hub genes critically influence the participation strength in the networks and thereby significantly impact up- and downregulation in several key biological pathways. Computational analysis of the PPI networks identifies key protein interactions and hubs in those modules, which opens up the possibility of precise identification and classification of host factors for viral infection in NSPCs.

Our previous study also showed that JEV infects neural stem/ progenitor cells (NSPCs) and decreases their proliferation. Statin, a commonly used class of cholesterol lowering drug, has been shown to possess potent anti-inflammatory and neuroprotective effects in acute brain injury and chronic neurodegenerative conditions. Using BALB/c mouse as an experimental model of viral infection, we observed that atorvastatin effectively reduces viral load in the subventricular zone (SVZ) of infected pups and decreases the resultant cell death. It also reduced interferon-β response in the neurogenic area. The neuroprotective role of atorvastatin is again evident from the rescue in neurosphere size and decreased cell death *in vitro*. It has also been observed that upon atorvastatin administration, cell cycle regulatory proteins and cell survival proteins are also restored to their respective expression level as observed in uninfected animals. Thus, the antiviral, immunomodulatory and neuroprotective roles of atorvastatin reflect in our experimental observations.

Publications

1. B Hazra, S Chakraborty, M Bhaskar, S Mukherjee, A Mahadevan, A Basu (2019) miR-301a regulates inflammatory response to Japanese Encephalitis Virus infection via suppression of NKRF activity. Journal of Immunology 5;203(8):2222-2238

2. S Mukherjee, I Akbar, R Bhagat, B Hazra, A Bhattacharyya, P Seth, D Roy, A Basu (2019) Identification and classification of hubs in miRNA target gene networks in human neural stem/ progenitor cells following Japanese encephalitis virus infection. mSphere 4(5). pii: e00588-19.

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5. S Mukherjee, I Akbar , B Kumari, S Vrati, A Basu#, A Banerjee (2019) Japanese Encephalitis Virus-induced let-7a/b interacted with the NOTCH-TLR7 pathway in microglia and facilitated neuronal death via caspase activation, Journal of Neurochemistry 149(4):518-534 (#joint corresponding author). (Cover page article)

Presentations

1. A Basu (2020) Drug repositioning/repurposing: Promising strategy to develop therapy against viral infections. Ramkrishna Mission Vivekananda Centenary College, Rahara, Kolkata, 10th February, 2020.

2. A Basu (2019) Drug repositioning/repurposing: Promising strategy to develop therapy against viral infections. Experts Opinion on Molecular Medicine, West Bengal State University, Barasat. 12th December, 2019.

3. A Basu (2019) Drug repositioning/repurposing: Promising strategy to develop therapy against viral infections. Indo-US Symposium on New Insights into the Inflammation, Immunity, and Pathobiology of Diseases, Port Blair, Andaman Islands, 3rd-8th December, 2019.

4. A Basu (2019) Innate Immunity in the central nervous system: Redefining the relationship between "Immune system" and "Nervous system". SNCI-Chennai Chapter, Dept. of Biochemistry, Madras University, 20-21st August, 2019.

5. A Basu (2019) Innate Immunity in the central nervous system: Redefining the relationship between "Immune system" and "Nervous system". Department of Biochemistry, AIIMS, New Delhi, World Immunology Day, 29th April, 2019.

Funding

1. microRNAs as a potential therapeutic target in Neurotropic Viral infection [Tata Innovation Fellowship from the Department of Biotechnology (BT/HRD/35/01/02/2014)] starting from 01/04/2018, for two years.
2. MicroRNA mediated regulation of neural stem/progenitor cell fate in neurotropic flaviviral infection [Department of Biotechnology (BT/PR22341/MED/122/55/2016)] starting from 29/12/2017, for three years.
3. Understanding the therapeutic role of adult stem cell derived exosome in combating virus induced neurodegenerative disease [Department of Biotechnology (BT/PR15984/MED/31/325/2015) starting from 20/03/2018, for three years.
4. Deciphering Antiviral Properties of Statins against Japanese Encephalitis Virus Infections [Department of Biotechnology BT/PR27796/MED/29/1301/2018, starting from 26/12/2018, for two years.
5. Elucidating the role of long non coding RNAs (lncRNAs) in neuronal cell death during Japanese Encephalitis (JE) [Department of Biotechnology (BT/PR126590/MED/122/113/2017) starting from 05/03/2019, for three years.

Collaborators

- Arpan Banerjee, Pankaj Seth, and Dipanjan Roy, NBRC
- Sunit Singh, Institute of Medical Sciences, BHU, Varanasi.
- Sudhanshu Vrati, Prasenjit Guchait, Manjula Kalia, and Arup Banerjee, RCB, NCR Biotech Cluster, Faridabad
- Anita Mahadevan, NIMHANS, Bangalore
- Vivek Sharma, Department of Biological Sciences, Birla Institute of Technology and Science Pilani, Hyderabad Campus, Hyderabad

Degree Awarded

Masood Ahmad Wani (M.Sc.)

Arpan Banerjee

Department of Computational Neuroscience,

Cognitive Neuroscience, Systems Neuroscience, Translational Neuroscience

Post-Doctoral Fellows

Dr. Dipanjan Ray
Dr Amit Naskar
Dr Soibam Shyamchand Singh

PhD Students

Neeraj Kumar
Priyanka Ghosh
G. Vinodh Kumar
Anagh Pathak
Ritu Moni Borah
Nisha Chetana Sastry
Kirti Saluja

MSc Students

Darshit Thakkar
Akanksha Gupta

Project Assistants

Varun Madan Mohan
Shubham Kumar

Neuro-cognitive network mechanisms using multimodal neuroimaging

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 cognitive impairments in epilepsy 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, 2019 - March, 2020. 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: Biophysical mechanisms governing large-scale brain network dynamics underlying individual-specific variability of perception

Perception necessitates interaction amongst neuronal ensembles, the dynamics of which can be conceptualized as the emergent behavior of coupled dynamical systems. Here, we propose a detailed neurobiologically realistic model that captures the neural mechanisms of inter-individual variability observed in cross-modal speech perception. From raw EEG signals recorded from human participants when they were presented with speech vocalizations of McGurk-incongruent and congruent audio-visual (AV) stimuli, we computed the global coherence metric to capture the neural variability of large-scale networks. We identified that participants' McGurk susceptibility was negatively correlated to their alpha-band global coherence. The proposed biophysical model conceptualized the global coherence dynamics emerge from coupling between the interacting neural masses - representing the sensory specific auditory/visual areas and modality non-specific associative/ integrative regions. Subsequently, we could predict that an extremely weak direct AV coupling result in a decrease in alpha band global coherence - mimicking the cortical dynamics of participants with higher McGurk susceptibility. Source connectivity analysis also showed decreased connectivity between sensory specific regions in participants more susceptible to McGurk effect, thus establishing an empirical validation to the prediction. Overall, our study provides an outline to link variability in structural and functional connectivity metrics to variability of performance that can be useful for several perception & action task paradigms (Figure 1)

Project 2: Large-scale Functional Integration, Rather than Functional Dissociation along Dorsal and Ventral Streams, Underlies Visual Perception and Action.

Visual dual stream theory posits that two distinct neural pathways of specific functional significance originate from primary visual areas and reach the inferior temporal (ventral) and posterior parietal areas (dorsal) (Figure 2). However, there are several unresolved questions concerning the fundamental aspects of this theory. For example, is the functional dissociation between ventral and dorsal stream driven by features in input stimuli or is it driven by categorical differences between visuo-perceptual and visuo-motor functions? Is the dual stream rigid or flexible? What is the nature of the interactions between two streams? We addressed these questions using fMRI recordings on healthy human volunteers and employing stimuli and tasks that can tease out the divergence between visuo-perceptual and visuo-motor models of dual stream theory. fMRI scans were repeated after seven practice sessions that were conducted in a non-MRI environment to investigate the effects of neuroplasticity. Brain activation analysis supports an input-based functional dissociation and existence of context-dependent neuroplasticity in dual stream areas. Intriguingly, premotor cortex activation was observed in the position perception task and distributed deactivated regions were observed in all perception tasks thus, warranting a network level analysis. Dynamic causal modelling (DCM) analysis incorporating activated and deactivated brain areas during perception tasks indicates that the brain dynamics during visual perception and actions could be interpreted within the framework of predictive coding. Effectively, the network level findings point towards the existence of more intricate context-driven functional networks selective of "what" and "where" information rather than segregated streams of processing along ventral and dorsal brain regions (Figure 3). The details can be explored in the recently published paper Ray, et al 2020.

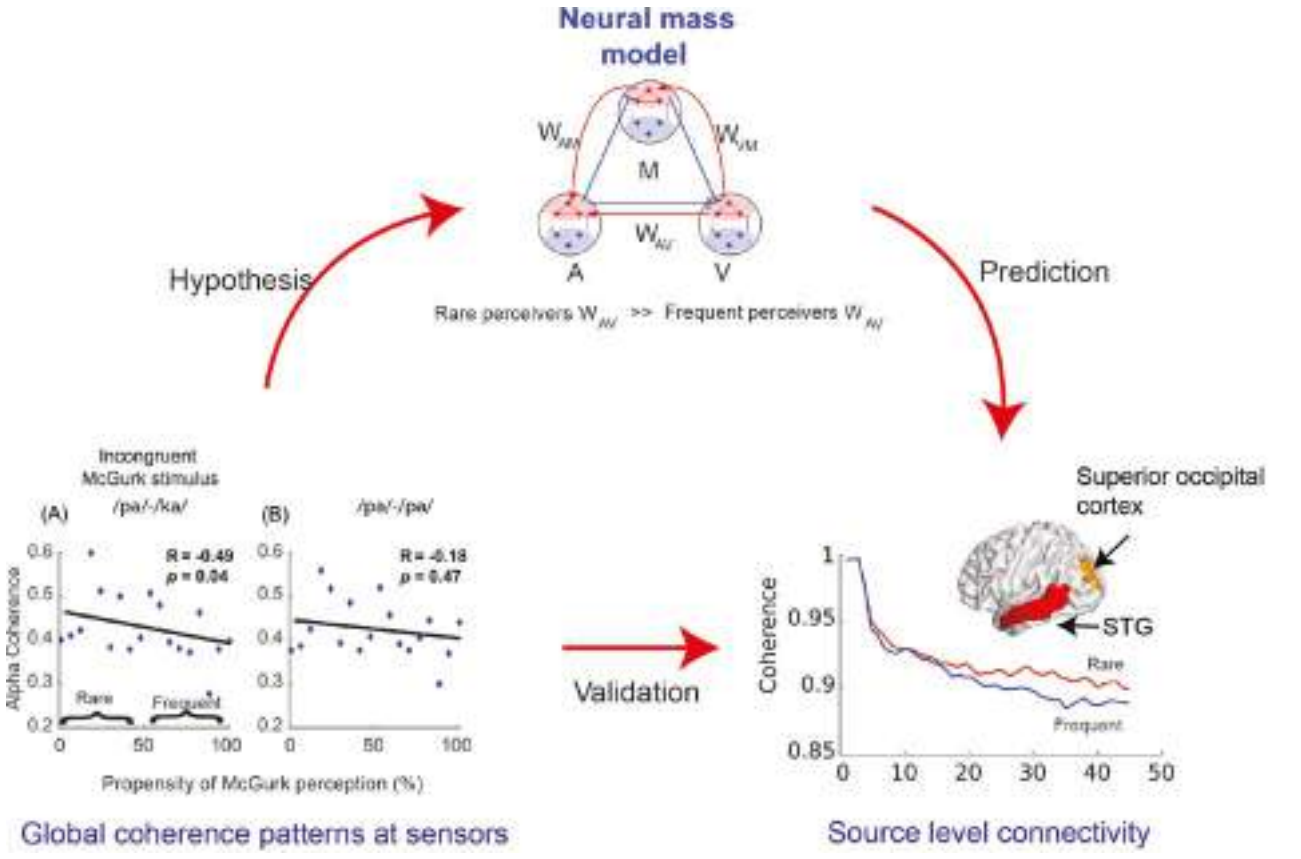

Figure 1: Pipeline of the study: We address an ongoing challenge of characterizing the neural mechanisms that govern the variability during multisensory speech perception. Employing the McGurk paradigm, we identify the neural signatures of the variability in the global coherence metric. Global alpha coherence among EEG sensors is inversely correlated to the degree of McGurk illusion. We then turn to test our hypothesis – 'dynamic and preferential coupling between sensory specific and multisensory regions underlie the observed variability', using a neural mass model. Finally, we validate the inferences drawn from the model by analyzing pairwise coherence in the source space between concordant cortical generators of neural activity.

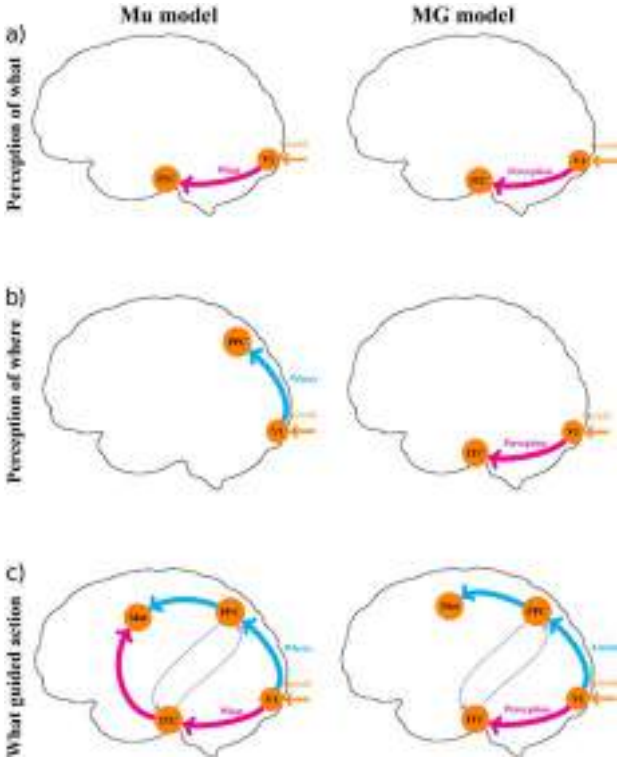

Figure 2: The plausible functional connectivity maps according to Mishkin-Ungerlieder (Mu) and Milner Goodale (MG) models of perception action.

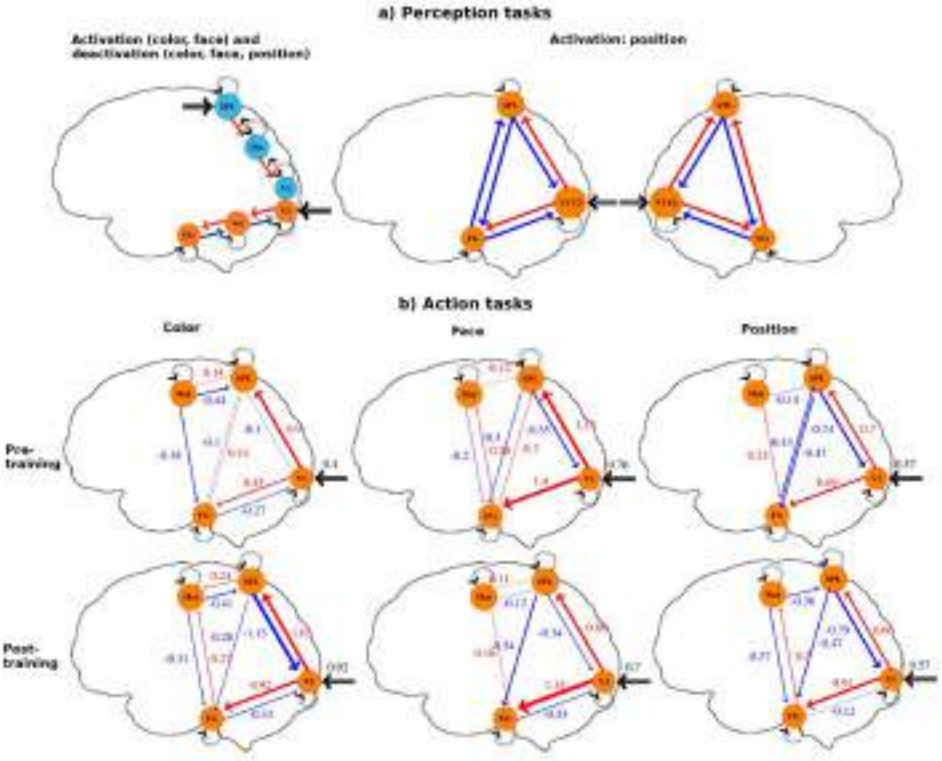

Figure 3: Effective connectivity using DCM during perception and action tasks. (A) Perception tasks: The winning model configuration for ventral stream activation and dorsal stream deactivation during color and face perception tasks and activation in primary and secondary visual cortex (V1V2), ventral (FG), and dorsal (SPL) stream regions during position perception tasks (positive modulation: red, negative modulation: blue). Pre- and posttraining analyses show similar values of estimated coupling parameters for each connection for color and face perception. (B) Action tasks: The winning model configuration for pre- and posttraining sessions. The color of the arrow represents the nature (positive modulation: red, negative modulation: blue), and the thickness of the arrow represents the mean value of the estimated coupling parameter for modulation of effective connectivity. VES = extrastriate ventral stream regions; DES = extrastriate dorsal stream regions; Mot = primary motor cortex.

Publications

1. Ray, D., Hajare, N., Roy, D., Banerjee, A. (2020) Large-scale Functional Integration, Rather than Functional Dissociation along Dorsal and Ventral Streams, Underlies Visual Perception and Action. Journal of Cognitive Neuroscience 32:5, 847-861.

2. Pal A.K., Roy, D., Kumar, V. G., Chatterjee, B., Sharma, L. N., Banerjee, A., & Gupta, C. N. (2020) Empirical Mode Decomposition Algorithms for Classification of Single-Channel EEG Manifesting McGurk Effect. In: Tiwary U., Chaudhury S. (eds) Intelligent Human Computer Interaction. IHCI 2019. Lecture Notes in Computer Science, vol 11886. Springer, Cham.

3. Halder, T., Talwar, S., Jaiswal, A. K., & Banerjee, A. (2019): Quantitative evaluation in estimating sources underlying brain oscillations using current source density methods and beamformer approaches. eNeuro DOI: https://doi.org/10.1523/ENEURO.0170-19.2019.

4. Dutta. S., Roy, D. & Banerjee, A. (2019): Generative framework for dimensionality reduction of large scale network of non-linear dynamical systems driven by external input. New Journal of Physics, 21 072001 (Published as fast-track communication)

Presentations

1. Arpan Banerjee: Introduction to Cognitive Neuroscience, Workshop on fMRI analysis at Symbiosis International University, Pune, June 2019.

2. Arpan Banerjee: Can data science lead us to the grand unified theory of brain function? NeuroAI: Aug 2019.

3. Arpan Banerjee: Can data science lead us to the grand unified theory of brain function ? Invited Talk Series at IIIT Delhi, Oct 2019.

4. Arpan Banerjee: The decoherence theory of perception at Brain Modes, Pokhara, Nepal, Dec 2019.

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

- Anirban Basu, Dipanjan Roy, Ellora Sen, NBRC
- Cota Navin Gupta, IIT Guwahati
- Ganesh Bagler, IIIT Delhi

Degree Awarded

- G. Vinodh Kumar(Ph.D)
- Kirti Saluja (M.Sc.)
- Leesa Joyce (M.Sc.) (Registered at IIISER Mohali, jointly supervised with Dr Somdatta Sinha): Multi-voxel pattern analysis of human brain fMRI data

Dipanjan Roy

Department of Computational Neuroscience,

Cognitive Neuroscience, Systems Neuroscience, Translational Neuroscience

Research Associate

Dr. Jasleen Gundh

PhD Students

Vanshika Singh
Abhishek Singh Narvaria
Gargi Majumdar
Azman Akhtar

MSc student

Vinsea Singh

Project Assistants

Fahd Yazin
Vivek Sharma
Priyanka Sigar

Atypical brain network dynamics with development and aging and relationship with Cognitive and sensory processing

Our Lab investigates the interaction among large-scale brain networks and dynamics during maturation or development of Cortex and healthy aging process. There are well documented stages from children to adolescence to adult lifespan 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. Here we used publicly available high throughput neuroimaging multimodal datasets and also collect our own multimodal data at NBRC during (during rest and variety of Cognitive tasks spanning multiple cognitive domains (namely perception, memory and language processing)) in collaboration with Cambridge Neuroscience Aging Consortium (***CAMCAN***) for both genders (male and female) of varying age groups. This is a truly large-scale data repository comprise of 700 individual subjects characterizing different stages of adult lifespan with multimodal imaging techniques and with unprecedented depth of cognitive phenotyping. Not only that but the data comprise 14 different Cognitive task spanning domains such as Visuo-spatial working memory, Verbal working memory, Fluid intelligence, Crystallized intelligence, Sensory-Motor processing, Visual and auditory perception, Passive movie watching, Emotional face processing to name a few and therefore, serves as a testing ground many hypothesis (e.g. Posterior-Anterior shift with aging (PASA), Slowing down Peak Alpha frequency (PAF), Neural noise hypothesis and increase in the noisy baseline, Compensation related utilization of resources (CRUNCH)) and developing regression and classification based advanced statistical models. To test and develop our own theories which departs or support previous models of cognition during development, aging and provides neural basis of Cognitive flexibility we track large-scale spatio-temporal changes in global coherence, synchronization between brain areas and sensors/sources and metastable brain dynamics among large-scale resting state brain networks where age as an independent variable. Specifically, we differ from traditional classification approach where

between group metrices are evaluated for pinpointing specifically age-related differences and develop predictive models. We have proposed completely novel approach and provided new understanding of how continuous change in dynamical patterns over the whole brain and specific modules of cognitive functions unfolds with maturation and age. We have further demonstrated that previous ways of categorial analysis on aging is not an entirely correct approach to get complete insight onto large scale brain network dynamics and quantify idiosyncrasy in the aging process. For example, our analysis reveals every aging brain is very different from others and there exists subject-wise variability in the data which purposefully add to the potential understanding of the aging process and pinpoint how individuals may allocate attention during variety of sensory and cognitive goal directed task. The questions we addressed here in details. For fMRI data, we addressed does activity or suppression and BOLD signal variability in salience / CEN/ default mode networks predict causally cognitive performance? Variations in neural circuitry may underlie individual differences in cognitive performance (High performing versus Low performing Elderly in memory task). The salience network comprises the dorsal anterior cingulate network (DAN) and orbital Fronto-Parietal, Insular cortices (FPN) with connectivity to subcortical and limbic structures (Cole et al. 2014). This network shows correlations with anxiety ratings, emotion regulation, mood alteration, and may serve for the identification of the most homeo-statically regulated sensory stimuli/inputs entering the nervous system. Hence, any homeostatic deregulation or disruption via change in E/I balance would immediately impact salience networks. Currently, we are investigating how causally the suppression in the DMN and CEN networks are strongly coupled with increase in activity in SN in the context of aging. Finally, we are also investigating what is the exact role of the common driver areas such as subcortical areas e.g. Thalamus, Putamen etc. in altering net causality between DMN, SN, and CEN networks with aging process.

Lifespan associated changes in global patterns of coherent communication revealed using neuro-electromagnetic signals and neural oscillations

Introduction

Healthy ageing is accompanied by changes to spontaneous electromagnetic oscillations. At the macroscopic scale, previous studies have quantified the basic features, e.g., power and frequencies in rhythms of interest from the perspective of attention, perception, learning and memory. On the other hand, signatures and modes of neural communication have recently been argued to be identifiable from global measures applied on neuro-electromagnetic data such as global coherence that quantifies the degree of togetherness of distributed neural oscillations and metastability that parametrizes the transient dynamics of the network switching between successive stable states. Here, we demonstrate that global coherence and metastability can be informative measures to track healthy ageing dynamics over lifespan and together with the traditional spectral measures provides an attractive explanation of neuronal information processing. Finding normative patterns of brain rhythms in resting state MEG would naturally pave the way for tracking task relevant metrics that could crucially determine cognitive flexibility and performance. While previously reported observations of a reduction in peak alpha frequency and increased beta power in older adults are reflective of changes at individual sensors (during rest and task), global coherence and metastability truly pinpoint the underlying coordination dynamics over multiple brain areas across the entire lifespan. In addition to replication of the previous observations in a substantially larger lifespan cohort than what was previously reported, we also demonstrate, for the first time, age related changes in coherence and metastability in signals over time scales of neuronal processing. Furthermore, we observed a marked frequency dependence in changes in global coordination dynamics, which, coupled with the long-held view of specific frequency bands sub-serving different aspects of cognition, hints at differential functional processing roles for slower and faster brain dynamics.

Methods

Participants

Cam-CAN is a multi-modal, cross-sectional adult life-span population-based study. The study was approved by the Cambridgeshire 2 Research Ethics Committee, and all participants have given written informed consent. The data presented here belonged to Stage 2 of the study. In Stage-1, 2681 participants had been home-interviewed and had gone through neuropsychological assessments and been tested for vision, balance, hearing and speeded response. Participants with poor vision (< 20/50 on Snellen test), poor hearing (threshold greater than 35 dB at 1000 Hz in both ears), past history of drug abuse, with any psychiatric illness such as bipolar disorder, schizophrenia, with neurological disease e.g. epilepsy, stroke, traumatic brain injury, or a score less than 25 in Mini-Mental State Examination were excluded from

further behavioral and neuroimaging experiments. 700 participants had been screened from Stage 1 to Stage 2, of which Magnetoencephalogram (MEG) data from 650 subjects were available.

Data acquisition

Data used in the preparation of this work were obtained from the CamCAN repository (available at http://www.mrc-cbu.cam.ac.uk/datasets/camcan/). For all the subjects, MEG data were collected using a 306-sensor (102 magnetometers and 204 orthogonal planar magnetometers) VectorView MEG System by Elekta Neuromag, Helsinki, located at MRC-CBSU. Data were digitized at 1 kHz with a high pass filter of cutoff 0.03 Hz. Head position was monitored continuously using four Head Position Indicator coils. Horizontal and vertical electrooculogram were recorded using two pairs of bipolar electrodes. One pair of bipolar electrodes were used to record electrocardiogram for pulse-related artifact removal during offline analysis. The data presented here consisted only of resting state, where the subject sat still with their eyes closed for a minimum duration of 8 minutes and 40 seconds.

Continuous and categorical analysis of aging data

In order to bring all aspects of age-associated neural communication we performed both continuous and categorical analysis of the aforementioned brain measures with age as an explanatory variable. The primary goal of the continuous analysis was to capture the pattern change over lifespan (e.g., whether changes of the patterns are increasing/ decreasing). For this analysis we divided the whole cohort into bins of 5 years starting from 18 years. The bins were non-overlapping and the center of each bin was considered as the representative age value of the bin. On the other hand, in the categorical analysis decomposing the whole data into cohorts with age ranges 18-35, 36-50, 51-64 & 66-88 allowed us to get finer and accurate insights in each stage of the adult span which has been well-documented in the fMRI literature (Chan et al., 2014) as well as the results obtained here can be contextualized with previous studies. The age ranges were unequally chosen because of the limitations posed by the CAM-CAN data set where different numbers of samples in each age group are available. However, in order to keep a reasonable number of samples > 120 in each cohort we chose the bins accordingly.

Results

We studied the effect of healthy ageing on the fundamental properties of the endogenous band-limited neural oscillations such as amplitude and center frequency. Since the Head Position Indicator (HPI) coil related noise can be unreliable at higher frequencies, we concentrated our analysis between 0-40Hz which fully contains the neural oscillations in the Delta (1-3Hz), Theta (4-8Hz), Alpha (8-12Hz), and Beta (16-25Hz) frequency bands. Alpha band power was estimated by averaging the estimated spectral values within 8-12 Hz. We further quantified age-effects in the beta band using a categorical approach and found significant differences in group means between Young Adult (YA) vs Middle Elderly (ME), Young Adult (YA) vs Middle Late (ML), Young Adult (YA) vs Older Adult (OA) and Middle Elderly (ME) vs Older Adult (OA) groups (as shown in **Figure 1**). Among various interesting findings one of key finding from this work Age trajectories in band-specific global network measures: coherence and metastability. Global Coherence in the delta and theta band was found to increase with age. In contrast, global coherence in the alpha band varied inversely with age while Beta band global coherence did not display an age effect (as displayed in **Figure 2A and B)**.

Metastability quantify variability in synchrony with aging

We estimated the variability of neuronal communication states using metastability as a function of age and frequency. We observed a dichotomous pattern in metastability as a function of frequencies in all age groups - a sharp decrease with increasing frequencies till 12 Hz and a gradual increase in the metastability indices across frequencies between 12 – 40 Hz (Figure 2C and D). Qualitatively, we found metastability to be higher for delta, theta and beta bands as compared to the alpha band. Interestingly, in all age categories, the variation of metastability with frequencies was consistent, essentially a U-shaped profile. From the continuous analysis we could establish that band-specific metastability increased with age across all frequency bands- Delta, Theta, Alpha, Beta.

Region-wise analysis of metastability reveals differential trends

In order to track changes in metastability in specific brain areas we segmented the sensors in 5 groups - Frontal, Centro-Parietal, Occipital, Left Temporal and Right Temporal regions. The region-wise analysis consisted of 14 randomly sampled sensors to compute metastability in each brain region. Next, we tracked the region-wise metastability with aging. Spearman rank correlation was performed to characterize trends in band and region specific metastability and effect sizes quantified using Cohen's d. Delta and Theta oscillations either stayed invariant or reduced as a function of age in the occipital, left temporal and right temporal regions. Beta band

metastability showed the highest age correlation (using Spearman rank test) in the centro-parietal sensors while staying invariant in the occipital and temporal sensors.

Relationship of between global network measures and Cognitive performance in Visuospatial short-term working memory (VSTM)

In order to evaluate the relationship of normative brain rhythms over lifespan we computed the correlations between global network measures and the performance metric of precision in a visual short-term working memory (VSTM) task available with the Cam-CAN cohort. We observed a significant correlation at 95% confidence levels between global coherence in the alpha band and precision in VSTM task after regressing out the effect of age (**Fig 3**). The global coherences and metastability computed in other frequency band were not significantly correlated with precision.

Discussion

Neuronal communication is the backbone of basic human brain functions and supports a myriad of cognitive functions at various scales of nervous system organization. While spectral estimates attempt to link neural oscillations with cognition, very few studies are available that provide normative mapping of neuronal oscillations across healthy lifespan aging. We observed a significant age-related decline in peak alpha frequency (PAF) at the sensor level as well as increase in broadband beta power in a healthy cohort consisting of 650 human participants from the CAMCAN repository. Out of all sensor specific spectral features such as frequency and amplitude of oscillations in narrowband and broadband, PAF and beta power varied exclusively with age in opposite ways. Subsequently we could track the global subspace that sculpts the alpha and beta topographies, and their corresponding overlap over lifespan. Interestingly the angular separation between the alpha and beta topographies increase with age indicative of segregation of underlying generators over lifespan. Integrative mechanisms operational at the macroscale of whole-brain MEG sensor-space were captured by two complementary mathematical frameworks – global coherence spectrum that parametrizes the strength of band specific synchronization in different frequencies over a set of network nodes (MEG sensors for the purpose of this paper), and metastability that captures the degree of intermittency that exists between two successive synchronization states. Together, the two measures along with the spectral estimates quantifies the dynamic repertoire of the state variables. We observed an emerging dichotomy with aging in pattern of global coherence across slow and fast time scales. The global alpha coherence decreases over lifespan followed a linear relationship whereas global beta coherences are unaffected by aging. The global coherences in slower frequencies - delta and theta on the other hand, are unaffected by aging up to a critical age of around ~45-50 years. Thereafter, the global coherence shows an increase with age up to ~70 years and decrease further upon reaching a peak value. While alpha global coherence could be fitted best with a linear curve, theta and delta variation over age was non-linear. Concurrently, metastability exhibited a monotonically increasing relationship over lifespan in all frequencies (best fitted by a linear curve), with a visible saturation for elderly (~70 years). Interestingly, while increase in metastability in alpha band was truly global, increases in metastability in other bands were region-specific. The decrease in PAF, prominently observed in our study, has been reported to be a biomarker of normal and pathological aging process, especially for dementia, mild cognitive impairment, and Alzheimer's disease. Patients with Alzheimer's disease show a significant decrease in PAF compared to age-matched control group. Parkinson's patients with dementia have a lower PAF compared to age-matched controls. Interestingly, developmental changes in spontaneous electrocortical activity is associated with an increase in PAF from early to late childhood. While the mechanistic explanation of this dichotomy still remains elusive, several computational attempts have suggested a link between the thalamocortical circuitry responsible for alpha rhythmogenesis and age-related morphological differences in thalamocortical circuits to explain slowing down of PAF. In fact, PAF may carry the signature of an ending of rapid neurodevelopmental process of human beings, behaviorally observed as trait developments from adolescence to young adults. Concurrently, cognitive task relevant EEG/MEG studies have linked PAF with scores on cognitive paradigms such as working memory and visual acuity suggesting a crucial role of PAF with age associated changes in attention and memory from YA to OA. We argue while alpha coherence decrease may be associated with neuro compensatory mechanisms, they may not have a direct bearing on performance for which delta and theta may be more informative. Studies have demonstrated that theta rhythms are crucial for information processing underlying sequence learning. Since metastability is a direct measure of the functional capacity of the brain and has been shown to confer cognitive flexibility in task-switching, information-processing and logical memory (Hellyer et al., 2015), this would argue in favor of a compensatory explanation of the global increase in metastability with aging. However, the neural noise hypothesis of aging would suggest a different interpretation. This theory argues that age-related cognitive decline is best explained as a consequence of an increase in the noisy baseline

activity of the brain. According to this framework, global phase inconsistencies as we observe here is an obligatory change resulting from change in underlying scaffold dictated by gradual change in white and grey matter volume that shifts the baseline and result in an unspecific lifespan-associated increase in neural noise. Within this framework, changes in global metastability and coherence reflect an epiphenomenon that occurs due to an increase in neural noise. Future efforts should focus on resolving this debate. One possible direction would be to study brain signals through measures of signal complexity using source reconstructed EEG/MEG, to elucidate the role of specific brain regions in bringing about metastable patterns of activity. More direct estimates of metastable state switching from electrophysiological data could be employed to disentangle the effects of noise. Recent works in this direction have proposed ways to directly estimate metastable switching between synchrony states. This is also necessary to reconcile the region specific metastability patterns we observe across frequency bands, with alpha band metastability increase being truly global versus region-specific enhancement and decrease of metastability in other frequency bands over lifespan. An ongoing research direction in the neuroimaging community is to relate resting state dynamics to performance measures also sometimes referred to as behavioral phenotypes. We use Visual short-term memory task (VSTM) in which the accuracy is anti-correlated linearly with increase in age. Interestingly only the global coherence in alpha band was correlated with precision when the age effects were corrected, while the global coherence in other frequency bands are uncorrelated with VSTM performance (**Fig 5**). On the other hand, metastability has no bearing on performance accuracy once the effects of ageing were considered for any frequency. Thus, except the global network captured by alpha global coherence, the others are non-specific measures of neurophysiological processing.

Within and between network thalamocortical interactions with healthy aging in Control, maintenance, and task switching networks of the human brain

Introduction

The human brain undergoes substantial structural and functional changes across the lifespan. On average, within network resting-state functional connectivity weakens in magnitude while between network connectivity strengthens. Although, few recent attempts demonstrate relationship between Cognition and effective connectivity change during rest over healthy lifespan, it still remains an open question to what extent age related change in thalamic drive reorganizes causality among these resting networks. Using directed connectivity and weighted net causal outflow measures on resting-state fMRI data, we examine both cortical and thalamocortical causal interactions within and between resting-state networks with age. To address this, we select commonly investigated triple large-scale brain networks (implicated in functions such as self-regulation and maintenance, salience and task switching and Cognitive control networks) Default Mode Network (DMN), Salience Network (SN), Central Executive Network (CEN) employing Independent Component Analysis (ICA) as well as spatially matching of hub regions with the important Resting State Networks (RSNs) previously reported. Thereafter, multivariate GCA was performed to test for causality index between ROIs with and without the inclusion of left and right thalamus. There are two major findings, progressively weaker within network causal connections, while strengthening of between network causal connections among core neurocognitive networks with age, primarily reflecting what was previously observed based on correlational analysis. Secondly, we find significant change in all cortical causal connections with thalamus which was not reported previously. Finally, we found that the thalamus plays a critical role in mediating within network causal flow, while salience network plays a critical role in mediating between network causal flow. Our findings strengthen the hypothesis that balancing within and between network causal connectivity is perhaps critical for the preservation of cognitive functions with aging.

Methods

Participants and data acquisition

25 young and 24 elderly individuals participated in this study after providing written consent. Young (13 females and 12 males) ranged in age from 18-33 years (mean age = 25.68 years) and Old (18 females and 6 males) ranged in age from 49-80 years (mean age=58.1 years). All participants gave written informed consent and the study was performed under the compliance of laws and guidelines approved by the ethics committee of Charité University, Berlin advanced Neuroimaging center. Resting state data was acquired from 49 healthy participants. Each fMRI dataset amounts to 661 time points recorded at TR=2s, i.e. about 22 minutes. In the same session, EEG was also recorded, but we do not use the EEG data for our current analysis. No other controlled task was performed. Resting state BOLD activity was recorded while subjects were asked to stay awake with their eyes

closed, using a 3T Siemens Trim Trio scanner and a 12 channel Siemens head coil (voxel size). Voxel time courses are averaged inside ROIs defined by the Desikan-Killiany atlas (Desikan et al., 2006) as implemented in FreeSurfer. The empirical BOLD time series signals from Regions of Interest (ROI) used in this paper for net causal flow estimations is generated by using an automated pipeline. The parcellation used in this study is Desikan–Killiany parcellation (Desikan et al., 2006) which consists of 68 cortical regions of interest (ROIs) with 34 ROIs in each hemisphere and 32 subcortical regions. For our present analysis along with 68 cortical regions, two thalamic regions, left and right thalamus were selected based on this parcellation. FC matrices generated from each subject's MRI data are averaged element-wise to obtain an averaged FC matrix for younger and elderly cohort.

Selection and extraction of three large-scale resting state networks

To identify RSN activity a spatial Group ICA decomposition was performed for the fMRI data of all subjects using FSL MELODIC (MELODIC v4.0; FMRIB Oxford University, UK) with the following parameters: high pass filter cut off: 100s, MCFLIRT motion correction, BET brain extraction, spatial smoothing, normalization to MNI152, temporal concatenation, dimensionality restriction to 30 output components. ICs that correspond to RSNs were automatically identified by spatial correlation with the 9 out of the 10 well-matched pairs of networks of the 29,671-subject Brain Map activation database (excluding the cerebellum network). Subsequently, the three key intrinsic networks were identified by spatially matching with pre-existing templates following widely accepted seven networks resting state parcellation proposed by Buckner and colleagues, each of the cortical regions were classified further down to seven parcellated resting networks.

The SN, which comprises the anterior insula and caudal, rostral anterior cingulate cortex, is important for detection of salience events and switching between other large-scale networks. Bilateral Rostral and Caudal middle frontal gyrus, superior parietal lobule was selected as nodes of CEN. The core DMN regions selected in this work consistently showed anticorrelation with SNs.

Directed connectivity estimation based on Multivariate Granger Causal Analysis

Brain signals of different nodes within and between networks are expected to follow a multivariate probability distribution. For instance, let be a time series of 3 nodes in a network. If there are joint dependencies between and if we calculate unconditional granger causality between ***X*** and ***Y,*** spurious causalities may occur due to common dependency on ***Z.*** Thus, to eliminate the possibility of spurious causalities between two time series Multivariate Granger Causality analysis (GCA) was performed to assess the causal influence between nodes of SN, CEN and DMN. In MVGC spurious causalities are eliminated by conditioning out the common dependencies.

Results

To investigate the effect of thalamus in shaping within and between network causality, we included thalamus as an additional node in our analysis. For each of the three resting state networks, for within network analysis, we included the right and the left thalami, as the seventh and the eighth nodes. Since the mechanism of the MVGC changes with the number of nodes, the causal strengths were not directly comparable between two networks having different number of nodes.

Central Executive Network (Control Network) In elderly group all the connections except, rRMFG to lSPL remained significant ($p < 0.05$, false discovery rate (FDR) corrected FDR corrected). Connections from the rrMFG to the lSPL was mediated by the left Thalamus (lthal). Some significant causal connections were emerging from both the thalami, from the lthal to the lRMFG, the rRMFG, the lSPL, the rSPL, from the rthal to the lRMFG, the rSPL, and the lSPL for the elderly groups (**Figure 4**). For young groups, all the connections without thalamus also found significant after inclusion of the thalamus (figure). Additionally, the left thalamus causally influenced the lRMFG, the lCMFG, and the rRMFG (**figure 4D**). Right thalamus influenced the node lRMFG. Net granger causal outflows were significantly changed after inclusion of thalamus for both the young and elderly groups. Effects of thalamus was greater in the younger individual's net causal values. Left thalamus acted as a causal outflow hub for both the groups. But the causal outflow in the left thalamus was higher in young compared to elderly group. Causal outflows were significantly different in both the groups for all the eight nodes aging.

Salience Network (task switching network) Among three resting state networks, the SN was least affected after inclusion of thalamus. No changes were found in causal structure after inclusion of thalamus in elderly individuals (**Figure 4**). In young individuals, significant causal connections were found from the lThal to the lInsula and from the rThal to the rInsula (**Figure 4**). No significant changes were found in the net causal outflow pattern in both the groups. Left thalamus exhibited positive outflow, higher in the case of old individuals

($p<0.05$). Right thalamus received marginally small negative outflow (inflow) for both groups.

Default Mode Network (self-processing and maintenance)

After inclusion of the thalamus in default mode network, there were restructuring in the causal connectivity pattern found in the elderly individuals. On performing multivariate granger causal analysis on DMN after addition of thalami, some of the earlier significant causal connections disappeared while some thalamo-cortical causal connections emerged as important connections for both the age groups (**Figure 4C, 4F**). Causal connection from rIPL to rMOF continued to be the strongest connection in elderly group as found in the previous section without thalamus (**Figure 4C**). Other than that, GCA revealed significant causal connections from the rMOF to the rPCC, from the rThal to the lIPl, from the lIPL to the rThal, from the rThal to the lMOF for the elderly people (**Figure 4C**). After the introduction of thalami, some of the connections between the left hemispheric nodes disappeared in elderly. For the young group, the effect of the inclusion of thalamus was more pronounced compared to the elderly individuals (**Figure 4F**). Instead of the connection from the lMOF to the lPCC, the connection from the lThal to the lPCC emerged as the strongest one after the inclusion of the thalami (though the lMFC to the lPCC connection also remained significant). In addition to that, other significant connections were from the lMOF to the lIPL, from the lThal to the lMOF, from the lThal to rThal, from the lThal to the rPCC, from the rThal to the lMFC, from the rThal to the rMFC, from the rMFC to the rPCC, and from the rMFC to the rIPC (**Figure 4F**) suggesting substantial effect of thalamus in reorganizing within network causality in cortical networks and also revealing the effect is the strongest in the younger group compared to elderly. This could be related to the thalamic decline with aging.

Net granger causal outflows were significantly changed after inclusion of the thalamus for the young individuals left thalamus emerged as a causal outflow hub for young group. Patterns in the net causal outflows were unchanged in elderly group (**Figure 5**). rIPL continued to be causal outflow hub for elderly group, even after inclusion of thalamus. Causal outflows were significantly different in both groups ($p<0.01$).

Between network directed connectivity involving changing role of Thalamus with age

Next we investigated between network causality in presence of the thalamus for both groups. Causal connections from the thalamus to all three network nodes, namely the DMN, the SN, and the CEN in both age groups were found significant ($p< 0.05$, false discovery rate (FDR) corrected). Thalamus was also causally driven by CEN and SN for both elderly and young groups (**Figure 6C and 6D**).

Weighted net causal outflows were significantly affected after inclusion of thalamus. Now thalamus acts as a causal outflow hub for elderly group. SN received highest causal outflow for young group (**Figure 6**). Unlike the within network results, in between network analysis causal outflows were greater in the elderly group. Among other three networks, the SN had positive outflow and the DMN had negative outflow for both the groups. After inclusion of thalamus, outflows in the CEN changed its direction in old cohorts.

Overall, thalamus had not changed the causal connectivity pattern between three resting state networks. With thalamus providing exogenous drive and afferent connections to various cortical areas, the causality dynamics between three resting state networks remained unaltered. However, thalamus received causal influences from both task switching network (SN) and Cognitive control network (CEN), and as a feedback influenced all the three resting state networks in succession. We further quantify these mutual directed information flow using weighted net causal outflows, in particular, causal outflows for the elderly group was affected in the presence of thalamus. The effect of thalamus was dissimilar in between network analysis compared to within network analysis. Effect was higher predominantly in elderly group.

Discussion In the present study, we employ multi variate granger causality analysis to probe within- and between-network causal relationships among three key intrinsic resting state brain networks or triple brain networks with the hope to facilitate more biologically meaningful interpretations with healthy aging. Every cortical region receives feedforward projections from the thalamus and in turn sends outputs to one or multiple thalamic nuclei**. T**halamocortical projections relay nearly all incoming information to the cortex as well as mediate corticocortical communication. Thus, a fuller insight into brain functional characterization certainly requires knowledge of the organization and properties of thalamocortical interactions. In our analysis with effective connectivity measures thalamus emerges as an important node to critically influence both within- and between- network connectivity patterns among RSNs. After inclusion of thalamus in the between network analysis, thalamus acts as a causal outflow hub and causally drives all three network nodes for both the age groups. In contrast, in within network analysis, the influence of thalamus in reorganizing within network causality is much more prominent in younger age group compared to the elderly. In DMN, left

thalamus emerge as a causal outflow hub for young group while patterns in the net causal outflows were unchanged in elderly group compared with the pattern when thalamus was not included in the analysis. After inclusion of thalamus in CEN within network analysis, though left thalamus acts as a causal outflow hub for both the groups, the causal outflow values are higher in young compared to elderly group. This preferential influence of thalamus on younger individual is consistent with the thalamic decline with aging as discussed above. Also, among three resting state networks, the SN remains least affected after inclusion of thalamus, both in within- and between- network analysis. No changes were found in causal architecture within SN after inclusion of thalamus in elderly individuals. In young individuals also changes are minimal. The net causal outflow pattern also does not change after inclusion of thalamus in both the groups. These findings are in concurrence with the observations made by the previous studies that in contrast to DMN and CEN, within network connectivity is preserved or increased in SN with aging. Our result suggests that this preservation of connectivity within task switching network (SN) is driven by thalamus.

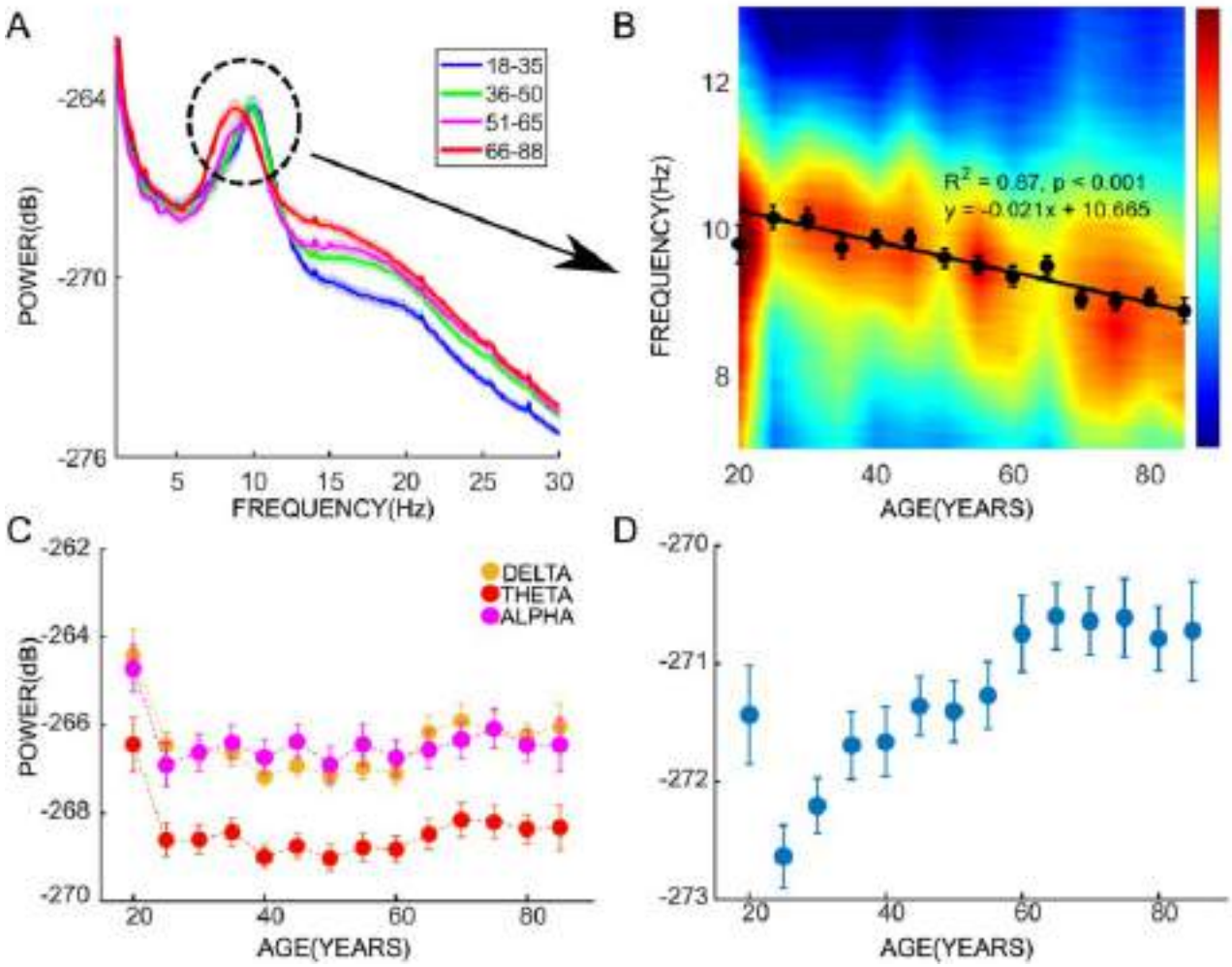

Figure 1. Relation between global spectral activity and age. A. Plots of mean power spectral density for 4 non-overlapping age groups i.e. 18-35, 36-50, 51-65 and 66-88. Shaded region denotes standard error of mean. B. Variation of alpha activity with aging. Center frequency in the alpha band for each age bin has been plotted as solid circles and solid black line is the linear fit of these points (labels indicate effect sizes, significance and correlation function) C. Spectra in the delta, theta and alpha bands as a function of age. D. Beta spectra as a function of age

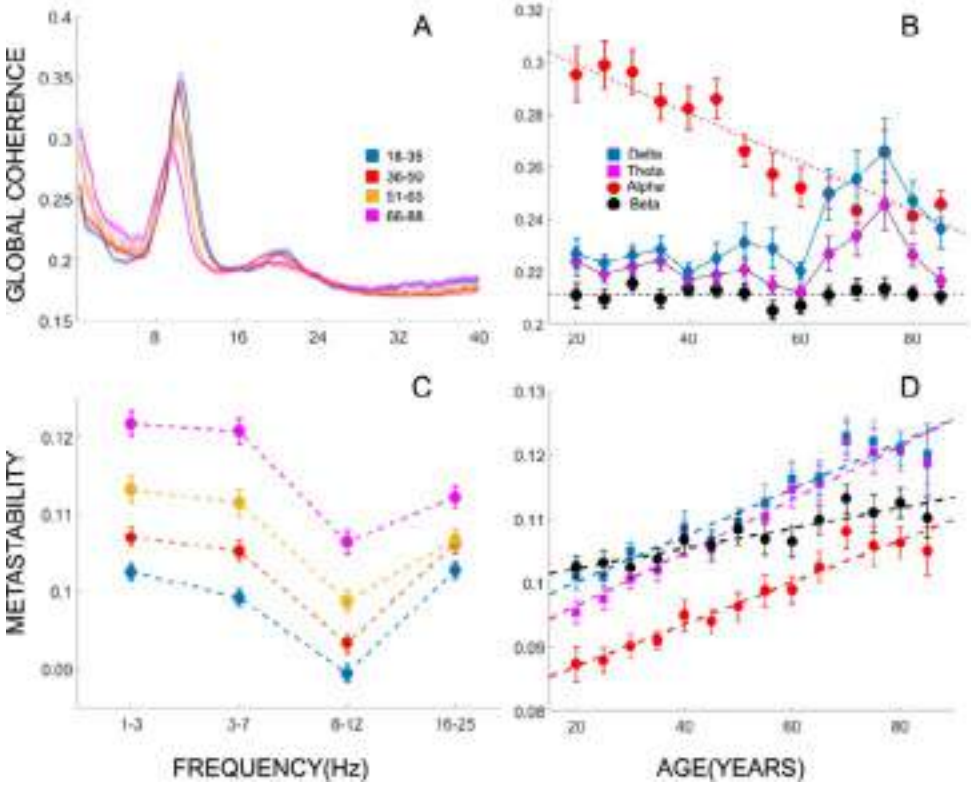

Figure 2. Differential changes in global coherence with aging. A. Plots of mean global coherency for the four age groups. Shaded region denotes s.e.m. B. Differential variation of global coherence for frequency bands. C. Metastability for four age groups in delta, theta, alpha and beta bands.

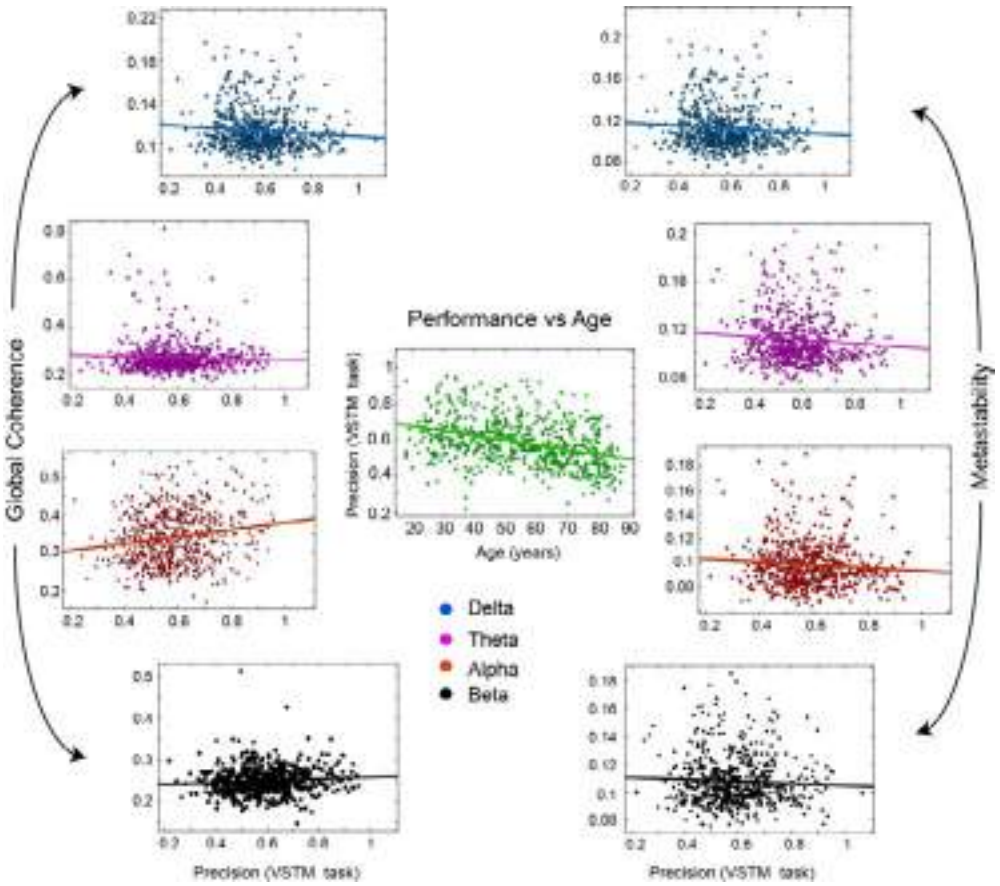

Figure 3: Correlation of VSTM precision with global coherence and metastability. Center: Scatterplot of precision with age. Left: Scatterplot of band-specific global coherence with precision in VSTM task. Right: Scatterplot of band-specific global coherence with precision in VSTM task

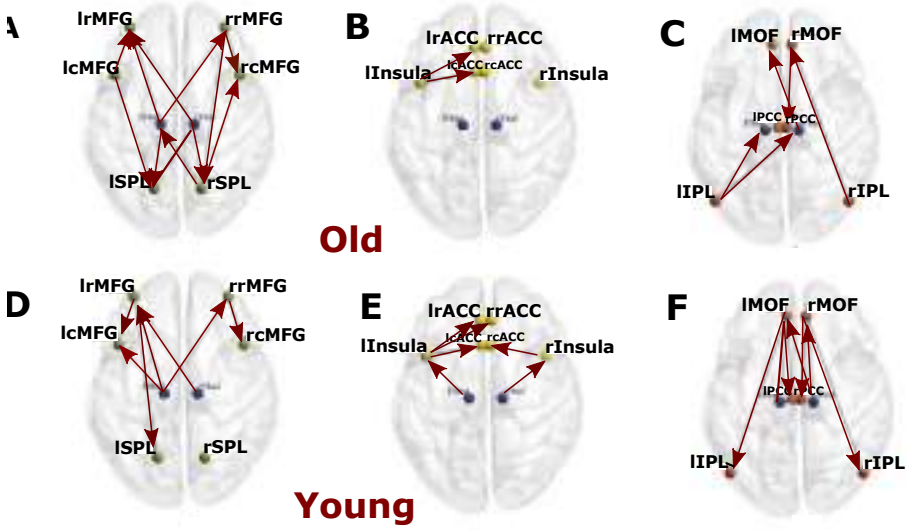

Figure 4. Directed Connectivity between the nodes of three resting state networks (CEN, SN and DMN) with thalamus. A. Directed connectivity between six key nodes of CEN (shown in green), B. six key nodes of SN (yellow), C. six key nodes of DMN (red) for elderly group in presence of thalamic nodes (blue). D. Directed connectivity between six key nodes of CEN (green), E. six key nodes of SN (yellow), F. six key nodes of DMN (red) for young group in presence of thalamic nodes (blue).

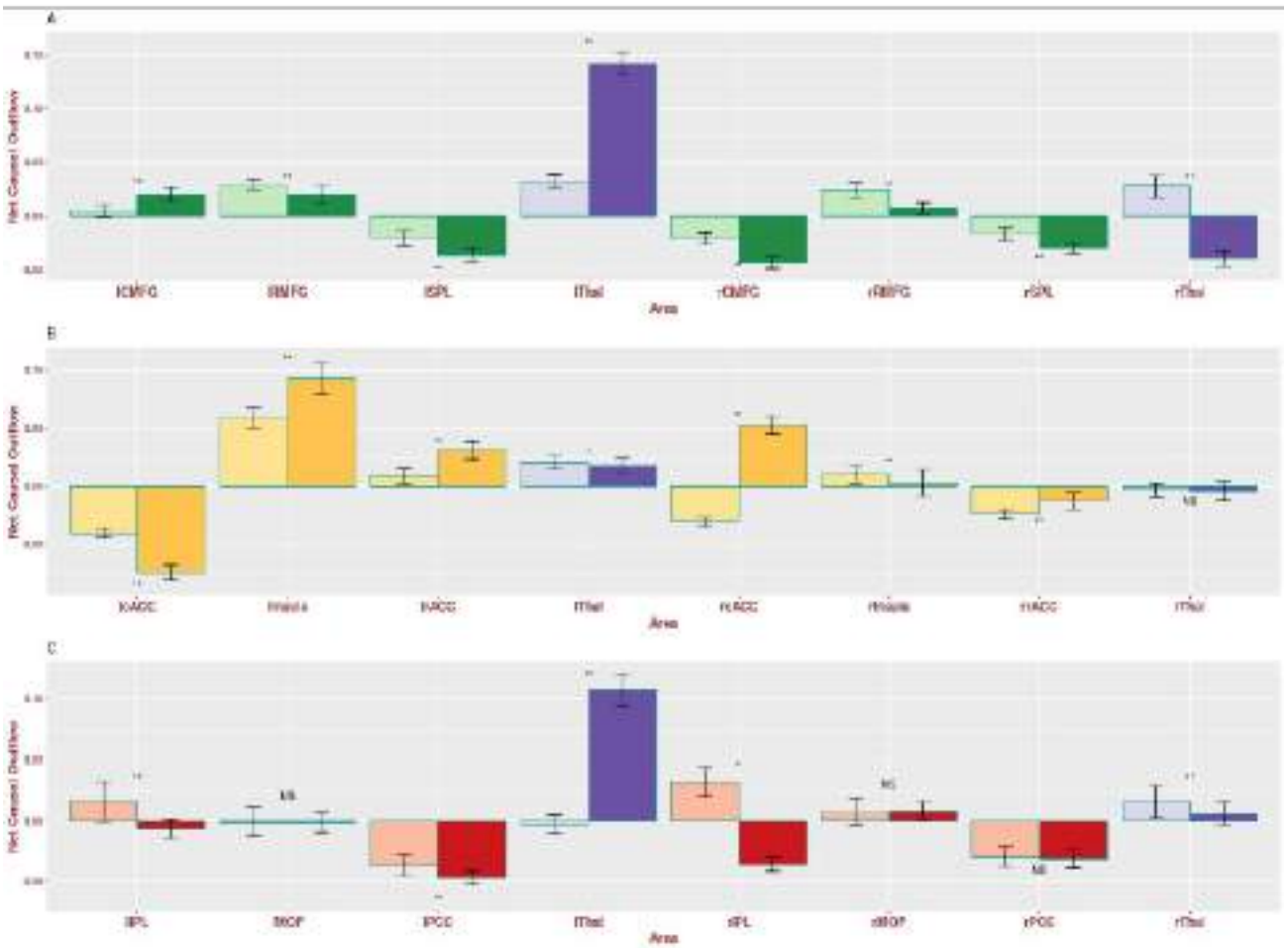

Figure 5. Weighted net causal outflow for within network effective connectivity analysis A. Weighted net causal outflow in nodes of the central executive network and two thalamic regions (left, right). B. Weighted net causal outflow in nodes of the salience network and two thalamic regions (left, right). C. Weighted Net causal outflow for default mode network and two thalamic regions (left, right). Weighted net causal outflows were significantly different in few nodes in each of the three RSN young and elderly group ($p < 0.05$ is indicated by '*', $p<0.01$ is indicated by '**', No significant difference is indicated by 'NS')

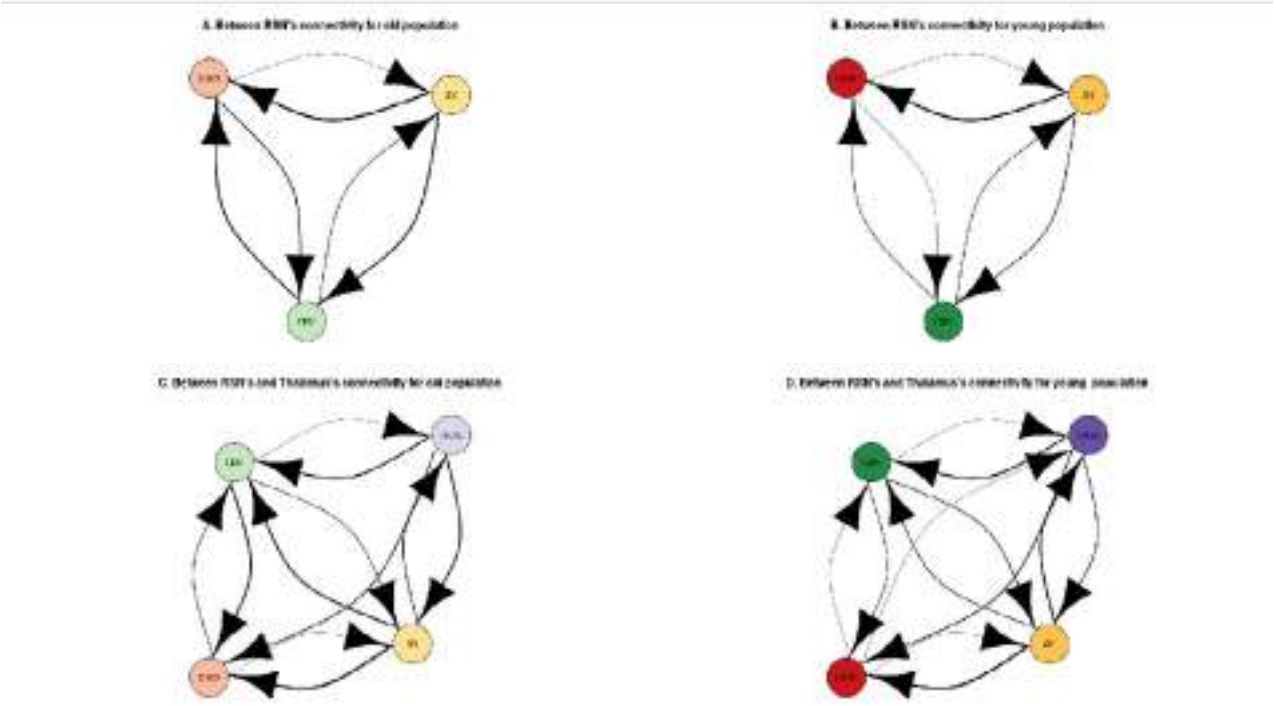

Figure 6. Directed connectivity between three resting state cortical networks including thalamus. A. directed connectivity between three nodes representing three RSN, SN (yellow), DMN (red), CEN (green) for older participants. B. Results for Effective connectivity between three nodes representing three RSN for young participants C. Directed connectivity between three nodes representing three RSN and fourth node representing the thalamus (blue) for older participants D. Effective connectivity between three nodes representing three RSN and fourth node representing the thalamus for young participants

Publications

1. Sahoo, B., Pathak, A., Deco, G., Banerjee, A.*, & Roy, D.* (2020) (*co-corresponding authors). Lifespan associated global patterns of coherent neural communications NeuroImage, 116824.

2. Kumar, G. V., Dutta, S., Talwar, S., Roy, D.*, & Banerjee, A.* (2020) (*co-corresponding authors) Biophysical mechanisms governing large - scale brain network dynamics underlying individual-specific variability of perception. Eur J. Neuroscience 2020 Apr 17. doi: 10.1111/ejn.14747

3. Ray, D., Hajare, N., Roy, D., & Banerjee, A. (2020). Large-scale functional integration, rather than functional dissociation along dorsal and ventral streams, underlies visual perception and action. Journal of Cognitive Neuroscience, 1-15.

4. Das, Moumita, Vanshika Singh, Arpan Banerjee, and Dipanjan Roy. "How do thalamocortical connections shape causal structure among resting state brain networks during aging?" BioRxiv (2019): 827451.

5. Surampudi, S. G., Misra, J., Deco, G., Bapi, R. S., Sharma, A., & Roy, D. (2019). Resting state dynamics meets anatomical structure: temporal multiple kernel learning (tMKL) model. NeuroImage, 184, 609-620.

6. Harlalka, V., Bapi, R. S., Vinod, P. K., & Roy, D. (2019). Atypical flexibility in dynamic functional connectivity quantifies the severity in autism spectrum disorder. Frontiers in human neuroscience, 13, 6.

7. Mukherjee, S., Akbar, I., Bhagat, R., Hazra, B., Bhattacharyya, A., Seth, P., Roy, D.* & Basu, A.*(* co-corresponding author) (2019). Identification and Classification of Hubs in microRNA Target Gene Networks in Human Neural Stem/Progenitor Cells following Japanese Encephalitis Virus Infection. mSphere, 4(5), e00588-19.

Presentations

1. Dipanjan Roy: Invited speaker International conference Brain Modes Conference 2019 "Unified principles of Brain function" Dec 13-14, 2019 Pokhara, Nepal.

2. Dipanjan Roy: Invited talk at Neuro-AI India's first symposium at the interface of Neuroscience and Data Science "Learning subject-specific brain state transitions using big data through a unifying framework in MEG, fMRI, and computational modelling" Aug 3-4, 2019 Bangalore.

Funding

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

2. Oscillatory Network Dynamics in Perceptual Learning SR/CSRI/21/2016 Department of Science and Technology (DST) Initiated in 2017 and for three years

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.

Collaborators

1. Arpan Banerjee, Anirban Basu NBRC

2. Bapi Raju, Avinash Shrama, Vinod Pallakad IIIT-Hyderabad

3. Gustavo Deco Institució Catalana de la Recerc Estudis Avançats (ICREA), Universitat Pompeu Fabra, Passeig Lluís, Companys 23, Barcelona, 08010, Spain

4. Petra Ritter Bernstein Center for Computational Neuroscience and Max Planck Institute Human development and Cognition

5. Viktor Jirsa (Director) institute system Neurosciences Aix-Marseille Université, Inserm, INS UMR_S 1106, Marseille, France

Ellora Sen

Department of Cellular & Molecular Neuroscience,

Translational Neuroscience

PhD Students

Sk. Touseef Ahmad
Pruthvi Gowda
Shruti Patrick
Kirti Lathoria
Shalini Sharma

MSc Student

Shashwati Tripathi

Technical Assistant

Shanker Datt Joshi

Lab attendant

Rajesh Kumar Kumawat

Metabolic - Inflammation cross-talk in Glioblastoma: Understanding immune evasive responses

Background and significance

Dysregulated metabolism characterized by the "Warburg effect" is an essential hallmark of tumor cells. Along with deranged metabolism, inflammation is also regarded as another indispensable participant in tumor progression. Glioblastoma multiforme (GBM) - the most malignant of brain cancers characterized by aberrant metabolic profile, is largely refractory to current therapeutic regimens. As there is significant overlap between metabolic, inflammatory and epigenetic pathways in cancers, studies from our laboratory are investigating how inflammation-metabolism cross-talk engages different signalling pathways and chromatin modifiers to target genes associated with survival and immune evasion in GBM.

(i) Silencing of Suppressor of cytokine signaling 1 (SOCS1) is associated with increased inflammation in GBM. SOCS1 is known to regulate Toll like receptor (TLR4) signaling and elevated TLR4 levels are observed in GBMs. On investigating the molecular and functional association between the two, we observed that mutational status of p53 impacts the transcriptional plasticity of SOCS1 promoter through differential recruitment of cofactors/epigenetic modifiers in response to TLR4 inhibition. The Cancer Genome Atlas (TCGA) dataset indicated that p53 mutational status effects TLR4 and SOCS1 levels. By elucidating a previously unrecognized novel dimension of mutant p53 in affecting regulators of inflammatory response, our study has the potential to uncover therapeutics targeting the link between p53 and inflammation in glioma.

(ii) Yes-associated protein 1 (YAP1) acts as a major mechano-transducer by sensing mechanical stimuli like cell density and relays them to the nucleus. Nuclear YAP1 associates with members of the TEA domain containing transcription factors (TEADs), and this YAP/TEAD complex regulates genes required for growth and oncogenic transformation. The role of YAP1 in hyper-proliferation and tumor formation is known. Somatic mutations in the isocitrate dehydrogenase 1 (IDH1) gene in glioma have been associated with better prognosis than those harboring wild-type IDH1. Importantly, IDH1 is increasingly being recognized as an independent prognostic marker in glioma as occurrence of IDH1 mutations (IDH1-MT) has been associated with improved clinical outcomes. Diminished YAP1 level was observed in IDH1-MT as compared to IDH1-WT. The role of YAP1 in affecting mitochondrial dynamics and redox homeostasis crucial for metabolic program in these mutants is currently being investigated.

(iii) As increasing evidences link disruption of circadian rhythms with metabolic reprogramming in cancers, we investigated the role of metabolism in orchestrating circadian rhythm and the involvement of the latter in regulating pro-inflammatory tumor microenvironment. Genetic and pharmacological manipulation of lactate dehydrogenase (LDHA) suggested the functional coupling between lactate, clock and pro-inflammatory cytokine IL1β. Our studies linking metabolism-inflammation axis with molecular clock suggests the importance of circadian rhythms for effective design of chronotherapies in cancers.

(iv) The biological activity of Tau - major neuronal microtubule-associated protein (MAP) is regulated by its degree of phosphorylation, with Tau hyperphosphorylation resulting in its dissociation from microtubule and aggregation that subsequently culminates in neuronal cell death. Abnormal tau phosphorylation is a pathological characteristic of traumatic brain injury (TBI). Altered brain metabolism in TBI is accompanied by dyregulated inflammation. As the role of TNFα- in chronic inflammatory conditions and metabolism is known, we are investigating whether TNF regulated metabolic program have a role in Tau expression in neuronal cells.

Presentations

1. Elloara Sen: Targeting metabolism – inflammation link in glioma: Implications in therapy. Neuglia 19, Dept of Biochemistry, University of Madras, Chennai, August 2019
2. Elloara Sen: Epigenetic landscape and p53 mutational status: Role in SOCS1 transcriptional regulation. INDO-US 2019 New Insights into the Inflammation, Immunity, and Pathobiology of Diseases, Port Blair, Dec 2019
3. Elloara Sen: Tumor heterogeneity in glioma: Therapeutic Challenges "Experts' Opinion on Molecular Medicine" West Bengal State University, 12th Dec, 2019
4. Elloara Sen: Tension at cross-border of determinism and causality: Reconciling phenomenological philosophy with reductionist sciences. The Nalanda Dialogues, Nalanda Jan 16th 2020
5. Elloara Sen: In search of Self. International Summit on Women in STEM Visualizing the Future: New Skylines. New Delhi 22nd Jan 2020
6. Elloara Sen: Philosophy as co-traveler in the journey of Science. National Science Day, Faculty of Interdisciplinary & Allied Sciences, Delhi University, 27th February 2020

Funding:

1. Inflammation regulated metabolic reprogramming: Implications in tumor progression. Unit of excellence in cancer biology DBT. (#BT/MED/30/SP11016/2015)
2. 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)

Neeraj Jain

Department of Systems Neuroscience,

Cognitive Neuroscience

Post Doctoral Fellow

Dr Prem Chand (until October, 2019)

PhD Students

John Thomas
Atanu Datta
Arti Kumari
Raghav Shankar

MSc Student

Mantosh Patnaik

Project Assistants

Dixit Sharma (until July 2019)
Arun E.V.R.

Technical Assistants

Mithlesh Kumar Singh
Hari Shankar

Organization of Somatosensory and Motor Systems and the Effects of Spinal Cord Injuries

Research in my laboratory is focused towards understanding the organization and information processing in the somatosensory and motor systems of the brain. The effects on spinal cord injuries on the organization of the brain is another major focus of our laboratory. We use rodent and non-human primate models, and different technical approaches that include functional Magnetic Resonance Imaging (fMRI), 2-photon imaging, electrophysiology, and neuroanatomy to address these research questions.

We have earlier shown that injuries to the dorsal columns of the spinal cord at cervical levels results in large scale reorganization of the primary (S1 or area 3b) and secondary (S2 and parietal ventral area) somatosensory cortex, and the medullary brainstem nuclei (e.g. Tandon et al., Journal of Neuroscience, 2009; Dutta et al., Brain Structure and Function, 2014; Halder et al., Cerebral Cortex, 2017). There are also significant changes in certain aspects of the movement representation of the thumb (D1) in the primary motor cortex or M1 (Kambi et al., Journal of Neuroscience, 2011). Our studies in rats have also shown changes in the organization of the M1 (Tandon et al., European Journal of Neuroscience, 2013). We have also established mechanisms of reorganization of area 3b using electrophysiological and anatomical approaches (Kambi et al., Nature Communications, 2014; Chand and Jain, Journal of Neuroscience, 2015).

More recently we have used functional Magnetic Resonance Imaging (fMRI) to study brain-wide changes in the organization and connectivity of the somatosensory cortex. We reported that in the primary somatosensory cortex (area 3b) of macaque monkeys and humans resting-state somatosensory functional network is characteristic for each body-part representation. This connectivity is broadly similar in monkeys and humans, and generally reflects the underlying anatomical connectivity (Thomas et al., bioRxiv 775569; https://doi.org/10.1101/775569; also see Annual Report for 2017-18).

We also determined how spinal cord injuries alter the somatomotor and other networks in terms of connectivity between nodes of a network, and interaction between different networks. We reported last year that the deafferented hand representation no longer remains a part of the somatomotor network, and its interaction with the default mode network (DMN) increases as a result of the lesion. DMN is a network that is traditionally believed to represent the correlated network which is active when no specific task is being performed by the subject.

Brain reorganization in non-human primates. Here we report on our continuing studies on how interaction of the nodes of the resting-state networks is affected by spinal cord injuries. We studied the effects of unilateral transections of the dorsal columns at cervical levels in two

adult macaque monkeys. Multiple resting state fMRI scans of the monkeys were acquired before and after the lesion. In addition, BOLD signal was acquired while the hand and the chin underwent tactile stimulation to establish the brain reorganization. T2 weighted MR images of the spinal cord were acquired before and after the lesions of the dorsal columns to determine the extent and level of the lesion (see Annual Report 2018-19).

The acquired BOLD signals for both the resting state and stimulation were analyzed after performing standard pre-processing steps. Data from stimulation experiments was analyzed by implementing General Linear Model to localize the brain activation regions. Results showed expansion of the chin representation in the deafferented hand region of area 3b (Fig. 1).

For the resting-state data region-to-region correlation analysis was performed to determine functional connections between specific brain areas. Here we investigated the effects on functional connectivity of the motor cortex. We have previously shown that the monkeys with injuries to the dorsal columns are no longer able to form precision grip. Moreover, in the M1 of these monkeys the movement representation for digits, particularly of D1, is no longer normal as determined by stimulation experiments. The results show that lesions of the dorsal columns, which is a sensory deafferentation, alter the functional network of the motor hand area. Due to the lack of somatosensory inputs, the functional connectivity of the hand representation in the primary area 4 had reduced functional connectivity with the ventral premotor area in the lesion affected hemisphere in both lesioned monkeys (Fig. 2).

Brain reorganization in rats. In order to understand mechanisms of brain reorganization it is important to compare across species. As mentioned above, our laboratory also studies the rodent system. We have observed that after transections of the dorsal columns of the spinal cord, unlike in monkeys, primary somatosensory cortex (S1) of rats does not reorganize. In order to understand mechanisms of this important difference between the brain reorganization in the two species, experiments were done to determine if subcortical somatosensory nuclei undergo reorganization following spinal cord injuries in rats. We made lesions of the dorsal columns in rats and mapped their S1 and brainstem nuclei. The results showed that in animals with complete lesions, in the deafferented S1 cortex there was no expansion of the face or any other intact inputs. Neurons in these parts of S1 remained unresponsive to touch on any part of the body even months after the injuries. Multiunit mapping of the brain stem nuclei revealed that the brain stem cuneate nucleus also does not reorganize unlike in monkeys. Neurons in the deafferented cuneate nucleus did not respond to touch on the face (Fig. 3). These data point to a fundamental difference in plasticity mechanisms of the two species.

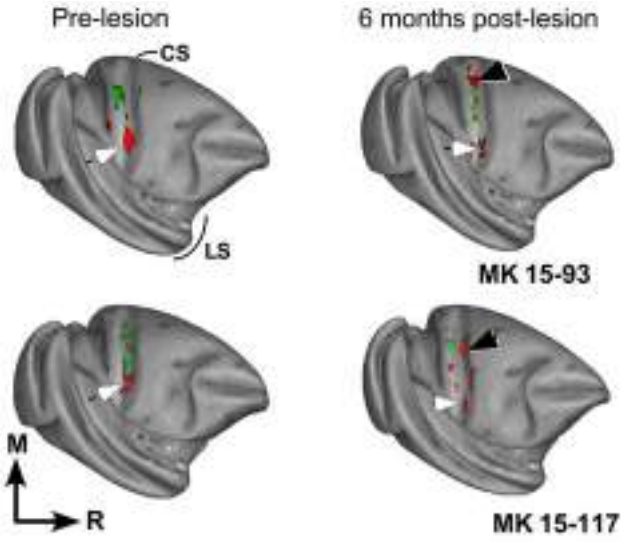

Figure 1. Organization of area 3b in monkeys (top row) MK15-93 and (bottom row) MK15-117 before transection of the dorsal columns (left) and 6 months after the transection (right) shown on partially inflated brain surface. BOLD signal following tactile stimulation of the chin (red) and hand (green) shows that in addition to the normal responses to the chin stimulation (white arrows), post-lesion responses to chin stimulation are evoked more medially in area 3b where hand responses are expected (black arrowheads). Responses to stimulation of the hand remain after the lesion because the lesion was partial. For normal chin responses, $p<0.005$, uncorrected; for hand responses, $p<0.005$, uncorrected; and for chin responses in the hand region; $p<0.02$, uncorrected. This figure is shown here for reference, and is same as shown in Annual Report for 2018-19. CS, central sulcus; LS, lateral sulcus; M, medial; R, rostral.

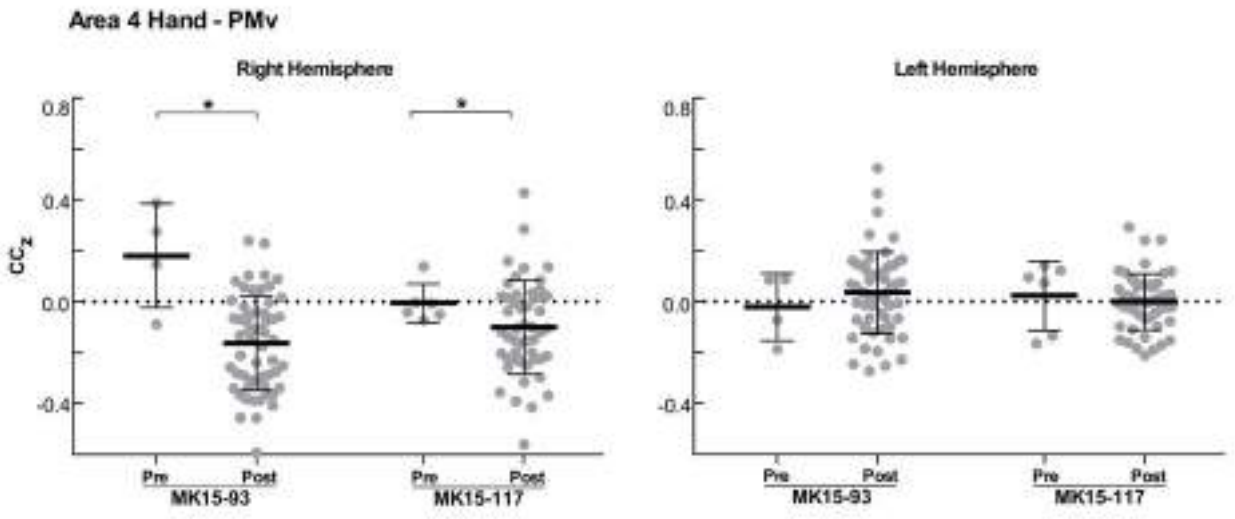

Figure 2. Resting-state functional connectivity of area 4 hand representation to ipsilateral ventral premotor area (PMv) before and after transection of the dorsal columns for monkeys MK15-93 and MK15-117. The left panel shows connectivity in the right hemisphere, which is contralateral to the spinal cord lesion; the right panel shows connectivity in the left hemisphere. For each hemisphere both pre- and post-lesion connectivity is shown. Each point denotes Fisher-z transformed correlation coefficient (CCZ) for each resting-state session. Asterisks* denote statistically significant difference ($p<0.05$, Welch's t-test).

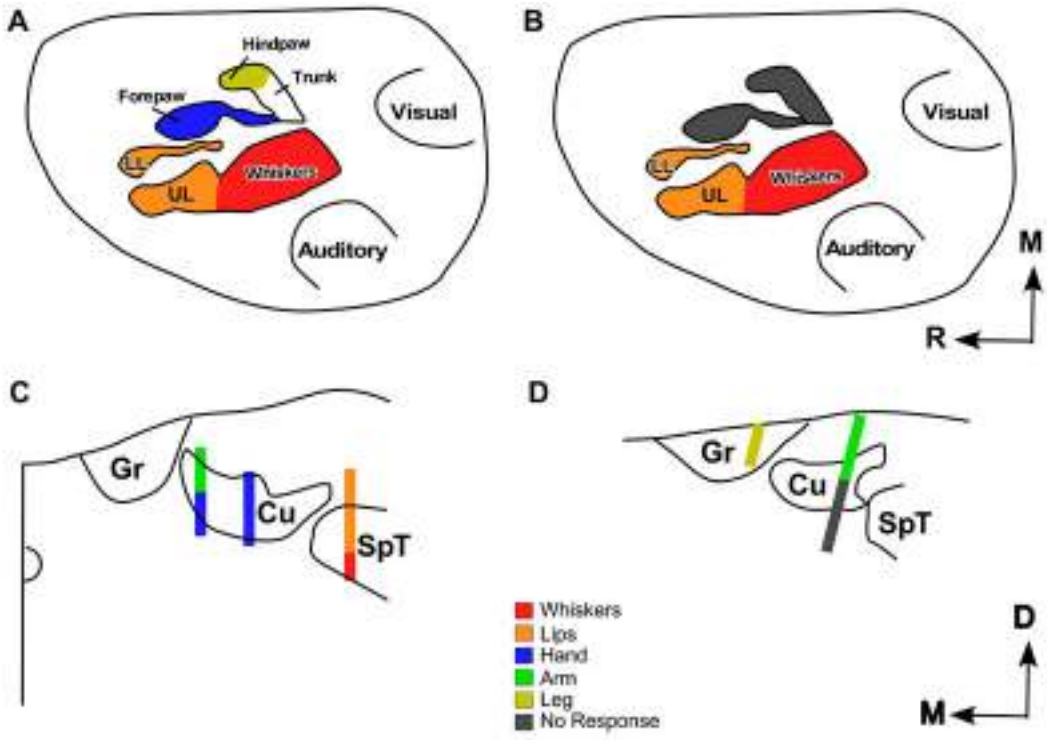

Figure 3. Organization of the primary somatosensory cortex and brain stem nuclei in normal rats and after dorsal column transections. (A) A schematic showing somatotopy in a normal rat. Locations of the primary visual cortex and the primary auditory cortex are shown for reference. LL, lowerlip; UL, upper lip. (B) A schematic showing effects of transection of the dorsal columns on the somatotopy in S1. The deafferented parts of S1 (grey) remain unresponsive to touch on any part of the body. (C) Somatotopy in the brain stem cuneate nucleus (Cu) and the spinal trigeminal nucleus (SpT) in a normal rat shown on outline diagram of a part of the coronal section through medulla. The vertical colored bars show the responses of neurons in three microelectrode penetrations (see the colour key). Nucleus gracilis (Gr) is also shown. (D) In a rat with complete transection of the dorsal columns at cervical levels there is no response to touch in the hand (grey bar). Neurons remain unresponsive to touch on any part of the body, although there are responses to touch in the arm because these inputs enter the spinal cord rostral to the level of the lesion. Responses in the nucleus gracilis also remain normal (yellow). R, rostral; M, medial; D, dorsal.

Publications

- Kamal Sharma, Neeraj Jain and Prabir K. Pal (2020). Detection of Eye Closing/Opening from EOG and its Application in Robotic Arm Control. Biocybernetics and Biomedical Engineering. 40:1-14.

Presentations

1. John Thomas, Dixit Sharma, Sounak Mohanta and Neeraj Jain 'Somatosensory Area 3b network is a composite of multiple distinct networks in macaque monkeys and humans', Neuroscience 2019, Annual Meeting of the Society for Neuroscience, USA. Oct 18-23, 2019; Chicago, USA.
2. Neeraj Jain, 'Intelligence: A neurobiologist perspective', International Workshop on Science of Intelligence, IIT Jodhpur, 18-19 January, 2020.
3. Neeraj Jain 'Spinal Cord Injuries and the Brain' Plenary Lecture at the 27th Annual Meeting of Indian Academy of Neurosciences, at AIIMS New Delhi; Nov 18-21, 2019.

Funding

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Collaborator

Prof P Raghunathan, NBRC

Award

Haryana Vigyan Ratna Award

Pankaj Seth

Department of Cellular & Molecular Neuroscience,

Translational Neuroscience

PhD Students

Chitra MS Singal
Hriday S. Pandey
Reshma Bhagat
Priyanka Singh
Himali Arora
Bindu
Guneet Kaur

MSc Student

Surbhi

Project Assistants

Paritosh Jaiswal,

Rishabh Kapoor

Technical Assistants

Durgalal Meena
Naushad Alam

Cellular and Molecular Mechanisms of HIV-1 and Zika Virus Neuropathogenesis

Despite the fact that India has millions of HIV/AIDS patients, very few researchers are engaged in studying molecular mechanisms of neurocognitive and motor deficits in AIDS patients. This is primarily due to complexities of the disease, lack of apt experimental models and challenges in the field. This laboratory of NBRC is among the very few labs not only in India, but also in world, that has successfully overcome these challenges by designing model systems of human origin. Our laboratory employs primary cultures of human fetal brain derived neural stem cells (hNSCs) and brain cells differentiated from them to understand the molecular mechanisms in the area of Human immunodeficiency virus-1 (HIV-1) and Zika virus (ZVKV). We are investigating the underlying mechanisms for HIV-1 and ZIKV mediated neurodegeneration in brain cells, particularly effect of their proteins on human astrocytes and neurons and hNSCs.

The field of neuroAIDS encompasses studies to understand how HIV-1 and its proteins cause neurocognitive disorders that are seen in HIV/AIDS patients. In current times, AIDS patients are treated with a cocktail of anti HIV drugs collectively called as combinatorial antiretroviral therapy (cART). The cART effectively inhibits viral replication in circulatory system of patients and hence the impact of the virus on immune cells ceases to a great extent. This has helped in preventing the mortality amongst the AIDS patients quite significantly. Unfortunately, the virus that traffics into brain, cannot be cleared due to poor penetration of cART drugs into brain. The brain hence serves as a *safe heaven* for the virus and it continues to harbor HIV-1 in glial cells (astrocytes and microglial cells) and produce the viral proteins like Transactivator of transcription (Tat). HIV-1 Tat has been reported in cerebrospinal fluid (CSF) of the AIDS patients that were successfully treated by cART, suggesting the presence of virus in brain even in the post cART period.

With advent of cART most of the damage to neurons is mediated through astrocytes, as the virus resides in these cells. Currently, we are focusing to understand how astrocytes mediate neuronal death using neuron glial co-cultures derived by differentiating human neural stem cells. We are investigating how HIV-1 viral protein, Transactivator of transcription (Tat) modulates the neuron-glia interactions that culminate into neuronal damage. We use cell and molecular biology approaches that include - live cell calcium imaging in human brain cells, time lapse microscopy, miRNA sequencing based assays, gene expression studies and bioinformatics tools.

Our laboratory is studying the importance of astrocytes in mediating neuronal damage and death by gaining insights into cellular and molecular mechanisms for astrocyte-mediated neuronal damage by HIV-1. We are studying the role of astrocyte on HIV-1 neuropathogenesis by multi prong approach. Firstly, we are probing into HIV-1 Tat induced alteration in EphrinA3 and EphA4, two

proteins involved in neuron-glia crosstalk. EphrinA3 is abundantly present on the astrocytes, while EphA4 - a tyrosine kinase receptor is present on the neurons. This line of investigation is based on the fact that EphrinA3 and EphA4 interaction alters spine density in neurons and glutamate levels in the synapse during neuron-astrocyte interactions under physiological conditions. Incidentally, both spine density and glutamate levels are altered during HIV-1 neuropathogenesis and with exposure of neuronal and glial cells to HIV-1 Tat, hence we hypothesized that EphrinA3 and EphA4 may be involved. Using human astrocyte-neuron co-culture system derived by differentiating primary human neural stem cells (hNSCs), we observed elevated expression of EphrinA3 in astrocytes in the presence of HIV-1 Tat. The glutamate levels in the supernatant of co-cultures were increased while the levels of glutamate transporters EAAT1 and EAAT2 were decreased. When we introduced EphrinA3 knockdown, it decreased the glutamate levels and glia mediated neurotoxicity. Studies for identifying the microRNAs regulating the EphrinA3 and EphA4 are in advanced stages. We performed Next Generation Sequencing (NGS) on astrocytes transfected with HIV-1 Tat and screened microRNAs that are downregulated and are also targeting the EphrinA3 3'UTR. Validation through qPCR reveals miR-4792, miR-181-a-2 and miR-4664-5p to be important for regulating EphrinA3 and EphA4.

Secondly, we are studying the role of Coronin-1a in astrocyte physiology. This approach is based on recent reports that suggest Coronin-1a to be important for cognitive abilities in a rat model and neurocognitive deficits are one of the hallmark features in neuroAIDS patients. Furthermore, Coronin-1a, an actin-binding protein, is associated with important cellular processes such as-cell migration, phagocytosis, morphogenesis, cellular trafficking, cytokinesis and many of these are impacted by HIV-1 Tat protein. Hence, we are investigating the role of Coronin-1a in modulation of astrocytic function by HIV-1 Tat. Our experiments with human astrocytes indicate that HIV-1 Tat can modulate the Coronin1A expression. In fact, knockdown of Coronin-1a using siRNA tools altered critical physiological functions of astrocytes that included decreased calcium flux and altered PLCy1 phosphorylation in ATP stimulated astrocytes. These observations encouraged us to study its role in astroglial activation. Knockdown of Coronin-1a alleviates the HIV-1 Tat induced astrocyte activation marked by measuring the levels of Glial fibrillary acidic protein (GFAP), cytokine, and glutamate release. These observations suggest important roles of Coronin-1a in modulation of astrocyte physiology and pathophysiology that may help explain mechanisms of glia mediated neurocognitive deficits in neuroAIDS cases. These findings would open new avenues for research in this field.

As mentioned earlier, we are also exploring mechanisms for neuropathogensis caused by Zika virus (ZIKV). This neurotropic virus causes microcephaly, a condition that results in abnormally smaller head size in around 7-10% of infants born to mothers infected with ZIKV during their first trimester of their pregnancy. Zika Virus consists a positive sense RNA genome and is spread through mosquitoes that cause dengue and Chikungunya. The viral genome encodes for a polyprotein with three structural proteins and seven non-structural proteins. Structural proteins are: capsid (C), premembrane/membrane (PrM), and envelope (E protein); non-structural proteins are NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5. ZIKV transmission has been reported in several countries, as well as in India. We have recently reported that E- protein of ZIKV severely affects the proliferation of human fetal brain derived neural stem cells via dysregulation of miRNA circuitry. For deeper insights into these observations, we performed detailed molecular studies and found that the differentially expressed miRNAs targeted the WNT signaling in hNSCs. Our follow-up study revealed that WNT2 is downregulated in response to ZIKV E protein in human fetal neural stem cells, as WNT2 is the molecular target of mir-204-5p, which was significantly increased in E-protein transfected hNSCs. Our studies have now provided conclusive evidence that mir-204-5p/WNT2 axis is involved in ZIKV induced impairment of the proliferation and immature differentiation of neural stem cells.

Publications

1. B. Prajapati, M. Fatima, M. Fatma, P. Maddhesiya, H. Arora, P. Seth and S. Sinha (2020, In Press). Temporal transcriptome analysis of neuronal commitment reveals the preeminent role of the divergent lncRNA biotype and a critical candidate gene during differentiation. Cell Death Discovery (In Press)

2. AS Channakkar, T. Singh, B. Pattnaik, K. Gupta, P. Seth, and YK. Adlakha (2020). MiRNA-137-mediated modulation of mitochondrial dynamics regulates human neural stem cell fate. StemCells May 38(5):683-697. doi: 10.1002/stem.3155. Epub 2020 Feb 8.

3. D. Singh, A. Agrawal A, CMS Singal, HS Pandey, P. Seth and SK Sharma (2020). Sinomemine inhibits amyloid beta-induced astrocyte activation and protects neurons against indirect toxicity. Molecular

Brain March; 13(1):1-10. doi: 10.1186/s13041-020-00569-6.

4. S. Mukherjee, I. Akbar, R. Bhagat, B. Hazra, A. Bhattacharyya, P. Seth, D. Roy and A. Basu. (2019) Identification and Classification of Hubs in microRNA Target Gene Networks in Human Neural Stem/Progenitor Cells following Japanese Encephalitis Virus Infection. mSphere Oct 2;4(5). pii: e00588-19. doi: 10.1128/mSphere.00588-19.

5. H. Pandey and P. Seth (2019). Friends Turn Foe-Astrocytes Contribute to Neuronal Damage in NeuroAIDS. Journal of Molecular Neuroscience Oct; 69(2):286-297 doi: 10.1007/s12031-019-01357-1.

Presentations

1. Pankaj Seth: Invited Speaker, Molecular mechanism of HIV-1 neuropathogenesis, NCR Cluster Meeting at National Brain Research Centre, Manesar, India February 26, 2020.

2. Pankaj Seth: Guest Speaker, Molecular Mechanisms for virus induced neuronal damage, at Workshop on Molecular Neurobiology from genes, Neurons to behavior in health and disease, at Regional Centre for Biotechnology (RCB), NCR Biotech Science Cluster, Faridabad, India February 24-29, 2020.

3. Pankaj Seth: Keynote Speaker, How viruses affect human brain – finding answers, at Recent Advances in Life Sciences (RALS 2020), DPG Degree College, Gurgaon, India February 22, 2020.

4. Pankaj Seth: Guest Faculty, What we know and what we need to know about how viruses affect human brain, at Workshop on Animal Cell Culture Techniques and Applications at Department of Zoology, Miranda House, New Delhi, India, December 17-24, 2019.

5. Pankaj Seth: Invited Speaker, Novel insights into Zika virus neuropathogenesis using human neural stem cells, at the 3rd Indo-US Symposium on "New Insights into the Inflammation, Immunity, and Pathobiology of Diseases", at Sinclairs Bayview, Portblair, Andaman Islands, India, December 3-8, 2019.

6. Pankaj Seth: Invited Speaker, Friends turn Foe - Glia mediated neuronal damage in virus induced neuropathogenesis, at the 37th Annual meeting of Indian Academy of Neurosciences, at All India Institute of Medical Sciences, New Delhi, India, November 19-21, 2019.

7. Pankaj Seth: Invited Speaker, Molecular insights into zika virus induced neuropathogenesis. NeuroCON 2019 at the Maharishi Markandeshwar Medical College and University, Mullana, India, November 15-18, 2019.

8. Pankaj Seth: Guest Faculty, Molecular mechanisms of zika virus induced microcephaly. IBRO-APRC School, at Panjab University, Chandigarh, India, Nov 9-16, 2019.

9. Pankaj Seth: Guest Faculty, Novel insights into Molecular mechanisms of zika virus induced microcephaly. IBRO-APRC School, at Banaras Hindu University, India, September 1-14, 2019.

10. Pankaj Seth: Guest Lecture, Molecular insights into virus induced damage to human brain cells. Indian Institute of Science Education and Research (IISER) – Mohali, India, September 24, 2019.

11. Pankaj Seth: Invited Speaker - TEDx talk, Decoding how viruses affect human brains at Heritage Xperimental School, Gurgaon. September 28, 2019.

12. Pankaj Seth: Invited Speaker, Molecular Mechanisms of Zika Virus Induced Microcephaly – some novel insights using human neural stem cell model. Society of Neurochemistry (India), Jamia Hamdard University, New Delhi, India, October 10-12, 2019.

13. Pankaj Seth: Guest Faculty, Zika virus - what we know and want we need to know about its effects on human neural stem cells, at the University extension lecture at Interdisciplinary Brain Research Centre (IBRC), J.N. Medical College, A.M.U., Aligarh, India on May 1, 2019.

14. Pankaj Seth: Guest Speaker, Novel insights into Zika Virus induced microcephaly at IBRO-APRC School, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala, India on April 26, 2019.

Funding

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Collaborators

- A. Basu, SK Sharma and S. Sinha, NBRC, Manesar, India.

- B. Sindhu, S. Sharma, and A. Singh, Civil Hospital, Gurgaon, India.
- A. Mahadevan, NIMHANS, Bangalore, India.
- M. Mukherjee, IGIB, New Delhi, India.
- S. Singh, BHU, Varanasi, India.
- S. Sen and P. Chattopadhyay, 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.

Award

Hriday S Pandey - Awarded International Travel Grant from International Society for Neurochemistry (ISN) for presenting a poster in the "2019, ISN-ASN Meeting" held at Montreal, Canada from August 4-8, 2019.

Degrees Awarded

- Guneet Kaur (M.Sc.)
- Reshma Bhagat, Integrated PhD student (Ph.D.)

Prof. Pravat Kumar Mandal

Department of Computational Neuroscience,

Translational Neuroscience

Scientist

Dr. Deepika Shukla

Research Scientist

Shallu Sharma

PhD Student

Khushboo Punjabi

MSc Student

Pratibha Ahirwal

Research Manager

Apoorva Misra

R&D Engineer

Anshika Goel
Saurav Roy
Kanika Sandal
Divya Dwivedi
Kuldeep Singh

Neuropsychologist

Shallu Joon

Clinical Coordinator

Ritwick Mishra

Project Assistants

Reshma Nimson
Mainak Ghosh

Imaging Based Biomarkers for early diagnosis of Alzheimer's and other Neurodegenerative disorders using Smart Model System with the integration of Advance Machine Learning and Artificial Intelligence.

Objective: Magnetic resonance spectroscopy (MRS) is the potent non-invasive investigative tool to monitor critical neurochemical information and the metabolic changes at an early stage of the disease. It can prove extremely useful in the investigation of causal molecular processes of Neurodegenerative disorders. Signal processing involved in the metabolic quantitation for MRS signals from the low abundance neurotransmitters is a sensitive process which requires a focused approach. We also develop a system "GAURI" using machine learning approach to investigate critical features from neurochemical, structural and neuropsychological studies on the various study groups.

Overview: The NeuroImaging and NeuroSpectroscopy (NINS) laboratory focus on identifying early diagnostic biomarkers for neurodegenerative disorders such as Alzheimer's disease (AD). AD is the most common form of dementia in the world with a whopping 47.5 million sufferers worldwide. An understanding of causal molecular process that transform a healthy brain to a diseased condition would help us for therapeutic advancements in AD and other neurodegenerative disorders. NINS lab is focusing in the study groups consisting of normal healthy control (HC), mild cognitive impaired (MCI), AD and Parkinson's Diseases for the following features:

- Glutathione (GSH) and Iron mapping at the Hippocampus.
- Working Memory Performance and Visuospatial Perception scale
- Retinal (Fundus) Imaging
- Neuropsychological test scores for cognitive reserve

The assessment of these neurochemical levels and functional performance in quantitative terms and its correlation with disease progression is a major focus of research in our laboratory using a model system GAURI. NINS lab also focuses on development of tools and platforms to aid processing of neuroimaging data using KALPANA Package. Major neuroimaging based database (ANSH) development for AD is in progress.

Major Projects

I. Integration of Multimodal Neuroimaging Data for Advanced Brain Research

Objective: To develop a methodology to spatially integrate multimodal neuroimaging data (fMRI, MEG, MRS, and QSM) and validate its functioning. The entire methodology for multimodal data integration as well as computation of common region has also been incorporated into a Graphical User Interface- the **Multimodal Data Integration (MDI) toolbox**. This methodology is also capable of spatially integrating outcomes from more than two modalities and has been qualitatively tested for combinations of three and four modalities namely MEG-MRS-QSM and fMRI-MEG-MRS-QSM respectively.

Project Summary: Neuroimaging techniques are widely used to non-invasively investigate macro-, micro-structural and functional changes and alterations in brain tissue physiology. Modalities such as (MRI), (fMRI), (MEG), (MRS), and (QSM) are important for studying structural, functional, neurochemical profiles and susceptibility alteration from different brain regions. These neuroimaging techniques are utilized in studying various aspects of brain development, ageing, and neurological and psychiatric disorders. Combining multimodal brain imaging data can provide valuable information for a better understanding of brain physiology. The trend of correlating outcomes of multimodal data in various clinical research has been observed in recent literature. However, these studies are constrained as they have independently analyzed and correlated the outcomes for each modality without integrating ROI coordinate information.

The MDI toolbox has been developed, which provides a platform to process and spatially integrate multimodal neuroimaging data. The methodology is validated on a group of healthy young participants for one focused region, the occipital cortex.

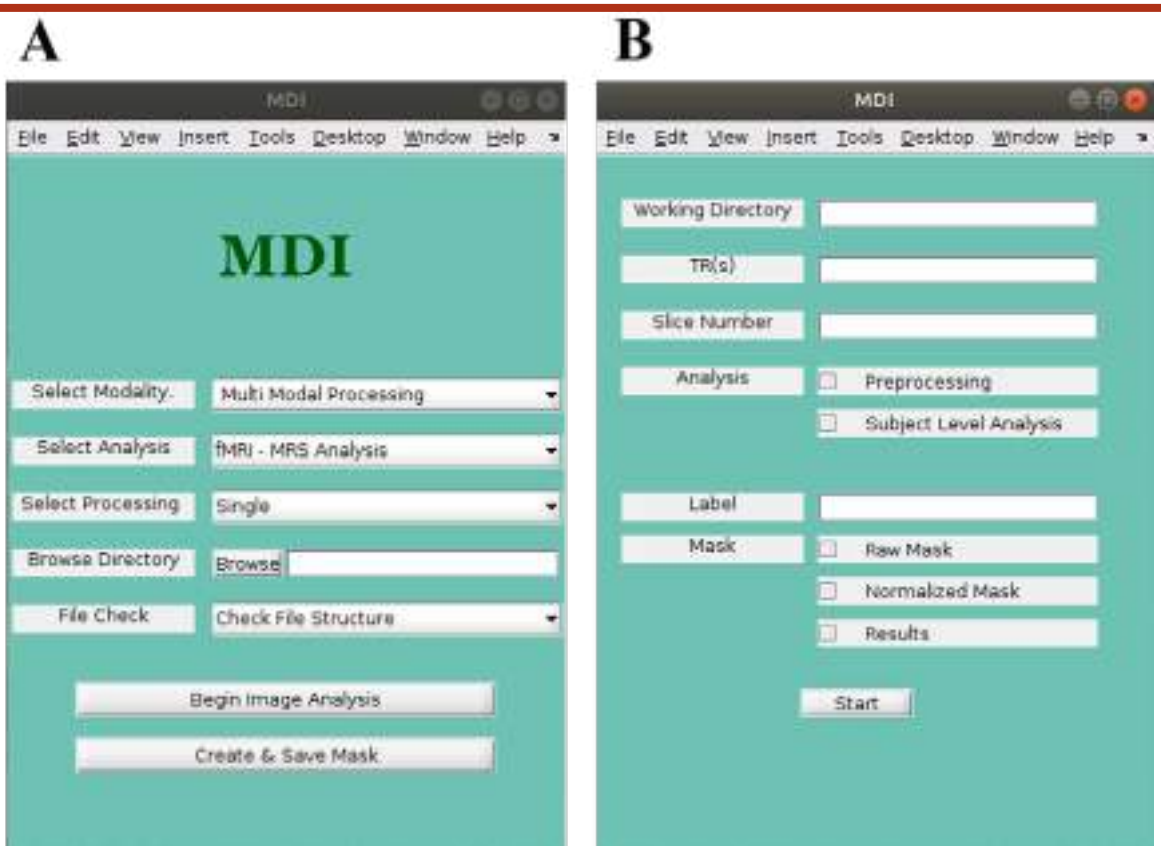

Figure 1: Primary and secondary window snapshot of the MDI Toolbox. A. The initial main window of the toolbox. The user has options for selecting between unimodal processing and multimodal processing, viz. fMRI-MRS, MEG-MRS, fMRI-QSM, and fMRI-MEG, for a single participant or a batch. A directory needs to be selected where the data is stored in the system. Option for generating as well as checking file structure is also available. **B.** Secondary window after selection of fMRI-MRS from multimodal processing option. The scan parameters from selected modalities such as TR, number of slices and processing options like pre-processing, single level analysis in case of fMRI, and label name of ROI, raw mask, normalized mask and results in case of MRS must be entered as a required field in the new window. The start option leads to the processing and integration of selected modality combination.

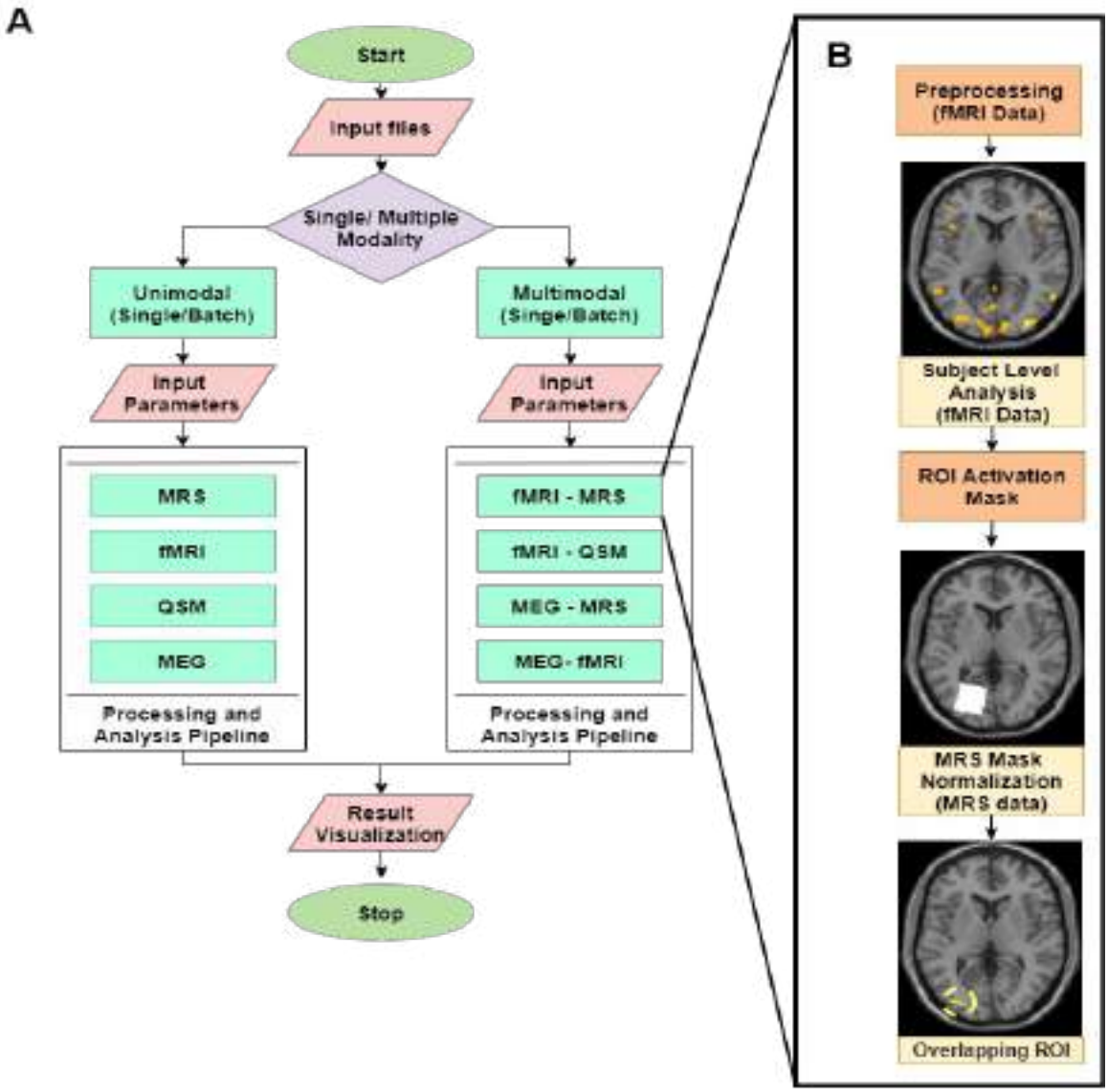

Figure 2: Multimodal Data Integration (MDI) Toolbox Execution Scheme: A. The pipeline begins with the input of data files and choosing between single and multimodal data processing, followed by the execution of the respective processing steps and visualization of the resulting common region. B. The processing of fMRI-MRS pipeline involves pre-processing of the fMRI data followed by single level analysis and creation of an ROI activation mask. This is followed by the generation of normalized MRS voxel masks. These masks are spatially integrated to get an isolated common region.

II. KALPANA: Advanced Spectroscopic Signal Processing Platform for Improved Accuracy to Aid in Early Diagnosis of Brain Disorders in Clinical Setting

Objective: Development of multinuclear signal processing scheme and absolute quantitation of metabolites (glutathione, GABA, ATP, PCr) and corelate these metabolites concentrations with disease conditions.

Present Status: This package is being released for Academic use (free of cost). KALPANA package is validated with other International toolboxes, Gannet, jMRUI (AMARES), LC Model and TARQUIN on a same of GABA data (blinded). Paper was presented at the International Society of Magnetic Resonance in Medicine (Montreal, Canada) (2019)

Title: Analyzing Big GABA: Comparison of Five Software Packages for GABA-Edited MRS

Authors: Mikkelsen M, Bhattacharyya P, **Mandal P, Shukla D**, Wang AM, Wilson M, Dydak U, Murdoch J, Near J, Oeltzschner, Edden R. (May 2019) (International Society of Magnetic Resonance in Medicine, ISMRM)

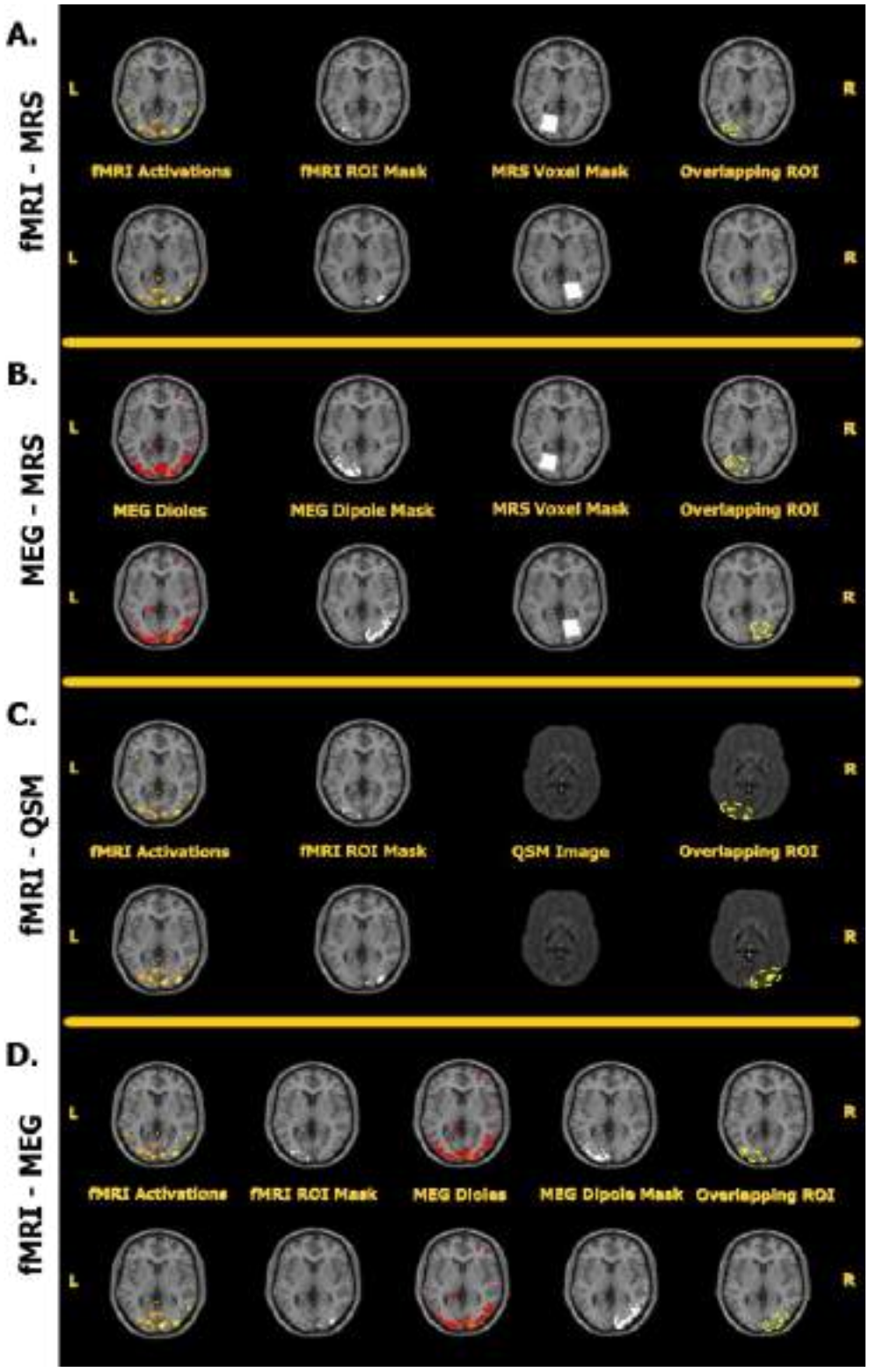

Figure 3: Representative results of unimodal data processing and intermediate steps of bimodal data integration. In each section, the first row represents LOC and the second row represents ROC. **A. fMRI-MRS Integration** shows the fMRI activations (checkerboard paradigm), fMRI activation mask for the respective ROI, and its corresponding normalized MRS voxel mask, followed by the resulting overlapping region. **B. MEG-MRS Integration** represents the MEG dipoles (checkerboard paradigm), MEG dipole mask, and the corresponding normalized MRS voxel mask for the respective ROIs followed by the resulting common region. **C. fMRI-QSM Integration** fMRI activations, fMRI activation mask for the respective ROIs, QSM image of the same brain slice, followed by the resulting overlapping region are shown. **D. fMRI-MEG Integration** shows the fMRI activations, fMRI activation mask for the respective ROI, MEG dipoles for the same paradigm, and MEG dipole mask for respective ROIs, followed by the resulting overlapping region.

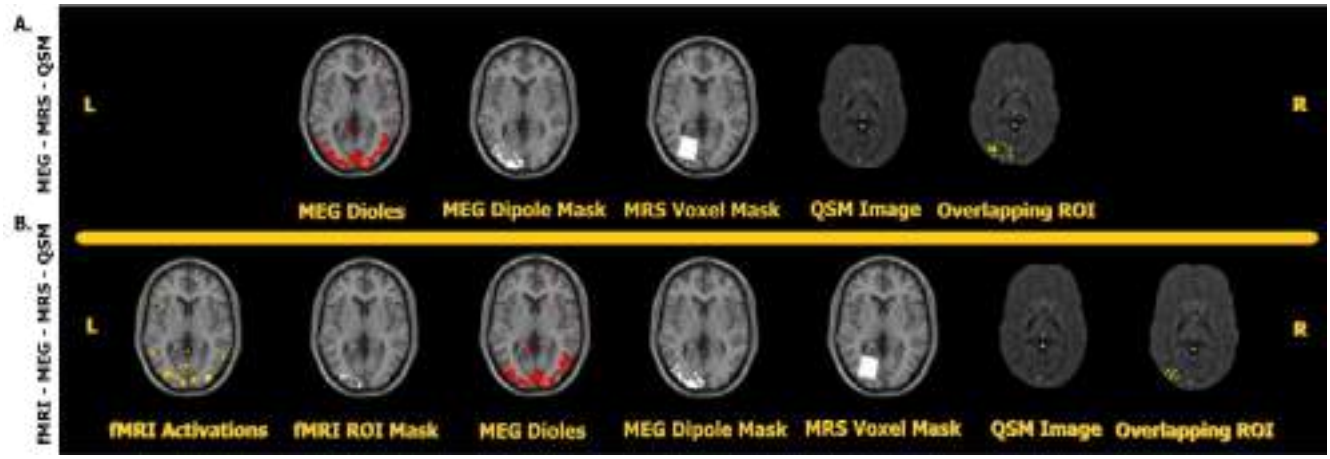

Figure 4: Multimodal Data Integration for combinations of three and four. A. MEG-MRS-QSM Integration, The first row shows the MEG dipoles observed as a result of the checkerboard paradigm, dipole mask, and the normalized MRS voxel mask for LOC followed by the QSM image and finally the overlapping common region from the three modalities. **B. fMRI-MEG-MRS-QSM Integration,** The second row represents the fMRI activations and MEG dipoles resulting from the checkerboard paradigm, each followed by their respective masks and MRS voxel mask and QSM image, and lastly the common region of the ROI obtained from these four modalities for LOC region.

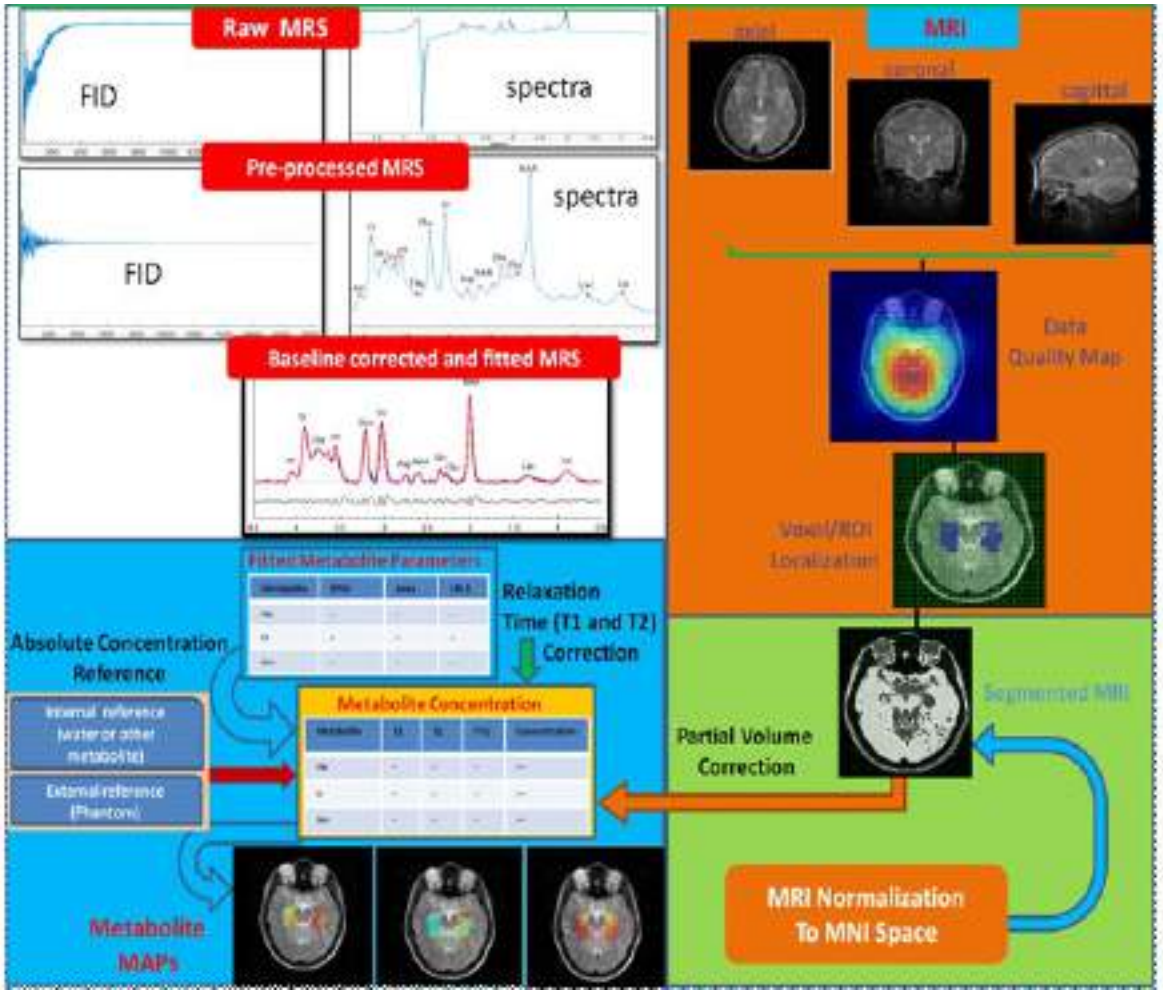

Figure 1: An illustrative representation for the multi-nuclei data processing, metabolic quantitation and outputs generated using KALPANA package

Publications

1. Pravat K. Mandal* and Deepika Shukla. "KALPANA: advanced spectroscopic signal processing platform for improved accuracy to aid in early diagnosis of brain disorders in clinical setting." Journal of Alzheimer's Disease Preprint Vol 75 (2) 397-402 (2020).

2. Divya Dwivedi, Kanu Megha, Ritwick Mishra, and Pravat K. Mandal*. "Glutathione in Brain: Overview of Its Conformations, Functions, Biochemical Characteristics, Quantitation and Potential Therapeutic Role in Brain Disorders." Neurochemical Research Vol 45 1-20 (2020).

3. Praful P. Pai, Pravat K. Mandal*, Khushboo Punjabi, Deepika Shukla, Anshika Goel, Shallu Joon, Saurav Roy, Kanika Sandal, Ritwick Mishra, and Ritu Lahoti. "BRAHMA: Population specific T1, T2, and FLAIR weighted brain templates and their impact in structural and functional imaging studies." Magnetic Resonance Imaging Vol 70 5-21 (2020).

4. Anshika Goel[#], Saurav Roy[#], Khushboo Punjabi[#], Ritwick Mishra, Manjari Tripathi, Deepika Shukla*, Pravat K. Mandal*, "Integration of Multimodal Neuroimaging Data for Advanced Brain Research." (in review Journal of Magnetic Resonance Imaging) # refers equal first Author

5. Deepika Shukla, Pravat K. Mandal*, Manjari Tripathi, Gayatri Vishwakarma, Ritwick Mishra, and Kanika Sandal. "Quantitation of in vivo brain glutathione conformers in cingulate cortex among age - matched control, MCI, and AD patients using MEGA - PRESS." Human Brain Mapping Vol 41 (1) 194-217 (2020).

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Collaborators

- Prof. (Dr.) Manjari Tripathi, MD, DM, Dept. of Neurology, All India Institute of Medical Science (AIIMS), New Delhi.
- Dr. Ashley Bush, MD, Head, Oxidation Biology Unit - Melbourne Dementia Research Centre, Florey Institute of Neuroscience and Mental Health, Melbourne, Victoria, Australia.
- Dr. Peter Barker, D.Phil, Professor, Dept. of Radiology and Radiological Sciences, Johns Hopkins, Baltimore, Maryland, USA.
- Dr. Vincenzo Fodale, MD, Professor, Dept. of Neurosciences, Section of Anesthesiology, University of Messina, *Italy*
- Dr. Lars Ersland, Ph.D, Professor, Dept. of Clinical Engineering, Haukeland University Hospital, Bergen, Norway

Ranjit Kumar Giri

Department of Cellular & Molecular Neuroscience,

Translational Neuroscience

MSc Student

Archana Mehta (Lab Rotation)

Lab Attendant

Lalit Bidla

Differential expression of CPEB alternative splice variants as a molecular marker of neuroblastoma cells

In recent years, cytoplasmic polyadenylation element binding (CPEB) protein has gained immense attention for its role in long-term memory formation. However, it was first discovered in *Xenopus* oocytes (first early cell of an organism), suggesting its role in cell division and in almost all cell types including cancer cells. Under basal condition, CPEB binds to cytoplasmic polyadenylation element (CPE) of several polyadenine tail containing mRNA and protect the mRNA from degradation and keep these mRNA in dormant or repressed state. Under translational stimulus, CPEB undergoes either phosphorylation or degradation which dissociates polyadenine specific ribonuclease and facilitate polyadenine elongation by Gld2 polyadenine polymerase from the same repressed which is a closed-loop structure between the 3'UTR and 5'UTR (untranslated region) of mRNA. Since CPEBs are regulators of cell cycle and cell senescence related transcripts, their participation in cancer seems highly conceivable. All CPEBs (CPEB1-4) has different splice variants, which are cell type specific. Alternative CPEB splice variants are used in prognosis and assertion of clinical stages of cancer patients. However, so far there is no report on the involvement of any CPEB splice variants in neuroblastoma, a cancerous state of neuroblast or early nerve cells derived from radial glial cells.

Last year, we reported that CPEB splice variants which are expressed in adult brain are either less expressed or not detected in neuroblastoma and the splice variants which are expressed predominantly in neuroblastoma are not again either less expressed or not expressed in mature brain. Such results tempted us to investigate, whether forceful differentiation of neuroblastoma will lead to shift in CPEB transcript splice variants expression. Therefore, in currents year, we differentiated N2a neuroblastoma cells by different doses of retinoic acid. Our results indicated that 20 μM of retinoic acid is sufficient to alter the morphology of neuroblastoma cells. Next we differentiated N2a neuroblastoma cells with 20 μM of retinoic acid and performed cell type analysis by immunofluorocytochemistry. Both undifferentiated and differentiated cells were incubated with anti-vimentin antibody (marker for neuronal precursor cells i.e., radial glial cells) and beta tubulin III (marker for neuron) or glial fibrillar acidic protein commonly known as GFAP (marker for astrocytes). Our results show, in undifferentiated neuroblastoma, almost all the cells express vimentin but not beta tubulin III or GFAP (Figure 1) suggesting N2a neuroblastoma cells are indeed derived from radial glial cells. However, beta tubulin III expression increased markedly when N2a cells are treated with retinoic acid but without any increase in GFAP expression. Moreover, retinoic acid treated cells have elongated cellular processes which are also positive for beta tubulin III expression. In addition, expression of vimentin is

also increased in retinoic acid treated N2a neuroblastoma cells. Collectively, our current differentiation procedure enabled us to push a highly cancerous neuroblastoma cells (doubling time roughly around 18 hours) to neuronal lineage but not towards astrocytic lineages. Therefore, N2a cells moving towards neuronal lineage will help us in finding CPEB transcript variants for neuronal lineage and will also strengthen our findings on specific transcript variants for cancerous neuroblastoma cells. Similar to this approach, in future, to associate CPEBs transcript splice variants specifically for astrocytes we will use CNS stem/progenitor cell cultures differentiate towards astrocytic lineage and also compare CNS stem cells specific CPEB transcript splice variants with neuroblastoma.

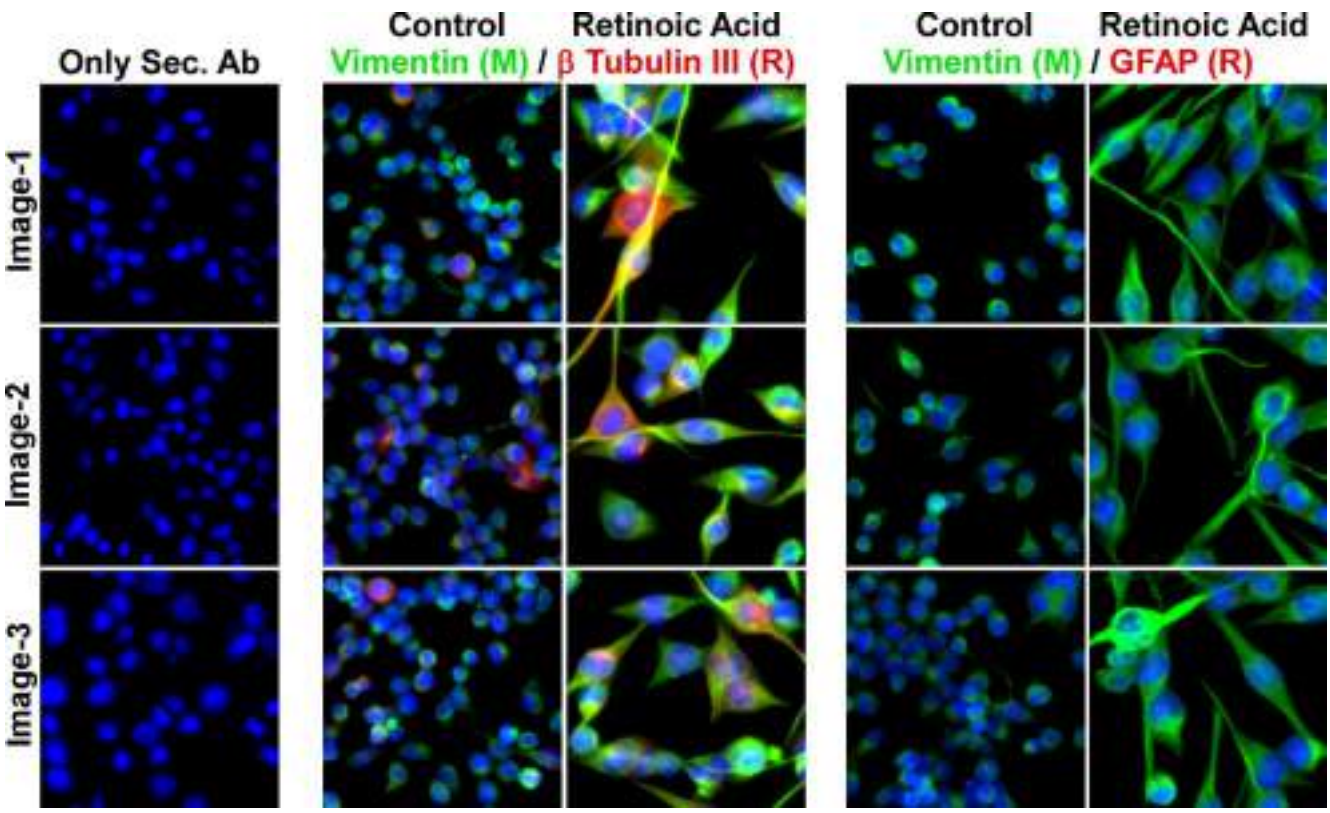

Figure 1. Differentiation of N2a neuroblastoma cells towards neuronal and astrocytic lineage by retinoic acid. N2a mouse neuroblastoma cells were cultured either in DMEM containing 2% fetal bovine serum (FBS) and 0.01% DMSO or in DMEM containing 2% FBS and 20 μM retinoic acid. After fixing the cells with 4% paraformaldehyde, cells were co-immunostained with vimentin and beta tubulin III or vimentin with GFAP. Nuclei were stained with DAPI. Microscopic imaging and image display settings were performed with similar setting across all the images. Briefly, N2a cells treated with retinoic acid differentiate towards neuronal lineage but not towards astrocytic lineage.

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Shiv K Sharma

Department of Cellular & Molecular Neuroscience,

Cognitive Neuroscience, Systems Neuroscience, Translational Neuroscience

Postdoctoral fellow

Deepali Singh

PhD Students

Kautuk Kamboj
Biswaranjan Sahoo
Apurva Agrawal
Tushar Arora
Deepti Dama

MSc Students

Ranjit Pradhan
Sharmishtha Panda

Project Assistant

Subhajit Jana

Technician

P. Manish (Part-time, informal arrangement)

Pattern-dependent synaptic plasticity and growth factor signaling

The focus of my laboratory has been to examine the mechanisms of memory formation, and to examine the processes that are involved in memory impairment in Alzheimer's disease, the most common form of dementia in the elderly population. Another aspect of our research is to understand the mechanisms that contribute to Down syndrome. We have made progress in all these projects. The above-mentioned personnel are working on different aspects of research going on in my laboratory. Previously, I have discussed our work on the research areas mentioned above. This year, I will present our work that relates to the mechanisms of memory formation.

The ability to make memories and recall them when needed is a remarkable feature of the brain. We know that memories play critical roles in our day-to-day lives. Based on previous experiences stored in the form of memories, we plan future activities. Considering the importance of memory in our lives, significant efforts are directed to understand how memories are formed in the brain. For this purpose, a wide variety of approaches including molecular, electrophysiological, behavioral and computational modelling are used to identify the processes that go into making memories. My laboratory has been using molecular, electrophysiological and behavioral approaches to elucidate the processes involved in memory formation. A combination of approaches is likely to provide better understanding of how memories are formed than any single approach.

Pattern-dependent memory: A very interesting feature in memory formation is the "spacing effect". In a multi-trial task, long-term memory formation is more robust if the trials during training are spaced in time than when the trials during training are massed together with little or no temporal spacing. The former pattern of training is referred to as the "spaced training", and the latter pattern of training is referred to as the massed training. The superiority of spaced training over massed training for long-term memory formation is referred to as the spacing effect. This phenomenon in memory formation was first described by Herman Ebbinghaus, a German psychologist. It is such a robust property of memory formation that it has been observed in systems ranging from invertebrates to humans. The important aspect of spacing effect is that the number of training trials remains the same during massed or spaced training. It is only the time interval between the trials that differs between the two training paradigms. And, short-term memory is unaffected by the training patterns. One of the aspects of our research on memory formation is to understand what makes spaced training superior to massed training for memory formation.

Pattern-dependent synaptic plasticity: Long-term potentiation (LTP) is studied as a synaptic mechanism of memory formation. LTP is a long-lasting increase in synaptic strength after an experience. Similar to memory, LTP also displays pattern dependence. Spaced

stimulation induces higher LTP than massed stimulation. We use hippocampal slices to examine properties of LTP. These experiments involve stimulation of the CA3 fibres and recording of the response in the CA1 region of the hippocampus. We previously reported that LTP induced by massed pattern of stimulation is enhanced when the level of protein acetylation in increased by sodium butyrate, a histone deacetylase inhibitor. Importantly, long-term memory induced by massed pattern of training is also facilitated by increasing the acetylation level in the cells. These results suggest that the level of acetylation plays a deterministic role in higher LTP induced by spaced pattern of stimulation, and in facilitation of memory formation by spaced training. Additionally, the results show that it is possible to enhance LTP and memory induced by massed patterns.

Continuing with our interest in spacing effect, we have started examining the effect of a growth factor in LTP induced by massed pattern of stimulation. For these experiments, we used a commonly used stimulation protocol referred to as the tetanic protocol. This stimulation procedure consists of 4 bursts of high frequency stimulation of the CA3 fibres. Each burst in turn consists of 100 stimuli which are applied at a frequency of 100 Hz. The response is recorded in the CA1 region of the hippocampus. Consistent with previous findings from our lab and other labs, we showed again that spaced stimulation of CA3 fibres induces LTP which is of higher magnitude than LTP induced by massed pattern of stimulation. We then asked whether a growth factor can enhance LTP induced by the massed pattern of stimulation. After recording the base line synaptic response, the growth factor was applied to the hippocampal slices for a short duration. Then, massed tetanic stimulation was applied to the slices. The results suggest that when the hippocampal slices are treated with growth factor and stimulated with the massed pattern, the LTP induced is of higher magnitude than the LTP induced by massed pattern of stimulation without the growth factor application. The slices used for the two groups in the experiments had similar input-output response. We are further examining the molecular mechanisms that may be involved in growth factor-mediated enhancement of LTP induced by massed pattern of stimulation.

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3. Kamboj K, Jana S, Sharma SK. Mechanisms of protein kinase C-induced sustained activation of extracellular signal-regulated kinase in the hippocampus. Biochem Biophys Res Commun. 520:453-458, 2019.

Presentation

- Shiv K. Sharma Delivered a lecture on "Alzheimer's disease: Molecular and synaptic mechanisms" on World Alzheimer's day, September 21, 2019, Interdisciplinary Brain Research Centre, Aligarh Muslim University, Aligarh.

Collaborator

Dr. Pankaj Seth, NBRC.

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Degree Awarded

Mr. Ranjit Pradhan (M.Sc.)

Soumya Iyengar

Department of Systems Neuroscience,

Cognitive Neuroscience

Integrated PhD Student

Utkarsha A. Singh

Technicians

Arvind Singh Pundir
Krishan Sharma
Ram Mehar

Expression of DARPP-32 in Adult Male Zebra Finches

Dopamine- and cyclic AMP-regulated phosphoprotein 32 kDa (DARPP-32) is localised mostly in dopaminoceptive neurons which are concentrated in different subdivisions of the basal ganglia. It is expressed by medium spiny neurons (MSNs) of the striatum which are parts of both direct and indirect pathways, which are important for movementsin both mammals and birds. The MSNs act as a hub for cortico-striatal and striato-nigral activity and receive glutamatergic input from the cortex and dopaminergic input from the substantia nigra. DARPP-32 is also distributed across cortical and subcortical areas which receive dopaminergic projections. Interestingly, modelling studies have demonstrated that DARPP-32 integrates glutamatergic and dopaminergic input in a time-locked manner, allowing it to function in various cognitive functions such as learning.

We have been studying the role of the endogenous opioid system on the acquisition of vocal learning in zebra finches, a species of songbirds. Zebra finches are sexually dimorphic and only males sing, in order to attract females during courtship. The song is learned during a sensitive period early in development, from a tutor, typically the father. Since the opioid system interacts extensively with the dopaminergic system, we decided to explore the targets of these neuromodulatory systems by studying the expression of DARPP-32 in the brains of zebra finches.

For these studies, we analyzed overall patterns of immunoreactivity for DARPP-32 in adult male zebra finches. Our results demonstrated that as in mammals and other avian species, DARPP-32 expression was highest in both medial and lateral striatum. Interestingly, a specific pattern of immunoreactivity emerged in the song control system, with 'core' song control regions, that is, cortical/pallial regions LMANcore (lateral magnocellular nucleus of the anterior nidopallium), RA (nucleus robustus arcopallialis) and HVC being less immunoreactive for DARPP-32 than 'shell' areas such as LMANshell, RAcup, AId (intermediate arcopallium) and HVCshelf (**Figure 1**). Our results suggest that whereas dopamine may modulate the shell pathways at various levels of the AFP, dopaminergic modulation of the core pathway occurs mainly through Area X, a basal ganglia nucleus. Furthermore, secondary sensory cortices including the perientopallial belt, Fields L1 and L3 had higher DARPP-32 immunoreactivity than primary sensory cortical areas such as the pallial basolateral nucleus, entopallium proper and Field L2, corresponding to somatosensory, visual and auditory systems, respectively. We also found DARPP-32-rich axon terminals surrounding dopaminergic neurons in the ventral tegmental area–substantia nigra complex which in turn project to the striatum, suggesting that there may be a reciprocal modulation between these regions (**Figure 2)**. Overall, DARPP-32 expression appears to be higher in areas involved in integrating sensory information, which further supports the role of this protein as a molecular integrator of different signal processing pathways.

The normative data presented above will be used in ongoing research to study whether the dopaminergic system in zebra finches undergoes any alterations when the levels of endogenous opioids are manipulated in the course of our experiments.

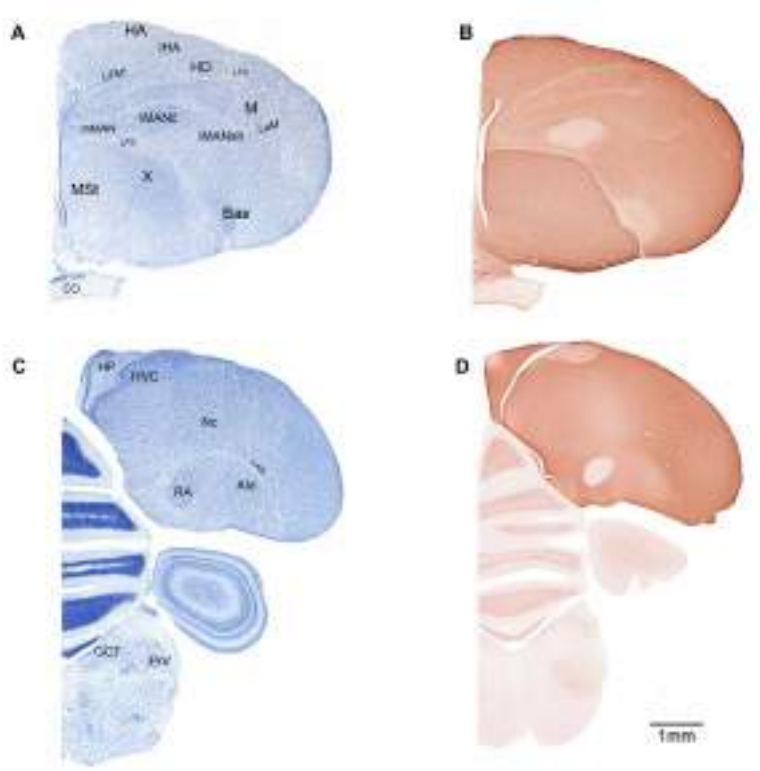

Figure 1: Nissl-stained sections (left panel; **A**) at the level of the song control nuclei LMAN and Area X of the anterior forebrain pathway and (**C**) from the caudal part of the zebra finch brain and corresponding coronal sections labelled for DARPP-32 (right panel, **B** and **D**).The central, magnocellular core of LMAN (LMANc) and Bas (Nucleus Basalis) are clearly delineated from the surrounding nidopallium (cortex) since they are devoid of DARPP-32 label. However, neuropil within LMAN shell (LMANs) is intensely labelled. Area X cannot be delineated from the medial striatum based upon DARPP-32 immunoreactivity pattern. In caudal sections (**D**), The vocal motor nucleus is particularly prominent since neuropil in this region which is negative for DARPP-32 can be clearly contrasted with higher levels of staining in the surrounding arcopallium. Low levels of immunoreactivity are present in the neuropil within the song control regions HVC and in AId, which is lateral to RA; whereas the brainstem is almost completely unlabeled at this level. Scale bar, 1 mm.

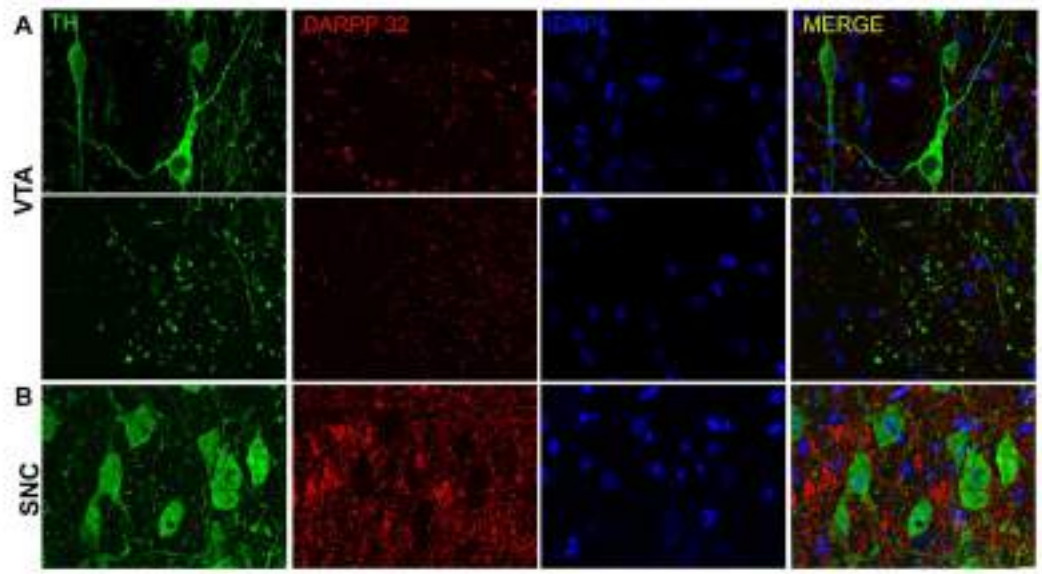

Figure 2: (A) TH-positive neurons and terminals surrounded by DARPP-32 afferents in VTA. (B) Large TH-positive neurons surrounded by a matrix of DARPP-32 positive terminals are observed within SN. Scale bar, 10 µm.

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1. Sen S*, Parishar P*, Pundir AS, Reiner AJ and Iyengar S (2018): The Expression of Tyrosine Hydroxylase and DARPP-32 in the House Crow (Corvus splendens) brain. * Joint first authors. J Comp Neurol. 2019 Aug 1; 527(11):1801-1836. doi: 10.1002/cne.24649.

2. Kumar S, Mohapatra AN, Sharma H, Singh UA, Kambi N, Velpandian T, Rajan R, Iyengar S (2019): Altering opioid neuromodulation in the songbird basal ganglia modulates vocalizations. Frontiers in Neuroscience, (Neuropharmacology) July 3 2019, DOI: 10.3389/fnins.2019.00671.

3. Singh UA and Iyengar S (2019): The Expression of DARPP-32 in Adult Male Zebra Finches (Taenopygia guttata). Brain Structure and Function, DOI: 10.1007/s00429-019-01947-0.

Presentations

1. S. Iyengar Corvid Brain Structure,Cognition and Mirror Self-Recognition. 15th - 16th March, 2019; Invited lecture, BIOSPARKS-2019, Organized by the School of Life Sciences, JNU, New Delhi.

2. S. Iyengar Brain Structure and Behaviour in Songbirds, Abstract submitted. 22nd - 24th April, 2019; International Workshop on Social Network of Animals in Extreme Environment of Antarctica with Special Reference to Penguins including Field Studies Zoological Survey of India, MoES (Ministry of Earth Sciences), Port Blair.

3. S. Iyengar The Role of the Opioid System in Singing and Song Learning in Zebra Finches. 24th Oct, 2019; Invited lecture, Dept of Psychology, Vanderbilt University, Nashville, TN, USA.

4. Singh UA and Iyengar S (2019): "Fine-tuning birdsong: The role of delta opioid receptors in the development of song structure". # 3655, Annual Meeting of the Society for Neuroscience, 2019, Chicago, USA. **This abstract has been selected as a Neuroscience 2019 Hot Topic (Only ~100 out of the over 14,000 abstracts submitted to Neuroscience 2019 are awarded this recognition. It was shared with the media as part of Neuroscience 2019's Hot Topics book and in the Neuroscience 2019 online press room.)

5. S. Iyengar Neural Plasticity and the Development of Axonal Connections in the Human Auditory Cortex. 19th - 21st Nov, 2019; IAN 2019, All India Institute of Medical Sciences, New Delhi

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DST Grant entitled "Effects of the δ-Opioid Receptor System on Singing and Song Learning in Zebra Finches", (EMR/2015/001422; September 2016 – September 2019).

Sourav Banerjee

Department of Cellular & Molecular Neuroscience,

Systems Neuroscience

Post Doctoral Fellow

M. Gopi

PhD Students

Balakumar Srinivasan
Sarbani Sammadar
Gourav Sharma
Dipanjana Banerjee
Kamakshi Garg

MSc Student

Rekha Singh

Project Assistant

Anupam Das,

Utsav Mukherjee

Technical Assistant

D. Narendar,
Musadik Hussein

Regulatory control of synaptic homeostasis by remodelling of miRNA-induced silencing complex

Adaptibility of neural circuits to changes in the environment requires proportionate tuning of synaptic strength or homeostatic scaling. Therefore, the molecular mechanisms regulating activity-dependent reversible and modular proteomic changes to adjust synaptic strength has gained a significant attention. Emerging studies have demonstrated the independent roles of protein synthesis and UPS-mediated protein degradation for the bidirectional modulation of synaptic strength. Identification of newly synthesized proteins including components of protein degradation machinaries during homeostatic scaling challenges the conventional view of stand-alone roles of these two processes in homeostatic scaling. Importantly, Synchronous control of protein synthesis and degradation or proteostasis has emerged as a key regulatory control point for modulating proteome composition necessary for maintaining physiological function of the cell. Seminal studies have indicated the synergistic involvement of translation and degradation pathways in proteome remodelling, no reports till date have demonstrated the existence of a spatial collaboration between these two opposing apparatus that potentially regulates the temporal dynamics of the neuronal proteome.

MicroRNAs (miRNAs) are small non-coding RNAs that play a pivotal role in the posttranscriptional control of gene expression necessary for synaptic transmission. miRNAs in association with the multi-protein RNA-induced silencing complex (miRISC) reversibly binds to 3' untranslated region (UTR) of target mRNA to regulate protein synthesis in response to synaptic activity. Recently, miRNAs have been functionally implicated in homeostatic synaptic scaling. These studies demonstrated that synaptic activity modulates a specific set of miRNA to govern the expression of synaptic AMPA - a glutamatergic receptor known to function as an endpoint effector of homeostatic scaling. These observations prompted us to investigate the mechanisms underlying synaptic homeostasis with special focus on compositional change in miRISC driven by cross-talk between the translation and degradation pathways.

To test the synergistic effects of protein synthesis and protein degradation by the proteasome in synaptic homeostasis, we measured miniature synaptic activity using whole-cell patch clamp recordings from cultured rat hippocampal neurons after pharmacological inhibition of protein synthesis and proteasome function either alone or in combination. We observed that inhibition of protein synthesis decreased and blockade of proteasome enhanced the miniature EPSC (mEPSC) amplitude – a parameter to quantitatively evaluate decrease or increase of synaptic strength respectively. Surprisingly, co-application of both restore the mEPSC amplitude comparable to basal level. However, we did not observe any significant change in mEPSC frequency following inhibition of protein synthesis and

degrdation either alone or in combination. These data convincingly demonstrates that interfering with either protein synthesis or proteasome disrupts the synaptic homeostasis whereas co-inhibition of protein synthesis and degradation restricts the deviation of synaptic activity from basal level (Figure 1A-C). Similar to previous observations, synaptic strength was significantly reduced when hyperactivity was elicited by bicuculline, a $GABA_A$ receptor antagonist. However, when protein synthesis and degradation was inhibited at the same time, bicuculline-induced down scaling of synaptic strength was restored to control levels (Figure D-F). Our observations deviate from commonly held perspectives supporting the regulation of homeostatic scaling by the stand-alone control of either protein synthesis or proteasome-mediated degradation. Therefore, we suggest a mechanism of homeostatic plasticity that involves a synergistic action of both these processes.

To correlate molecular changes that influence synaptic strength, we measured the post-synaptic surface AMPA receptor (AMPAR) expression - a consensus end-point effector of homeostatic plasticity. We have analyzed the level of GluA1 and GluA2 subunits of AMPAR.

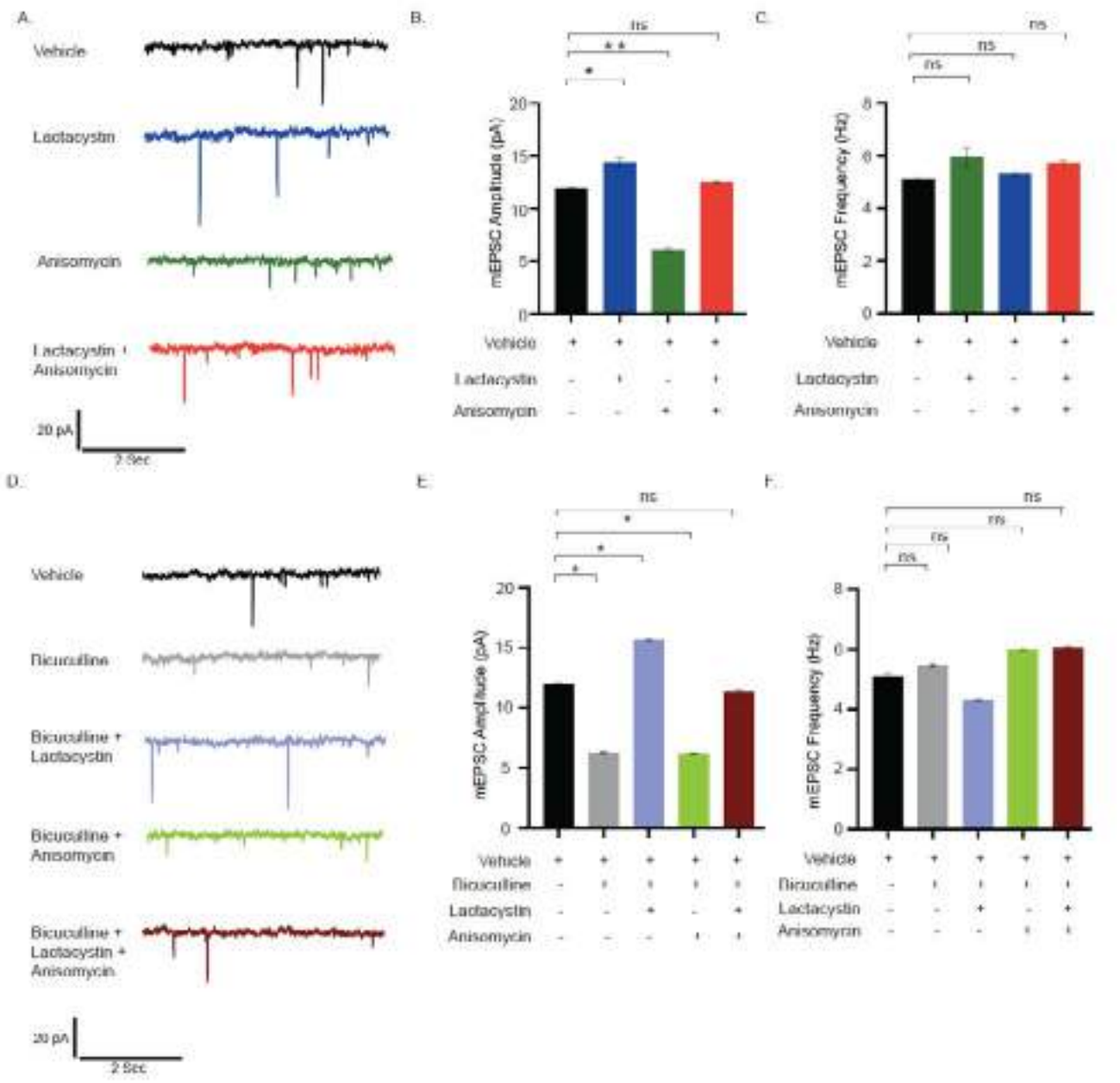

Figure 1: Synergistic control of protein synthesis and degradation modulates synaptic strength. (A - C) mEPSC amplitude and frequency after inhibition of protein synthesis and proteasome either alone or in combination. (D-F) mEPSC amplitude and frequency after inhibition of protein synthesis and proteasome in presence of bicuculline.

While bicuculline treatment alone significantly reduced the receptor expression, we were intrigued to find that co-inhibition of protein synthesis and proteasome function during bicuculline-induced elevation of synaptic activity restored the AMPAR levels at the post-synaptic surface (Figure 2). Taken together, our data provides a compelling evidence for resetting the synaptic strength from hyperactivity -mediated offset via synergistic control of protein synthesis and proteasome-mediated protein degradation.

These observations point toward an intriguing question – How synchronous control of protein synthesis and degradation regulate synaptic homeostasis? To evaluate this, we analyzed the polyribosome-associated translating RNA fraction or polysomes from hippocampus. We have assessed whether the sedimentation pattern of proteasomes matches those of actively translating, polyribosome-associated mRNA fractions. We have fractionated cytoplasmic lysates obtained from the rat hippocampus on 20 – 50% linear sucrose gradient and

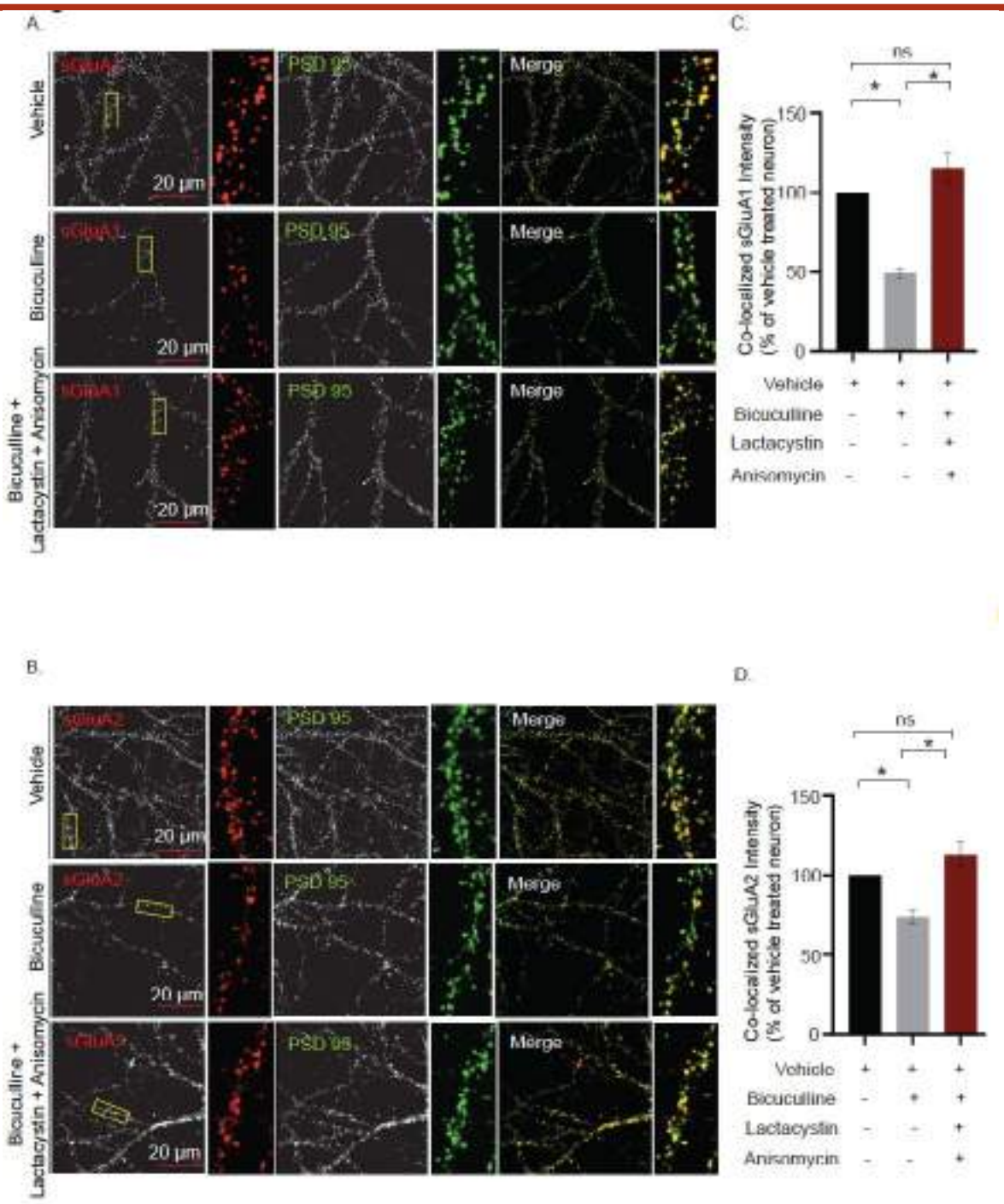

Figure 2: Synaptic surface expression of AMPAR is regulated combinatorial control of protein synthesis and degradation. Surface GluA1 (A) GluA2 (B) expression were measured after dual inhibition of protein synthesis and degradation in presence of bicuculline.

monitored the absorbance at O.D.$_{254}$ during fractionation. The sedimentation profile showed distinct peaks for non-translating (80S ribosome or monosome) and actively-translating polysomes. We observed that several components of the proteosomal machinary such as a7 subunit of 20S; Rpt1, Rpt3 and Rpt6 subunits of the 19S proteasome co-sedimented with translation initiation factors such as Eif4E and p70S6 kinase, the regulatory kinase of mTOR-mediated protein synthesis (Figure 3A-B). A possible causality for the observed co-sedimentation could be that these protein complexes have similar densities.

However, application of RNAse or EDTA led to dissociation of polysome-associated protein complex and complete loss of co-sedimentation of protein synthesis components as well as proteasome subunits (Figure 3C-F). Furthermore, we observed that proteasome associated with polyosome fractions are active as detected by fluroscence following peptide cleavage. The proteasome activity was blocked by application of epoxymycin, a 20S proteasome inhibitor (Figure 3G – H).

We further analyzed the proteins interacting with ribosomes in excitatory neurons to assess the direct interaction between proteasome and translation regulatory complexes (Figure 4A). We expressed Hemagglutinin (HA) tagged ribosomal protein Rpl22 (HA-Rpl22) in the excitatory neurons of hippocampus using a transgenic mouse where HA-Rpl22 expression is driven by Cre recombinase under the control of the CamK2a promoter (Figure 4B). We confirmed that HA-Rpl22- ribosomes preferentially co-sedimented with actively-translating polysome fractions (Figure 4C-D).

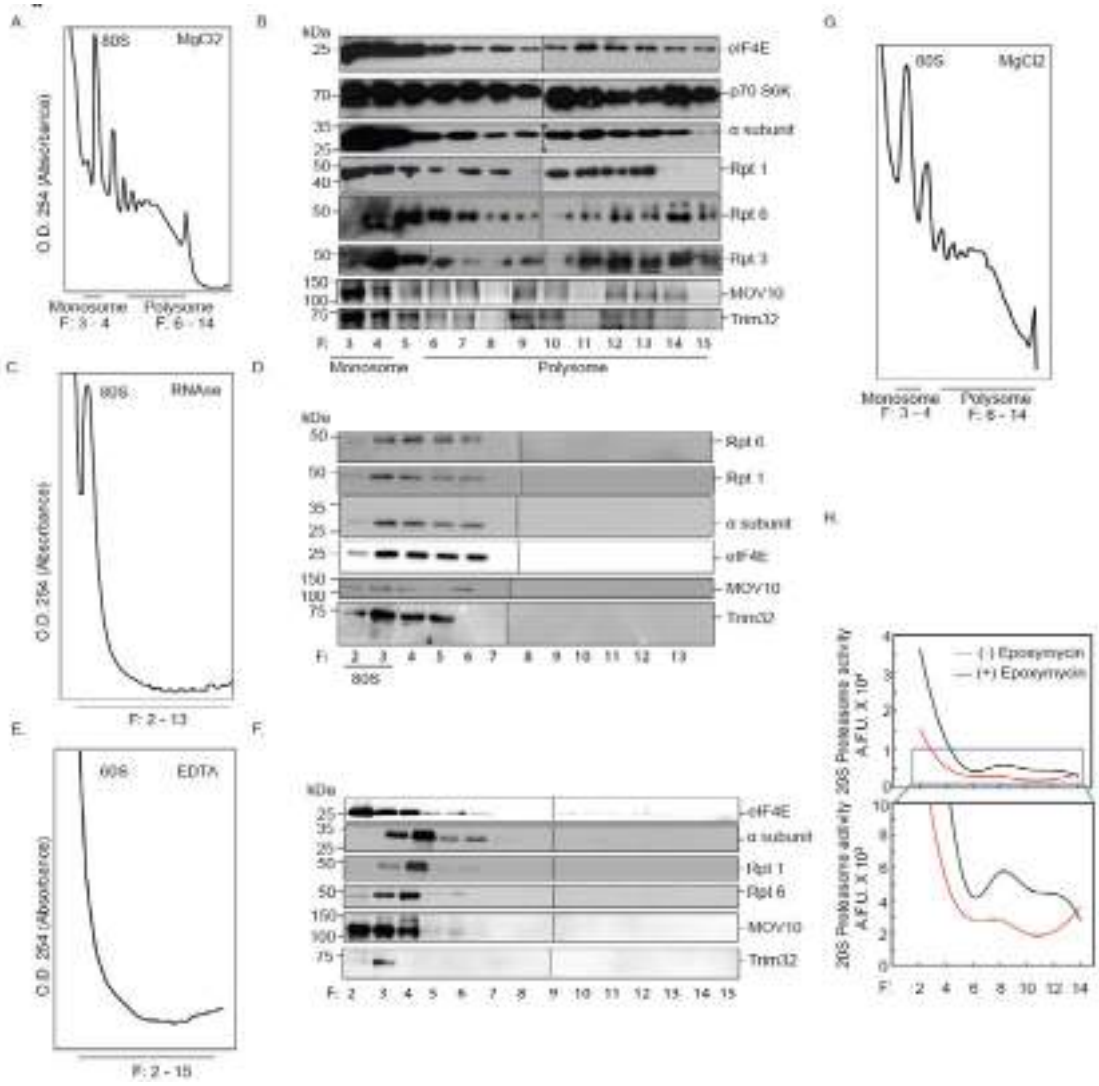

Figure 3: Active proteasomes are associated with translating transcripts. (A-F) O.D.$_{254}$ absorbance profile of hippocampal lysate and western blot analysis of surcrose density gradient fractions obtained from lysate treated with $MgCl_2$ (A-B), RNAse (C-D) and EDTA (E-F). (G-H) O.D.$_{254}$ absorbance profile of hippocampal lysate treated with $MgCl_2$ (G) and proteasome activity assay performed in prescence and absence of epoxymycin.

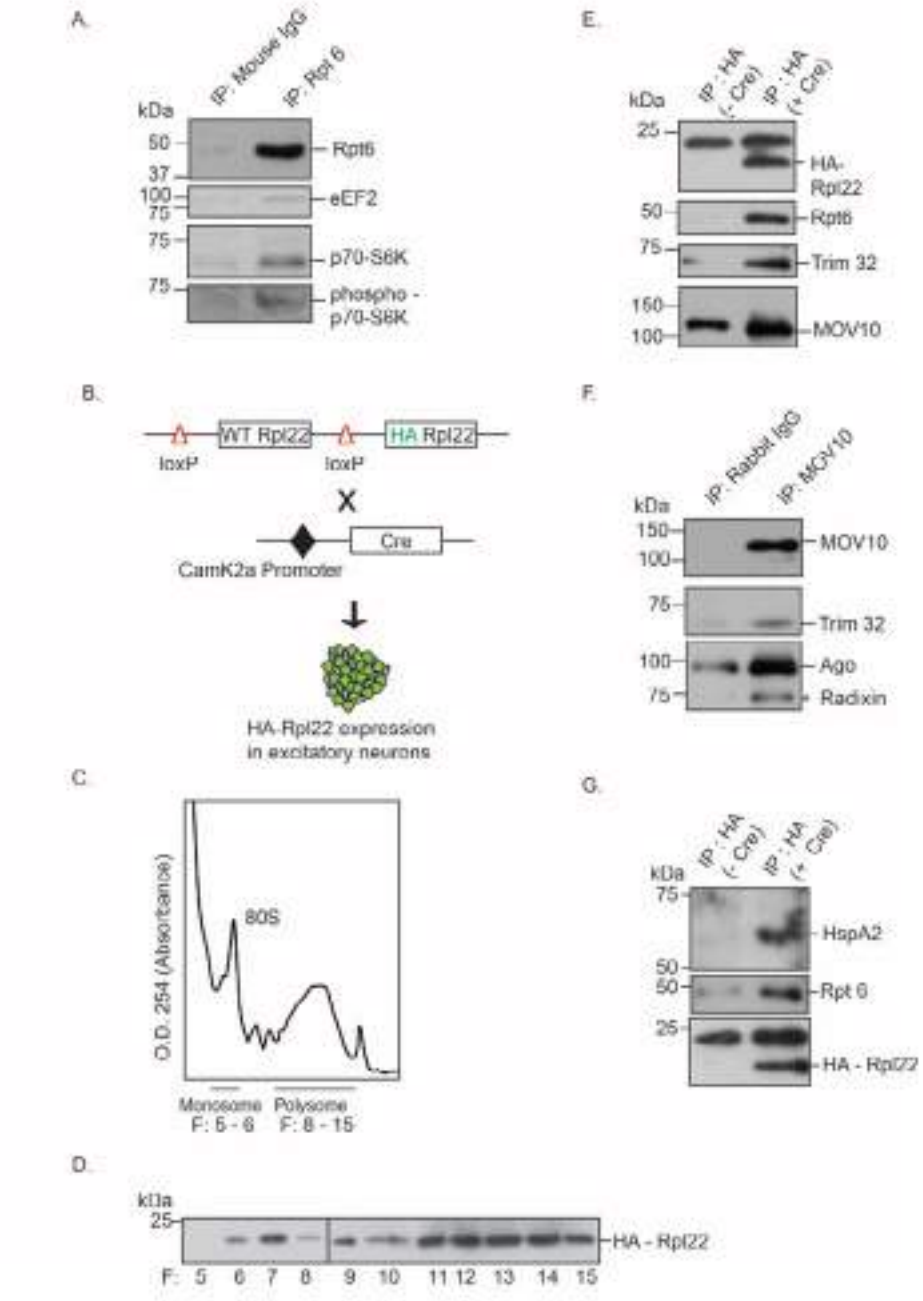

Figure 4: Interaction between proteasome and actively translating RNA-associated polyribosomes. (A) Proteasome interacts with protein synthesis regulators involved in mTOR pathway. (B-D) Schematic representation showing genaration of transgenic mouse expressing HA-tagged ribosome in excitatory hippocampal neurons. (B) $O.D._{254}$ absorbance profile from hippocampus expressing HA-tagged ribosomes. (C) Western blot analysis showing HA-tagged ribosomes are incorporated in actively-translating polysomes. (E) HA-affinity purification followed by western blot analysis showed direct interaction with E3 ligase Trim32, 19S subunit Rpt6 and MOV10 (F) Immunoprecipitation of MOV10 followed by western blot analysis showing Trim32 is integral component of miRISC. (G) Western blot detection of HspA2 in HA-Rpl22 affinity purified protein complex.

We reasoned that the analysis of HA-Rpl22-affinity purified complexes would confirm whether the polysome-associated protein translation and degradation machinaries directly interact with each other. Affinity purification of translating mRNAs from excitatory neurons of mouse hippocampus confirm a direct interaction between translation regulators involved in mTOR pathway, such as p70S6 Kinase and its phosphorylated form and the 19S proteasome subunits Rpt6 and E3 ligase Trim32 (Figure 4E). Our affinity purification of translating transcripts associated with the components of proteasome also co-purified core miRISC factors, such as MOV10 and Argonaute. Immunopurification of miRISC demonstrated that the Trim32 is an integral constituent

of miRISC (Figure 4F). These observation confirmed a RNA-dependent cross-talk between protein synthesis and degradation machanries. How is proteasome tethered to translating transcripts? We have detected both the 19S proteasome subunit Rpt6 and Hsp70-like protein A2 (HspA2) in the HA-affinity purified fraction (Figure 4G). HspA2, a Hsp70 family of chaperone protein has been shown to co-sediment with subunits of proteasomes and also known to regulate protein synthesis. Our observations prompted us to speculate that HspA2 may function as an adaptor protein between proteasome and polyribosome-associated actively-translating transcripts.

As several neuronal miRNAs have been shown to regulate AMPAR expression during homeostatic scaling, we focused on the miRISC remodeling by the combined actions of protein synthesis and proteasome-dependent protein degradation. We observed that bicuculline-induced synaptic activity triggered mTOR-dependent synthesis of Trim32, which promoted proteasome-mediated degradation of MOV10 - a previously characterized key regulator of the miRISC complex. Our data showed inhibition of Trim32 translation by protein synthesis inhibitor blocked MOV10 degradation by proteasome (Figure 5A-C).

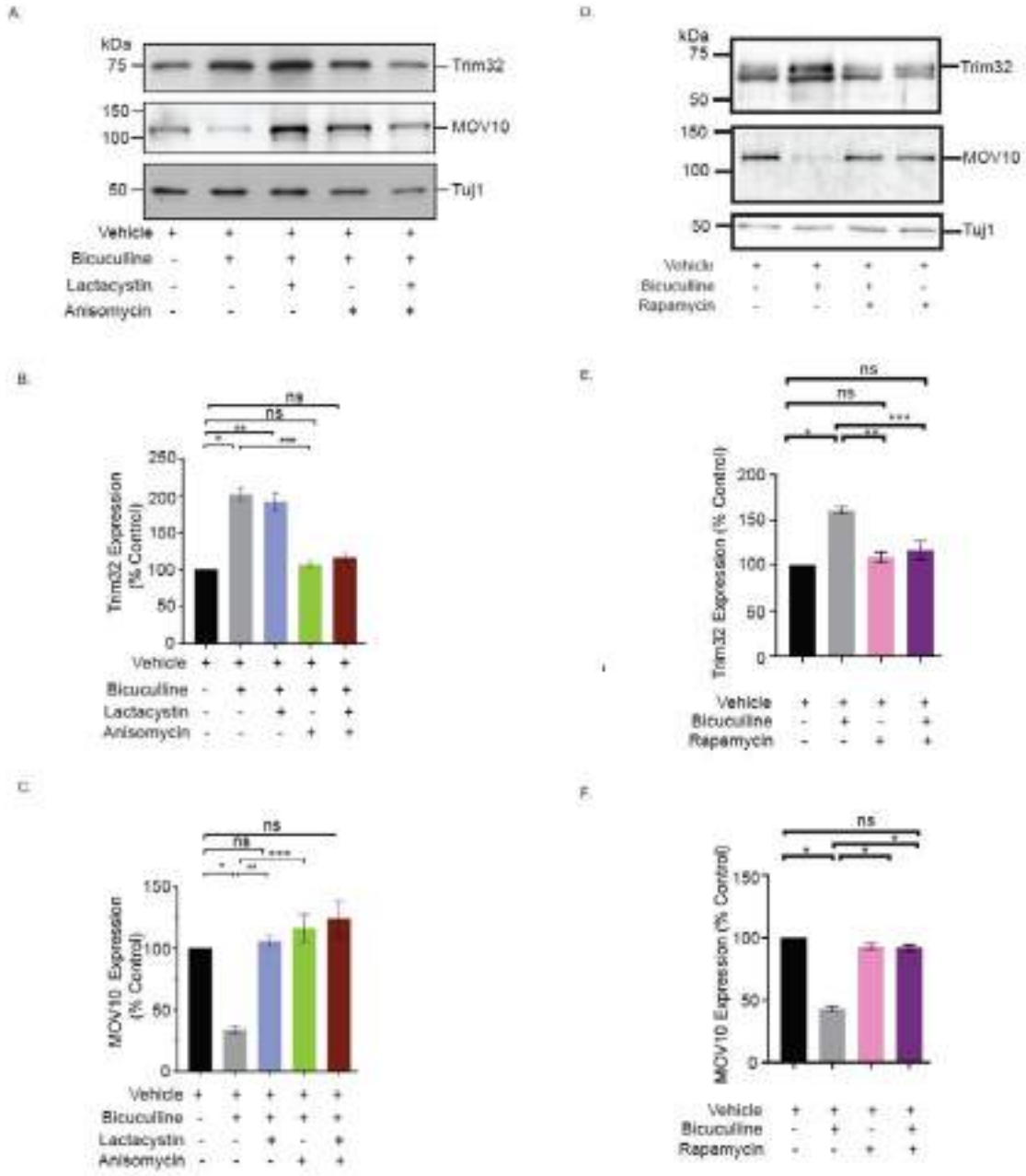

Figure 5: m-TORC1 -dependent remodelling of miRISC via dual control of protein synthesis and degradation. (A-C) Trim32 synthesis drives proteasomal degradation of MOV10 (D-F) m-TORC1 inhibition block Trim32 synthesis and subsequent degradation of MOV10.

We were able to show that inhibition of protein synthesis or mTOR activation prevented proteasome-dependent degradation of MOV10 (Figure 5D-F). This data provides specific mechanistic evidence supporting a counter intuitive model of miRISC remodeling *via* the combinatorial control by protein synthesis and proteasome-mediated degradation.

We analyzed the importance of the miRISC remodeling in homeostatic scaling by evaluating synaptic AMPAR expression following knockdown of MOV10. Indeed, we observe significant reduction of synaptic surface AMPAR following loss of MOV10.

Loss of MOV10 by lentivirus-mediated RNA interferance (RNAi) significantly reduced amplitude of mEPSC. However, we did not observe any alteration of mEPSC frequency. This observation recapitulates similar dynamics of AMPAR and subsequent reduction of synaptic strength following chronic elevation of synaptic activity upon bicuculline treatment. How AMPARs are downregulated by miRISC remodelling upon synaptic hyperactivity? Knockdown of MOV10, that mimics synaptic hyper-activity driven degradation by proteasome, significantly enhanced the expression of Arc – an immediate early gene known for AMPAR endocytosis from post-synaptic membrane and its subsequent degradation (Figure 7).

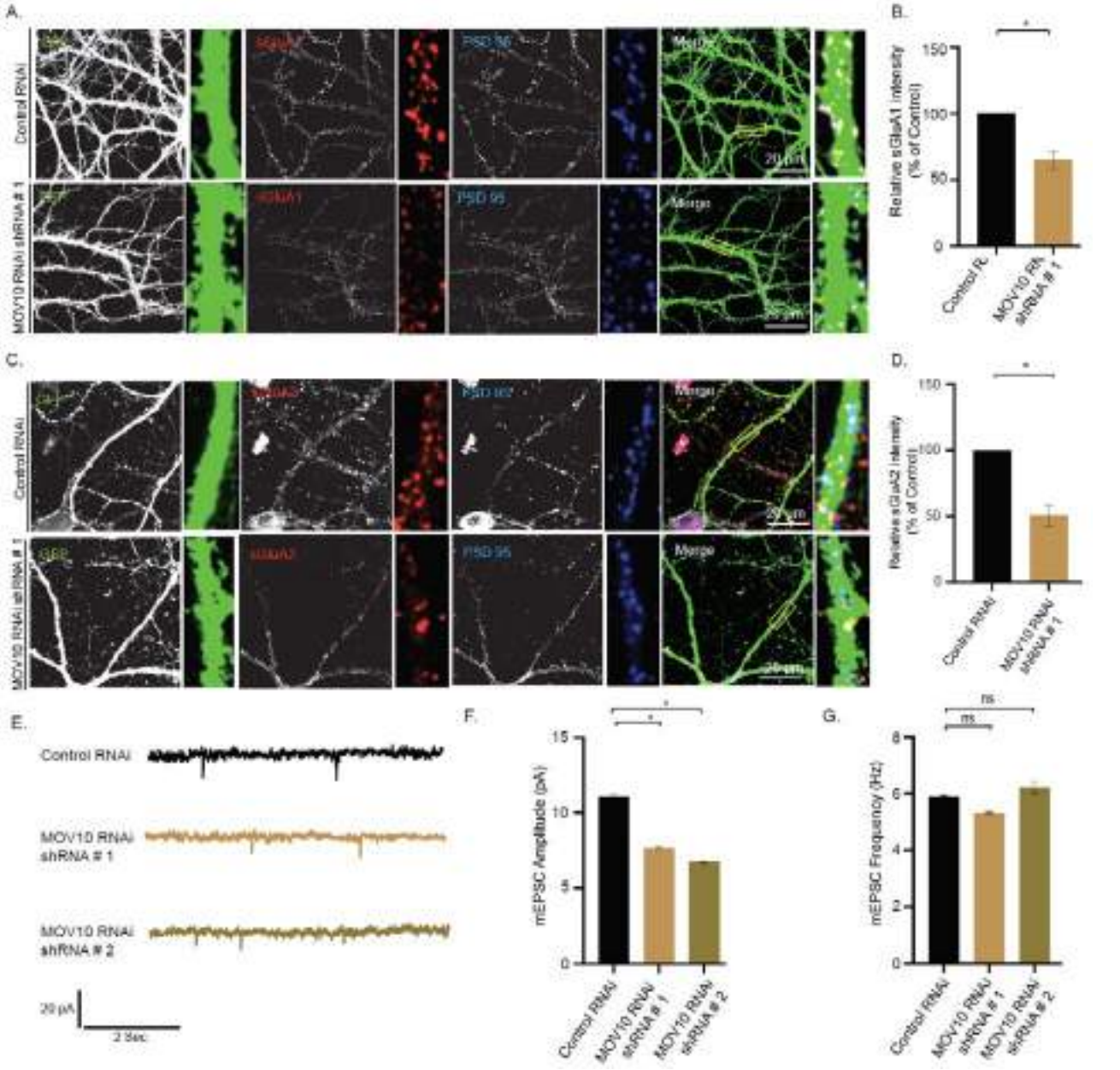

Figure 6: MOV10 knockdown reduces AMPAR-mediated synaptic strength. (A-D) Loss of MOV10 by lentivirus-mediated RNAi reduces surface expression of GluA1 and GluA2 subunits of AMPARs (B) MOV10 knockdown led to reduction of mEPSC amplitude but not frequency.

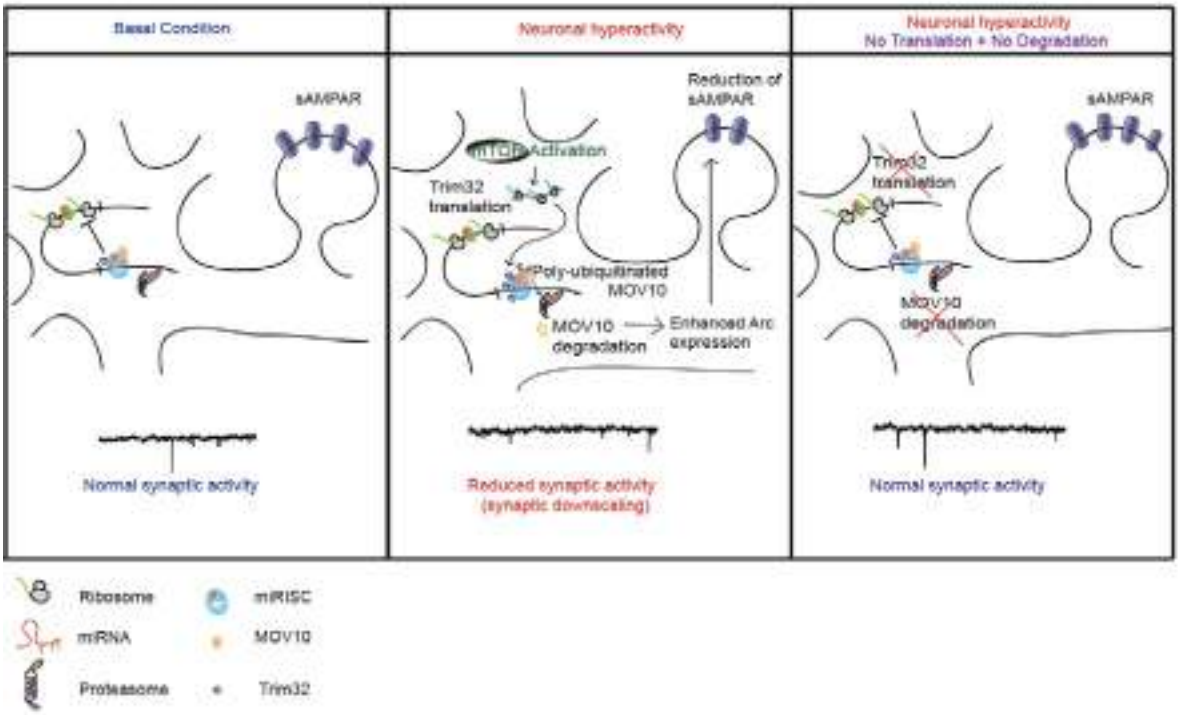

Figure 7: Schematic representation of synaptic homeostasis mechanism involving miRISC remodelling via synchronous control of protein synthesis and degradation.

Taken together, our study provides a unique mechanism of synaptic homeostasis involving dynamic remodeling of a protein complex through the synergistic actions of protein synthesis and proteasome-mediated protein degradation. Our data presents much-awaited biochemical evidence for the steady-state protein dynamics during synaptic remodeling that rely on the interplay between two opposing processes. We envisage that this regulatory control could potentially govern a diverse array of nervous system functions, including but not limited to synaptic homeostasis. Impairment of synaptic homeostasis emerged as a key pathological condition in various neurodevelopmental disorders, such as Autism Spectrum Disorders, Schizophrenia and Fragile-X-syndrome. This study is likely to stimulate further investigations to evaluate how deficits in homeostatic scaling contribute to pathological conditions of the central nervous system.

Presentations

1. Sourav Banerjee, Sarbani Sammadar and Balakumar Srinivasan. Mechanisms of local protein synthesis at the synapse by miRNA decay and its implications in synaptic plasticity, The Annual Meeting of the Japan Neuroscience Society and Japanese Society for Neurochemistry, July 2019.

2. Sourav Banerjee, Balakumar Srinivasan and Sarbani Samaddar. Balancing act : Mechanism of homeostatic synaptic scaling by synergistic control of protein synthesis and degradation, National Centre for Biological Sciences, September 2019

3. Sourav Banerjee, Balakumar Srinivasan and Sarbani Samaddar. RISCy Business: Regulation of homeostatic synaptic activity by remodeling of miRNA induced silencing complex, Annual meeting of Indian Academy of Neuroscience, AIIMS, New Delhi, November 2019

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Collaborators

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

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Bhavani Shankar Sahu

Technician

Mahendra Singh

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

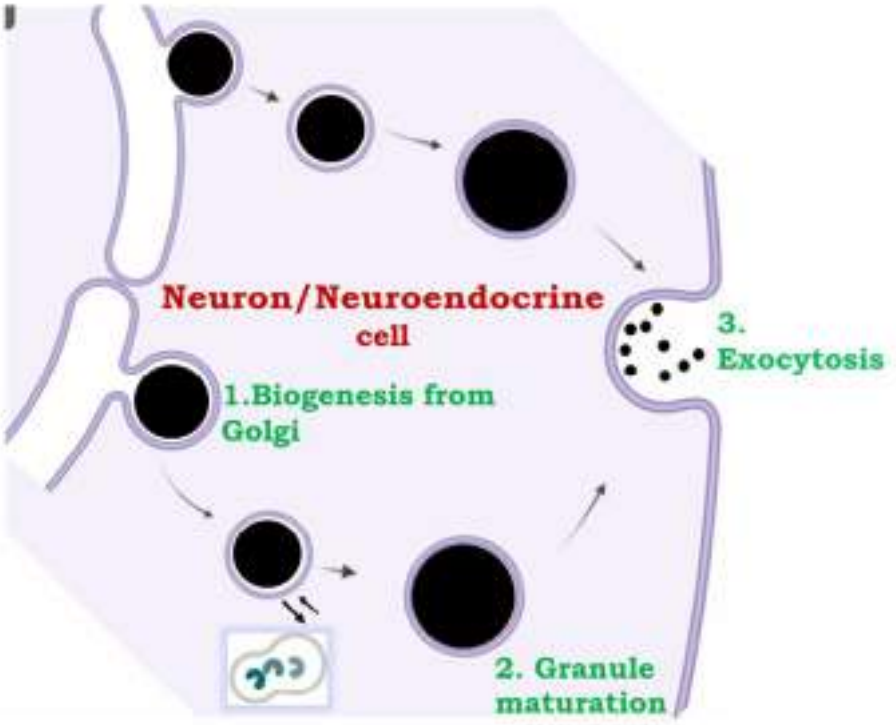
Our lab investigates vesicular trafficking pathways in neuroendocrine cells. Towards understanding the specialised vesicular trafficking pathways, we study a specific type of vesicles called dense-core vesicles (DCVs). DCVs are specialised sub-cellular organelles present in specific neurons/neuroendocrine 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 from the past four decades, many aspects related to sub-cellular trafficking/secretion is unknown, and we study this in our lab in two broad themes.

Research Theme I: Investigating DCV Biogenesis

We are specifically interested in understanding the fundamental mechanisms related to post Golgi vesicular trafficking pathways in DCV biogenesis and the proteins associated with regulated exocytosis, a phenomenon of controlled secretion in neuronal/neuroendocrine cells. To understand this, we employ Rat PC-12 and INS-1 neuroendocrine cells as model systems to study. The main goal is to discover novel proteins regulating DCV formation, maturation and secretion. To address this, we use gene manipulation (gene knockdown & CRISPR/Cas9), subcellular fractionation, proteomics, electron and confocal microscopy as tools. In this theme, for a specific project, we are investigating the role of adaptor protein complex-3(AP-3) in DCV formation and function by using inducible shRNA systems. We have established a stable cell line enabling inducible shRNA depletion of Ap-3 complex and currently in the process of carrying out the functional studies. In a second project, we are investigating the role of clathrin heavy chain, in neuronal differentiation using differentiated PC-12 cells. Our futuristic studies include characterisation the role of novel proteins associated with DCV formation and function.

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

Besides the fundamental biology, we are also interested in understanding how DCV proteins regulate metabolic and physiological functions at the cell/organism level. Towards this, we are investigating the



Schematic: INVESTIGATING THE BIOGENESIS OF DENSE CORE VESICLES AT THREE DIFFERENT STAGES 1,2&3.

role of Chromogranins and related peptides co-stored and released by regulated exocytosis from DCVs of neuroendocrine cells in regulating cellular and physiological functions by using cell culture and mice models. In a specific project, we are studying the role of DCV derived peptides, catestatin and TLQP-21 in modulating glial cell functions by using rodent N9 and BV-2 microglial cell lines. We are also interested in investigating the regulated exocytosis in neuronal diseases. In a specific project, we plan to understand the functional status of regulated exocytosis in Huntington's disease by using cell culture and mice models. Our futuristic projects include the use of knock out mice of DCV proteins to characterise the physiological phenotypes and functional characterisation of gene variants of DCV proteins associated with clinical conditions such as mental health disorders and metabolic syndrome (Diabetes, Obesity and Cardiovascular disease).

Presentations

1. Sahu BS Organellar proteomics reveals the crucial role of clathrin in dense-core vesicle biogenesis. M2T2-2019 – Molecular Motors, Transport and Trafficking 18-20th October 2019 at NBRC- Manesar.
2. Sahu BS TLQP-21 neuropeptide and the complement 3a receptor (C3aR1) regulate a novel calcium-dependent pro-lipolytic pathway. International Society for Chromaffin cell Biology meeting -2020 January 23-26, 2020 at IIT Madras.

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Collaborators

- Professor Sushil Mahata, University of California, Sandiego, USA.
- Dr Alessandro Bartolomucci, University of Minnesota, Twin Cities, USA.
- Dr Samuel Stephens, University of Iowa, Iowa City, USA.
- Dr Dileep Vasudevan, DBT- Institute of Life sciences, Bhubaneswar, India.

Nivethida Thirugnanasambandam

Investigating the role of nicotinic neuromodulation on levodopa-induced dyskinesias

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by loss of dopaminergic neurons in the basal ganglia. The motor and cognitive dysfunction associated with PD can be extremely debilitating and levodopa has been the most effective medical treatment. However, almost 70% patients on levodopa therapy develop severe complications such as abnormal involuntary movements or levodopa-induced dyskinesias (LID). Despite a critical need for new drugs to treat LID, due to insufficient knowledge about the disease etiology, only a few candidates have been identified. Recent studies suggest that nicotinic neuromodulation could contribute significantly to the pathophysiology of LID. Preclinical studies in animal models also show that nicotine and its agonists can reduce dyskinesia by >50% in mouse and monkey models of LID due to their neuroprotective and antidyskinetic effects. Epidemiologically, history of never smoking is associated with increased risk of early onset LID. Hence, it is conceivable that nicotinic neuromodulation plays a significant role in the pathophysiology of LID, which could be exploited for identifying new drug targets.

The primary goal of this project is to demonstrate the role of nicotinic neuromodulation in the pathophysiology of LID using neuropharmaco-physiology studies in patients. We will focus on certain neurophysiological and behavioral deficits in LID that are resistant to dopamine replacement such as cortical inhibition, cortical plasticity and connectivity. Our hypothesis is that nicotine will modulate dopaminergic response to restore these deficits in LID patients.

I. PD patients have less motor cortical inhibition when they are OFF medication. The lost inhibition can however be restored by levodopa in non-dyskinetic PD patients. In contrast, dopamine fails to restore the inhibition in patients with LID suggesting that motor cortical inhibitory circuits play a crucial role in the disease pathophysiology. My hypothesis is that nicotine will modulate dopaminergic response and restore the impaired motor cortical inhibition in dyskinetic patients. Motor cortical inhibition will be assessed using transcranial magnetic stimulation (TMS), electromyography (EMG), electroencephalography (EEG) and response inhibition task.

II. PD patients have difficulty in learning new motor skills due to impaired neuroplasticity. However, motor skill learning is crucial for rehabilitation of these patients. Dopamine restores motor plasticity and motor learning in non-dyskinetic PD patients but not in those with LID. Further, studies have shown that impaired plasticity could be due to reduced connectivity of the motor cortex and restoring cortical connectivity improves plasticity. We hypothesize that nicotine-modulated dopaminergic

activity will restore the cortical plasticity in dyskinetic PD patients and thus improve their motor learning. We will induce motor cortex plasticity non-invasively using TMS. Nicotine-induced changes in cortical excitability and motor learning performance will be assessed.

III. The functional connectivity of the cortico-basal ganglia network is altered in PD patients who develop LID. Our hypothesis is that LID patients will exhibit impaired cortico-basal ganglia connectivity that is not restorable by dopaminergic medication. Functional connectivity of the cortico-basal ganglia network is critical for reinforcement learning. We will use functional MRI to explore the differences in the cortico-basal ganglia network connectivity of dyskinetic and non-dyskinetic patient groups and their response to dopaminergic medication.

We expect that the results of this project will demonstrate that nicotinic neuromodulation is critical in the pathophysiology of LID and that nicotinic agonists in combination with dopamine can potentially restore some of the neurophysiological and cognitive deficits in LID. Thus, we can get valuable insight into the possibilities for new drug targets and also rationalize the use of nicotine agonists like varenicline as promising disease modifying agents.

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Collaborators:

- Arpan Banerjee, NBRC
- Dipanjan Roy, NBRC
- Dr. Roopa Rajan, Department of Neurology, AIIMS, New Delhi.

Swagata Dey

MSc Student

Nitish Kumar

Regulation of cytoskeletal dynamics in dendrite development and regeneration

For proper neurological functions, an organism requires neurons with intact axons and dendrites that can form right connections with their neighboring tissues. Various mental retardation pathologies like Schizophrenia, Down, Rett, Fragile X, Angelman's, and Williams and Rubinstein-Taybi syndrome have been symptomized by loss of structural connectivity in certain cognitive centers in the brain. Due to their sensitivity towards excitatory and inhibitory inputs, dendrites often undergo dystrophy like formation of dendritic varicosities, loss of dendritic spines, mitochondrial swelling and dysfunction, and disruption of microtubules often observed in focal stroke or anoxic depolarization, mild Traumatic Brain Injury (mTBI), and epilepsy. Although, these features appear to be neuroprotective and reversible in favorable conditions, their chronic occurrence may lead to permanent loss of neurological function or fatalities. It is therefore imperative to understand the processes and regulators of dendritic remodeling in different physiological conditions.

Dendrites grow and mature from the undifferentiated neurites following axon specification in the nascent neurons. Extracellular factors like OP-1, CPG 15, and neurotrophins along with MAP2, CHOI/MKLP1 are required for induction of dendrite. Dendrite maturation begins with the neurites undergoing a phase of longitudinal and circumferential growth and attaining molecular signatures of a typical dendrite. Cytoskeletal and signaling factors like Cdc42, RhoA, Rac, ROCK, Lis1, Dynein, and Notch are critical for the process. Concomitant to the growth of the dendrites, extracellular guidance cues and cellular receptors ensure correct targeting of the dendrites. Following the growth phase, the dendrites branch and form territorially restricted arbors and may acquire morphological characteristics like dendritic spines. My work pertains to understanding the dendritic remodeling processes during development and following injury, focusing specifically on the cytoskeletal processes and regulators.

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 transports 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 dendritic arbor. Dendritic arborization also depends on the microtubule and actin nucleators in the form of Golgi outposts, kinetochore proteins, endoplasmic reticulum, 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.

Unlike axon regeneration, dendritic injury and regeneration have not been well characterized. In the event of axonal injury, massive cytoskeletal reorganization is required to enable the formation of growth cone and regrowth of the axon. Upon injury, the intracellular calcium levels increase locally which further induces downstream pathways to ensure the regeneration program like increase in Cyclic Adenosine monophosphate (cAMP) levels and activation of Protein Kinase A (PKA) and Mitogen activated protein kinase kinase kinase (MAPKKK) such as Dual Leucine Zipper Kinase (DLK-1). DLK-1 initiates local microtubule (MT) remodeling and initiates the transcription through Ets/CEBP-1 to promote axon regeneration. On the other hand, dendrite regeneration is found to be independent of DLK and JNK signaling however, effectors like AKT and ROR and Wnt effectors regulate the dendrite regeneration in *Drosophila*. Also, MT regulatory molecules like Patronin are required for the regrowth following axon and dendrite injury. Although there are indications of the signaling effectors and cytoskeleton regulatory molecules that regulate dendrite regeneration, it is unclear how the signaling effectors may regulate the cytoskeleton during regeneration.

PVD neurons in *Caenorhabditis elegans* have an extensive stereotyped dendritic arbor spread in the anterior (major) to posterior direction (minor) and a ventrally directed well-defined axon (Figure 1A-B). PVD dendrites branch orthogonally in anatomy and hierarchy with a distinct cytoskeletal organization. Primary dendrites, axons and sometimes secondary branches are rich in microtubules while tertiary and quaternary branches are actin rich (Figure 1C). Using fluorescent protein reporters, these neurons can be visualized and observed *in vivo* thus making them a great system to study dendritic remodeling during development and regeneration.

Role of microtubule depolymerizing Kinesin-13, KLP-7 in dendritic arborization

In most of the model systems, dendrites either have mixed orientation or minus end out orientation of microtubules. PVD neurons has two microtubule rich primary dendrites with the major having minus-end out and minor having plus-end out orientation of microtubules. Among the candidates regulating the minus-end out microtubule orientation in the dendrites, major ones are Patronin, and motors, Dynein and Kinesin-1 which regulate the microtubule dynamics and transport, respectively. Dynein and Kinesin-1 regulate the overall dendritic transport thus having a greater impact on maintenance of dendritic arbor, however, role of cytoskeletal dynamics regulators is elusive. Another question is how the major and minor dendrites of PVD neurons are differentially populated with the specific orientation of microtubules.

KLP-7, an ortholog of KIF2A is a motor of the Kinesin-13 family that depolymerizes the microtubules at both its plus and minus ends however, at minus ends, Patronin imparts an antagonistic role. Originally, discovered as a kinetochore associated protein, Kinesin-13 (KIF2A) plays a role in axonal pruning, dendro-axonal

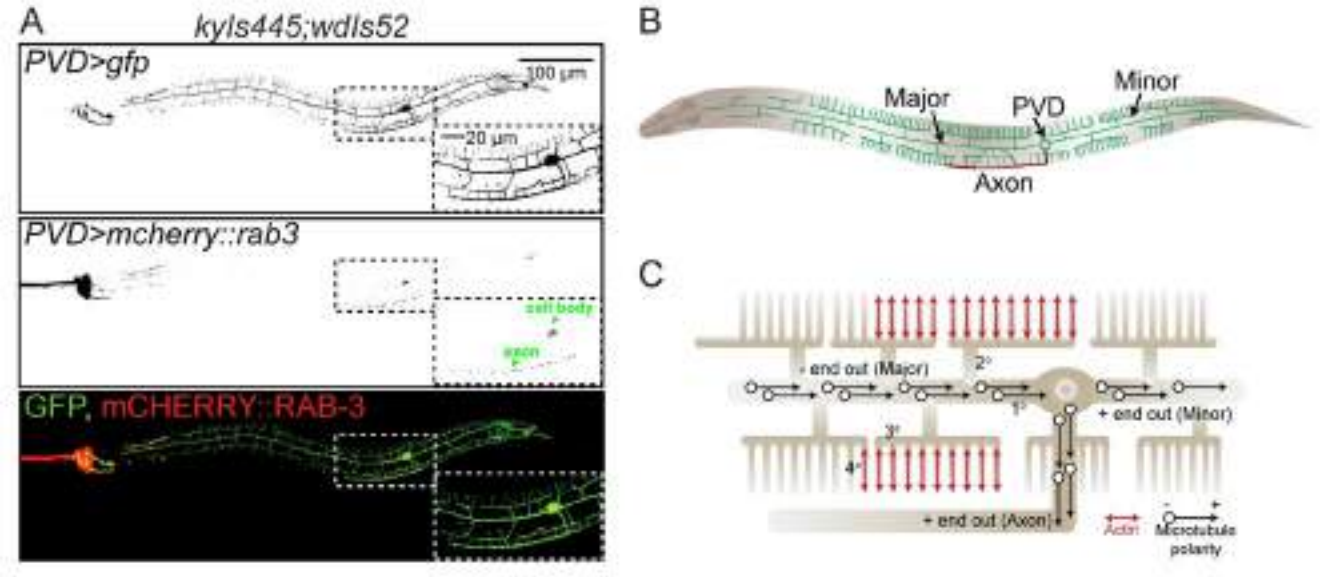

Figure 1. PVD neurons in *C. elegans*. (A) Representative images of PVD neuron labeled with GFP (*pF49H12.4>gfp*, green) and mCHERRY::RAB-3 (*pdes-2>mcherry::rab-3*, red) with the region of interest (white dashed rectangle) magnified in the respective insets. mCHERRY::RAB-3 punctae localized to the cell body and axon (marked in the inset). (B-C) Schematic depicting the neurite arbor of PVD neurons (B) and the cytoskeletal constitution (C).

conversions and neurite outgrowth. Role of KLP-7 as a microtubule depolymerizing factor is uncharacterized in the maintenance of dendritic arbors.

We investigated the dendritic arbor of GFP labeled PVD neurons which were grossly similar in both wild type and *klp-7* loss of function mutant animals (Figure 2A-B). Though loss of *klp-7* did not change overall density of secondary and tertiary branches remained unchanged (Figure 2B), the total number and density of quaternary branches were increased (Figure 2B). It is possible that increased microtubule stability in *klp-7(0)* facilitated the formation of new neurites or deficient pruning as previously observed in KIF2A knockout. Alternatively, KLP-7 can associate to the kinetochore machinery found to be enriched in the developing dendrites. These kinetochore complexes may serve as a secondary nucleating centers where KLP-7 may increase the microtubule dynamics by depolymerization.

Further investigation is necessary to understand the secondary roles of KLP-7 in dendritic arborization. I will be doing imaging the PVD dendrites in the adult stages to investigate role of KLP-7 in dendritic pruning. Observation of fluorescent reporter of KLP-7 and γ-tubulin will clarify its role in dendritic branching.

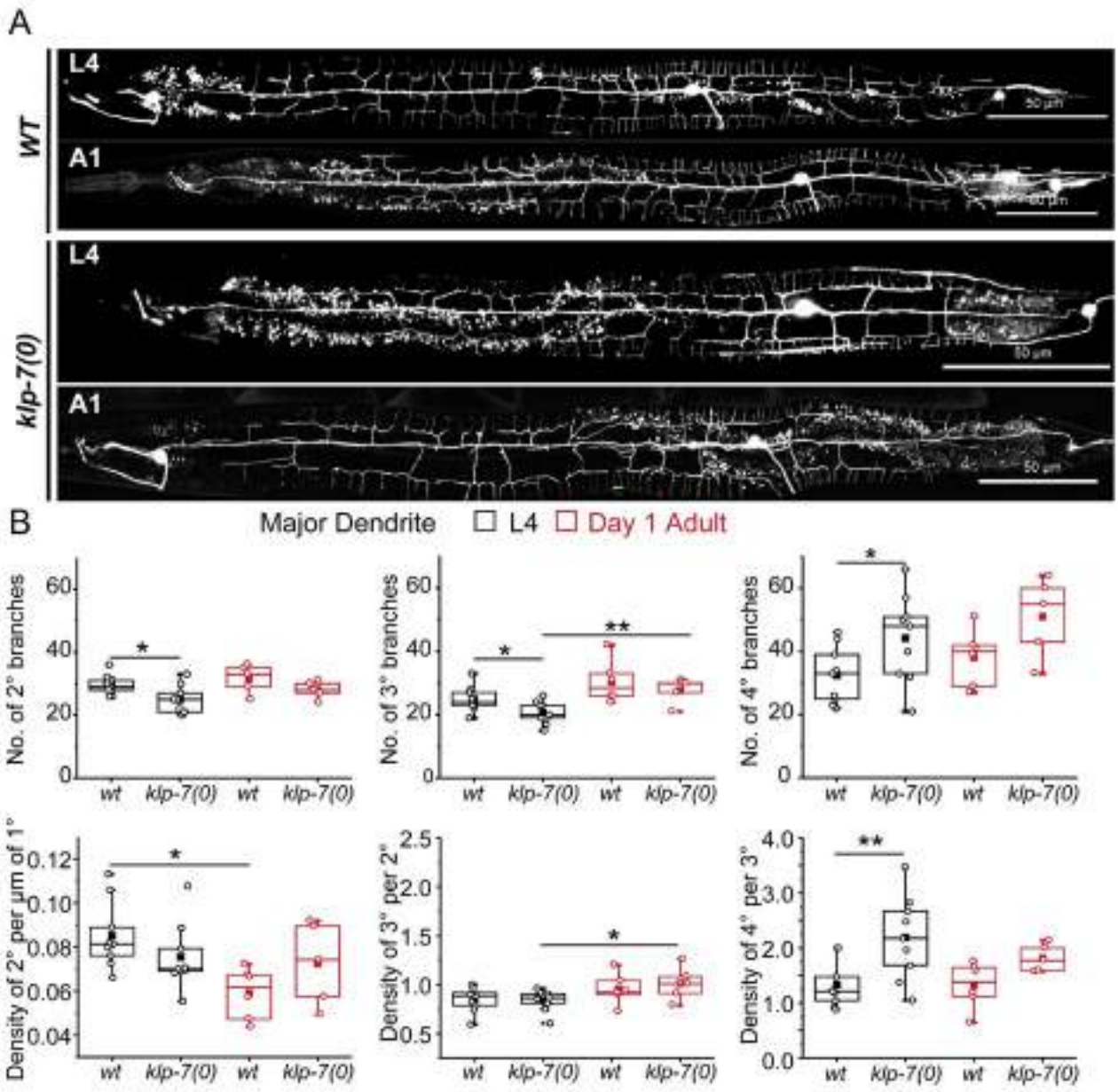

Figure 2. PVD neurons in the wildtype and *klp-7(0)*. (A) Representative images of the L4 and Day 1 adult stages in the wildtype and loss of *klp-7* function mutants. (B) Quantification of the branch number (upper) and density (lower) in wildtype and *klp-7* loss of function mutant at L4 and Day 1 adult stages. Comparison of means is done using ANOVA with $p<0.05$*, 0.01**.

KLP-7 is required for maintaining the microtubule dynamics and neuronal polarity

During neuronal polarization, taxol induced stabilization of microtubules causes conversion of nascent neurites to axons. Similar observations of neurite conversion were previously documented in the KIF2A (Kinesin-13) knockout mice primary neuron cultures. We investigated if KLP-7 also regulated microtubule orientation and neuronal polarity in PVD neurons by observing the EBP-2::GFP comets and compartmentalization of mCHERRY::RAB-3.

EBP-2::GFP dynamics was restricted to the primary dendrites and the axon, however, due to loss of *klp-7*, it was observed in the secondary and ectopic branches as well (Figure 3A-B). Loss of *klp-7(0)* is expected to stabilize the microtubules and decrease the microtubule dynamics in all processes. Contrary to our expectations, microtubule dynamics were only ceased in the axon and minor dendrite (Figure 3B). Major dendrite in *klp-7* mutant showed robust polymerization dynamics with no change in the orientation (Figure 3B). This might be possible due to Patronin (PRTN-1) mediated minus end stabilization and polymerization. Further investigation with Patronin reporter and mutant is required to understand the combinatorial effect of KLP-7 and PTRN-1.

mCHERRY::RAB-3 localized mostly to the cell body and of PVD neurons in the form of punctae with some occurrence in the dendrites (Figure 4A-B). Due to loss of *klp-7* function, dendritic localization of the mCHERRY::RAB-3 punctae was considerably increased in the secondary (2°) and tertiary (3°) dendrites as compared to wild type neurons indicating loss of neuronal polarity (Figure 4A-B). In the absence of *klp-7* function, the microtubules became highly stable which might cause the dendrites to convert to axons.

These results indicate that regulators of microtubule dynamics may define dendritic polarization and arborization. Other regulators of microtubule dynamics like severing proteins and post translational modifications can be investigated for dendrite morphogenesis. Clear understanding of this process will allow us to investigate extracellular signaling molecules like Wnt that also affect dendrite morphogenesis.

As the neurite growth happens as a result of concerted dynamics of microtubule and actin, our next set of experiments will be focused on regulators of microtubule and actin in PVD neurons. Understanding role of actin in the process of dendrite morphogenesis will provide insight about other regulators of actin assembly. We can investigate the multivalent proteins like Doublecortin like Kinases (DCLK) and Cdc-42/Rho/Rac pathway that can affect microtubules and actin. This will further elucidate the coregulation of actin and microtubule dynamics in restructuring of neurites.

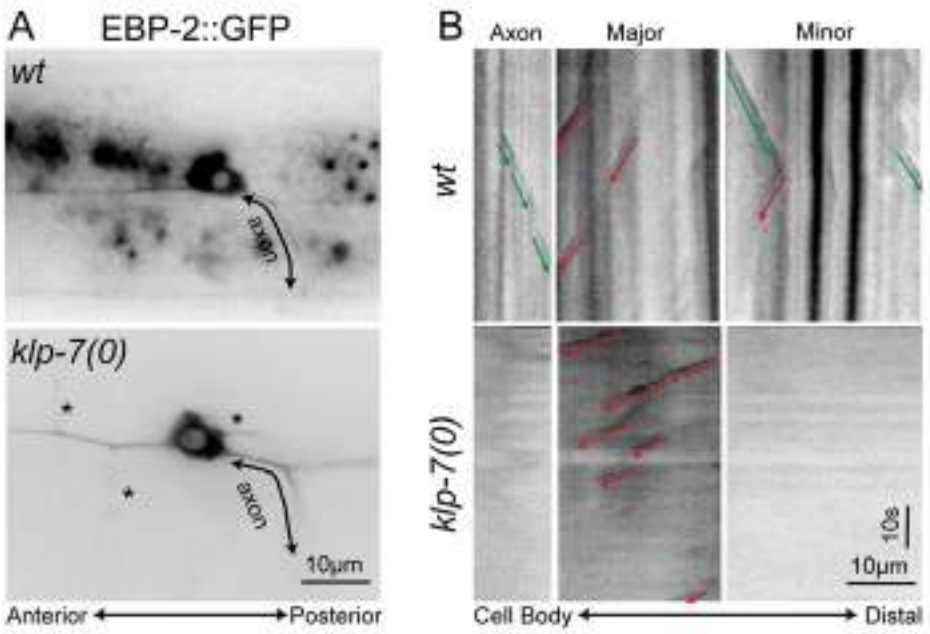

Figure 3. Microtubule dynamics in the wildtype and *klp-7(0)*. (A) Representative images of PVD neurons labeled with EBP-2::GFP at the L4 stage in the wildtype and loss of *klp-7* function mutants. Ectopic localization of EBP-2::GFP was indicated by asterisk. (B) Kymographs representing movement of EBP-2::GFP comets in the axon, major and minor dendrite of wildtype and *klp-7* loss of function mutant at L4 stage. Plus end out and minus end out movement was indicated by green and red arrows, respectively.

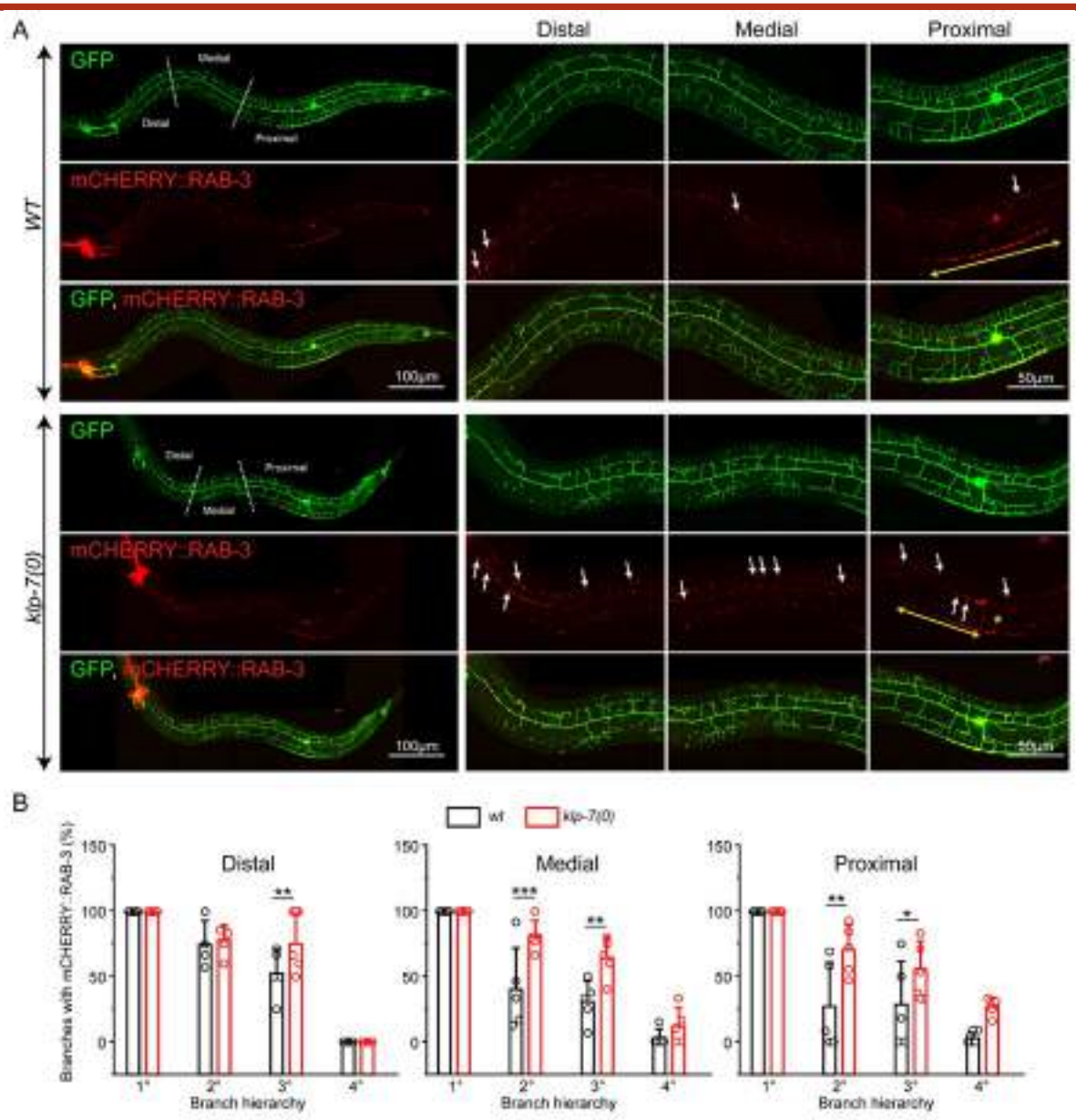

Figure 4. Neuronal polarity in the wildtype and *klp-7(0)*. (A) Representative images of PVD neurons labeled with GFP and mCHERRY::RAB-3 at the L4 stage in the wildtype and loss of *klp-7* function mutants. The major dendrite was sectioned into distal, medial, and proximal segments. White and yellow arrow mark the mCHERRY::RAB-3 punctae in dendrites and axons, respectively. Note formation of an ectopic axon (yellow asterisk) in the *klp-7(0)* mutant. (B) Quantification of the percentage of branches containing mCHERRY::RAB-3 punctae in distal, medial, and proximal sections of major dendrite of wildtype and *klp-7* loss of function mutant at L4 stage. Comparison of means is done using ANOVA with p<0.05*, 0.01**, 0.001***.

Characterization of axon and dendrite regeneration in PVD neurons of *C. elegans*

Dendrite remodeling following injury has been a less explored area in the field of neurite regeneration. Most of the molecular pathways of neurite regeneration have been elucidated in axon injury models. From the recent observations of dendrite regeneration in invertebrate neurons, it appears that dendrite regrowth following injury does not follow the conserved pathways of axon regeneration. In order to find the cytoskeletal basis of dendrite regeneration, PVD neurons can serve as a model system where the axon and dendrites are clearly differentiated with distinct cytoskeletal composition.

We used a reporter for mCHERRY::RAB-3 to mark the axon of PVD neurons and quantified the branches that acquired mCHERRY::RAB-3 as a readout of axonal regeneration (Figure 5A-B). In the wild type conditions at 3 hours (h) after transection, the severed end retracted considerably but it regrew at 24h after the injury from

the severed end (Figure 5B-F). In most of the cases, the most adjacent tertiary dendrite became like an axon directing their processes towards the VNC with some ectopic branches appearing from the axon and converted neurites (Figure 5B-F). We observed an increase in the length of the severed axon (original axon) from 3-48h suggesting continued development (Figure 5C), in the regrowth from the severed axon (Figure 5D), conversion of tertiary dendritic branches (Figure 5E), number and length of ectopic branches (Figure 5F).

Transection of the major or minor dendrite showed extensive non-stereotyped outgrowth with spurious branches and reconnection with the severed remnants. We severed the major and minor dendrite at 30 µm distance from the cell body. The dendrites did not show any regenerative process at 3h, however, at 24h after injury, the dendrite expanded in a non-stereotyped pattern (Figure 6A). The regrowing branches often reconnected to the severed remnants of the original arbor. As PVD dendrites are known to fuse, we expect fusion to occur at the regions where the branches cross each other. We found the regrowing dendrite to connect with primary and tertiary and continuing their regrowth. In majority of the cases, we found that the tertiary dendrites of the adjacent menorah merge corroborating the earlier observation of menorah-menorah fusion. A similar observation was made on the other primary (minor) dendrite with the plus end out microtubules (Figure 6B).

Furthermore, we are delineating the molecular players that are critical for dendrite regeneration. DLK-1/MLK-1 pathways were observed to be required for the axon (Figure 7) but not dendrite regeneration.

Together, these results have established a neurite regeneration model using PVD neurons which have a diverse cytoskeletal organization and regeneration of different processes can be investigated. Further, we will be exploring the immediate effectors of the cytoskeleton and polarized trafficking in these neurons to understand their regenerative mechanism.

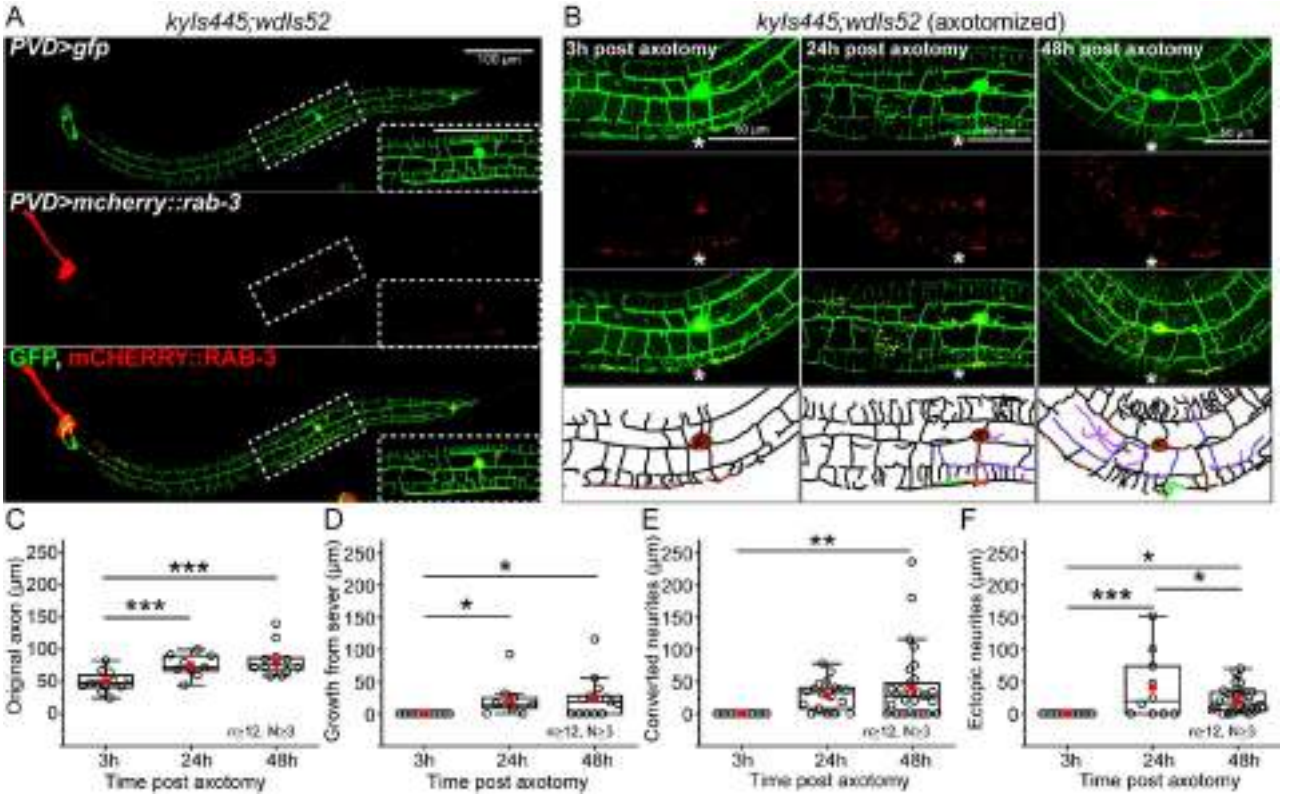

Figure 5. Axon regeneration in wildtype PVD neurons. (A) Representative images of PVD neurons with GFP and RAB-3::mCHERRY axons in the wild type neurons. (B) Representative images and schematic of axon regeneration in PVD neurons 3, 24, and 48 h following axotomy. In the schematic red dots depict RAB-3::mCHERRY punctae, green trace represents growth from the severed end, blue traces show converted neurites and purple traces depict ectopic branches. (C-F) Quantification of the length of original axon (C), growth from the severed axon (D), converted neurites (E), and ectopic branches (F) at 3, 24, and 48 h after axotomy. Comparison of means is done using ANOVA with $p<0.05$*, 0.01**, 0.001***.

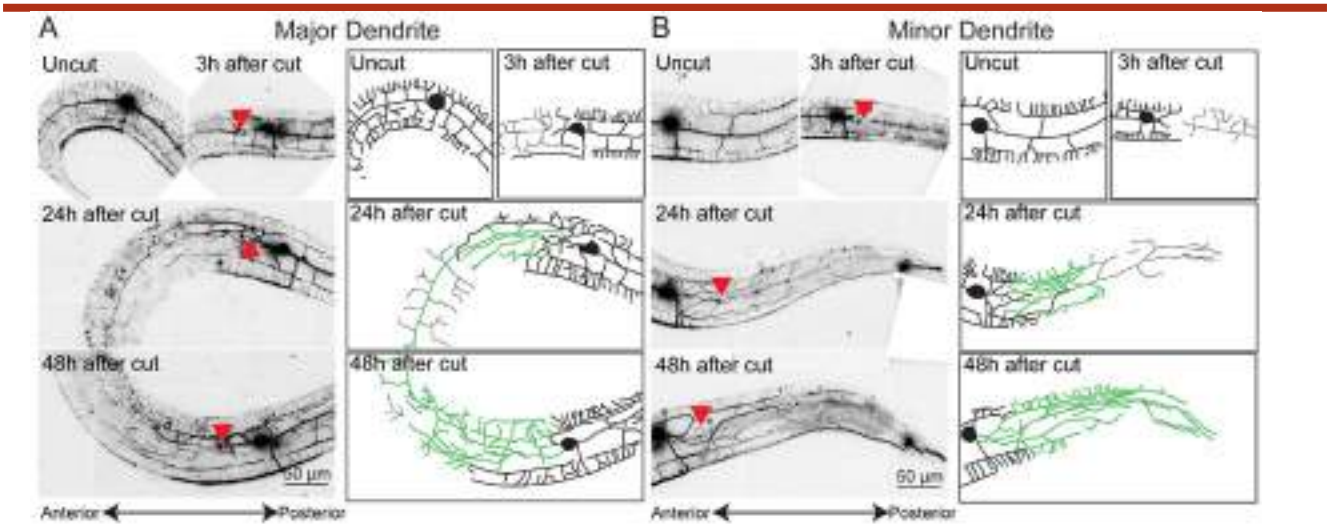

Figure 6. Dendrite regeneration in PVD neurons. (A-B) Representative images of PVD major (A) and minor (B) dendrite in the uncut condition, and 3, 24, and 48 h after injury. Red arrowheads depict the location of the injury. Panel on the right side illustrates the process schematically with original branches (black) and regrowing branches (green).

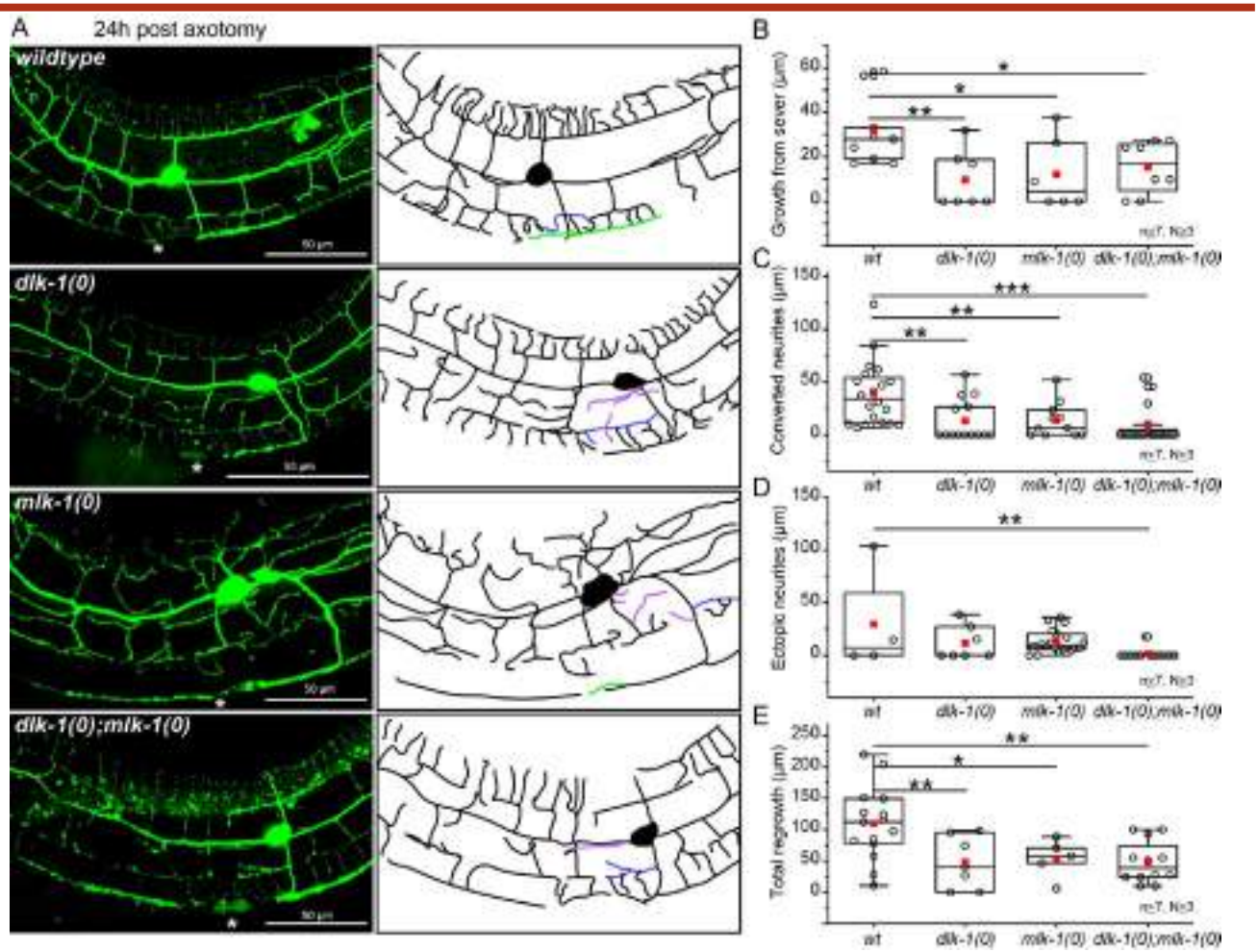

Figure 7. Axon regeneration in wildtype, dlk-1, and mlk-1 mutant PVD neurons. (A) Representative images and schematics of GFP labeled PVD neurons in the wild type, loss of function mutants of *dlk-1 (dlk-1(0))*, *mlk-1 (mlk-1(0))*, and double mutant of *dlk-1* and *mlk-1* neurons at 24 h after axotomy. In the schematic green trace represents growth from the severed end, blue traces show converted neurites and purple traces depict ectopic branches. (B-E) Quantification of growth from the severed axon (B), converted neurites (C), and ectopic branches (D) and total growth (E) in these mutants with respect to the wildtype at 24 h following axotomy. Comparison of means is done using ANOVA with $p<0.05$*, 0.01**, 0.001***.

Presentations

- Swagata Dey: Studying dendrite regeneration in PVD neurons of *Caenorhabditis elegans*. National Brain Research Centre, Manesar, India, Molecular Motors, Transport, and Trafficking Meeting. October 2019.

Funding

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Award

DBT/Wellcome Trust India Alliance Early Career Fellowship (2019)

Yogita K. Adlakha

DST Inspire Faculty

Department of Cellular & Molecular Neuroscience

Investigation of neurodevelopment using human neural stem cells derived from induced pluripotent stem cells

Human brain development is a beautifully orchestrated event which involves a complex series of dynamic and adaptive processes that function in a highly constrained and genetically organized context. Appropriate differentiation, maturation and function of neuronal networks is the utmost requirement for cognition and behavior. Interruption of these processes can lead to neurodevelopmental disorders such as Autism, Huntington's disease or Intellectual disability. Consequently, the processes underlying neural development, including neural stem cell self-renewal, differentiation, fate specification, neuronal migration, maturation, and integration have been well established at transcriptional level. However, recently, post-transcriptional control of gene expression has emerged as an additional, and equally important, regulatory layer. In particular, microRNAs (miRNAs), an abundant class of small non-coding RNAs, have been shown to regulate neuronal differentiation, maturation and their function by modulating gene expression via mRNA translation inhibition. Although the transcriptional machinery during neural development has been studied extensively, understanding the miRNA mediated regulation of neurodevelopment remains as uncharted territory.

Several studies have revealed essential roles of miRNAs in brain development and function using animal models with deficiency in miRNA biogenesis pathway genes. For example, loss of Dicer caused impeded brain development and the abnormal phenotype of brain in zebrafish. These effects could be rescued by ectopic expression of miR-430. Further, mice deficient in Ago2 (miRNA maturation pathway gene) displayed defects in neural tube closure and mis-patterning of the forebrain. Participation of Dicer in neural stem cell proliferation and differentiation was revealed by the conditional knockout of Dicer in mouse neural stem cells which led to smaller cortex. With progress in miRNA research, it is evident that miRNAs are frequently dysregulated in neurodevelopmental disorders, suggesting a role for miRNAs in the etiology and/or maintenance of neurological disease states.

MiR-137 is a brain enriched miRNA that plays an important regulatory role in brain function. This miRNA is associated with the regulation of adult neurogenesis, dendritic development and neuronal maturation as well as control of the dynamics between neural stem cell proliferation and differentiation during neural development. Emerging evidence implicates dysregulation of miR-137 with the etiology of neurodevelopmental disorders including Schizophrenia, Autism, Huntington's disease, Rett syndrome or Intellectual disability. Dysfunction of miR-137 has also been shown to contribute to neuroblastoma and glioblastoma multiforme. Owing to its significant functions in several neuropsychiatric/neurocognitive/oncological disorders, consequently, this miRNA may have great potential as a

biomarker and in treatment of human diseases where dysregulation of this gene or its pathways are involved.

Studies using mouse models have established that expression of miR-137 gets upregulated significantly when ESCs and neural stem cells differentiate into neuronal lineage. However, molecular role of miR-137 underlying neural development remains elusive.

We have made some novel discoveries in understanding the molecular mechanism underlying miR-137 mediated effects as to how it regulates the dynamics of proliferation and differentiation of neural stem cells. To pursue this goal, we generated human neural stem cells (NSCs) from iPSCs which were derived from peripheral blood of healthy subjects in-house. The NSCs stained positive for neural stem cell markers i.e. Nestin and Sox2. These NSCs were differentiated into neurons using neuronal differentiation media until day 21 and neuronal population was stained positive for neuronal markers including Tuj1 and Map2. We observed enhanced expression of miR-137 in iPSCs and mature neurons as compared to NSCs. Being enriched in brain, we questioned the role of miR-137 in NSCs, therefore, we modulated miR-137 levels in NSCs using overexpression and knock down experiments and immuno-stained the cells with Ki67 antibody for proliferation assay. Overexpression of miR-137 reduces proliferation of NSCs. Next, we assessed the effect of miR-137 on NSC differentiation and observed significant increase in the transcript levels of neuronal markers i.e. Tuj1, Map2, NeuroD1 and Ascl1. MiR-137 also increased punctate expression of DCX in new born neurons and percentage of TUJ1 positive cells. Thus, miR-137 induces neuronal differentiation and reduces proliferation of NSCs. Migration and sprouting of neurons from neurospheres were accelerated in miR-137 mimic transfected neurospheres. This result suggests that miR-137 increases migration of neurons also.

MiRNAs function by reducing the expression of their target gene. We found Myocyte Enhancer Factor 2A (MEF2A) as target gene of miR-137 using TargetScan. Using reporter vector, we observed that miR-137 binds to 3'UTR of this gene and reduces its expression. MEF2A is a transcription factor that regulates peroxisome proliferator activated receptor-gamma coactivator (PGC1α) transcription MEF2A, which led us to examine whether miR-137 modulates mitochondrial biogenesis to achieve enhanced neuronal differentiation. We found that miR-137 diminished the protein levels of PGC1α by 1.8-fold while increased the expression of NRF2, TFAM, SIRT1, and AMPK significantly. Further, we investigated the impact of miR-137 on mitochondria fusion and fission. Ectopic expression of miR-137 increases the transcript levels of genes that participate in mitochondrial fusion i.e. MFN1, MFN2, and OPA1. MiR-137 also increases the transcript levels of genes involved in mitochondrial fission i.e. DRP1 and FIS1. These results suggest that miR-137 also enhances mitochondrial fusion and fission in NSCs. Further, miR-137 increases the mitochondrial DNA content, activates oxidative phosphorylation (OXPHOS) and enhances oxygen consumption rate. These results confirm that miR-137 increases the mitochondrial biogenesis irrespective of PGC-1α status in NSCs. Thus, these experiments confirm that miR-137 alters mitochondrial dynamics to achieve enhanced neuronal differentiation of NSCs. Thus, we have revealed the molecular mechanisms underlying miR-137 mediated effects on neural development.

Since, neurogenesis decreases throughout the life span of an adult and results in compromised regenerative and repair capacity of the brain. Therefore, novel molecules/strategies responsible for enhancing NSC commitment and differentiation, especially for aging-associated neurodegenerative diseases, are needs of the hour. Thus, miR-137-based intervention might be useful for the management of aging-associated neurodegenerative diseases in future.

Publications

1. Asha S. Channakkar#, Tanya Singh, Bijay Pattnaik, Pankaj Seth, Yogita K. Adlakha#*. MiRNA-137-mediated modulation of mitochondrial dynamics regulates human neural stem cell fate. STEM CELLS. 2020, Feb 3. doi: 10.1002/stem.3155. *Corresponding Author. # Equal Contribution as first author. (Our work made headlines, "NBRC scientists pave the way for a better understanding of Autism" in Hindu Business Line and Vigyan Prasar "India Science Wire" and Biotechnika.)

2. Kaya KD, Chen HY, Brooks MJ, Adlakha YK, Welby E, Swaroop A. Transcriptome-based molecular staging of human stem cell-derived retinal organoids uncovers accelerated photoreceptor differentiation by 9-cis retinal. Molecular Vision, 2019; 25:663-678. Preprint, bioRxiv 733071.

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1. Ke Jiang, Anupam Mondal, Yogita K. Adlakha, Matthew Brooks, Linn Gieser, Jessica Gumerson, Kim Jung-Woong, Raul Covian Garcia, Anand Swaroop. "Mitochondria Defects Constitute an Early Step in Retinal Degeneration". ARVO Annual Meeting, Vancouver, Canada, July, 2019.

2. Yogita K Adlakha, Invited Resource person. "Elucidation of regulation of neural development by non-coding RNAs: Employing statistical tools". Faculty Development Program on Biomathematics, Shivaji College, University of Delhi, New Delhi, India, Aug, 2019.

3. Yogita K Adlakha, Invited Speaker. "Role of non-coding RNAs in the regulation of brain development: Applications of induced pluripotent stem cells". National seminar Shivaji College, University of Delhi, New Delhi, India, Sep, 2019.

4. Yogita K Adlakha, Speaker. "Role of microRNAs in the regulation of human brain development: Applications of induced pluripotent stem cells (iPSCs) and 2D neural stem cells (NSCs)". XXVII Annual Meeting of Indian Academy of Neurosciences (IAN), All India Institute of Medical Sciences (AIIMS), New Delhi, India, Nov, 2019.

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Collaborators

P. Seth and A. Basu, NBRC, Manesar, India.

Major Research Programs

Dementia Science Programme

A national level research programme funded by

Department of Biotechnology

Coordinate by

National Brain Research Centre

Dementia is a devastating condition. It is a progressive disorder that is characterized by impairment in memory and other cognitive abilities. Alzheimer's disease accounts for majority of the dementia cases. Other conditions include vascular dementia, fronto-temporal dementia and Lewy body dementia. With increase in the number of people with advanced age due to increase in life expectancy combined with other risk factors, the prevalence of dementia is predicted to increase substantially in the coming years. This will lead to tremendous increase in the burden on families, the care givers, the healthcare system and the society at large. The increase in dementia cases is predicted to be more in the developing countries including India than the developed countries. For these reasons, it is important to understand the processes involved in the development of dementia, and to identify potential window of therapeutic interventions for this devastating condition.

This chronic disorder is relatively less explored in our country. Given that it is extremely important to understand different aspects of Dementia, Department of Biotechnology provided funding for Dementia Science Programme aimed at comprehensive investigation on different facets of this disorder. The Programme aims to collect reliable data regarding prevalence, incidence, biomarkers and risk and protective factors for this disorder. This multi-centric Programme involves researchers and clinicians from across the country. As part of the Programme, long-term population-based and hospital-based cohorts of dementia patients will be established, and followed up. A unique feature of the Programme is that for diagnosis and classification of dementia, all the participating centres will use robust and uniform criteria that have been internationally accepted and validated in the Indian context. The Programme also involves imaging, basic biology and genetic studies. Another important aspect of the Programme is to set up a Bio-repository of samples from normal individuals and dementia patients, and to establish a long-term data storage facility at NBRC. The samples stored in the bio-repository and the data stored in the data storage facility will serve as very valuable resources for further studies.

The Dementia Science Programme is coordinated by Director, NBRC with Dr. Shiv Sharma, NBRC and Dr. NK Arora, INCLEN Trust International, as co-coordinators. The participating sites, in alphabetical order, are given below. All India Institute of Medical Sciences, New Delhi.

- Bangur Institute of Neurosciences, Kolkata.
- National Brain Research Centre, Manesar.
- National Institute of Mental Health and Neurosciences, Bengaluru.
- North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong.

- Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram.
- The INCLEN Trust International, New Delhi.
- University of Calcutta, Kolkata.

In order to formulate robust and uniform criteria for diagnosis and classification of Dementia, several discussion meetings with participating investigators and other experts were held. These meetings helped shape the final Protocol, which is now ready. Standard operating Procedures have almost been finalized for different aspects of the study. Before starting large scale recruitment of participants, it was necessary to conduct pilot studies in using the uniform Protocol. Thus, pilot studies were undertaken in Bengaluru, an urban community site, and in Palwal, a rural community site. These pilot studies identified certain limitations. Discussion meetings were then held to tweak the Protocol in the light of the lessons learnt during the pilot studies. After these important activities, the participating sites are almost ready to start recruiting the participants.

NBRC Flagship program

Coordinator
Proj Neeraj Jain

PIs (Brain Imaging)

Dr Arpan Banerjee
Dr Dipanjan Roy

PIs (Bio-banking and genetic analysis)

Dr Shiv Kumar Sharma
Dr Anindya Ghosh Roy

Tracking mental health over lifespan
The science of well being

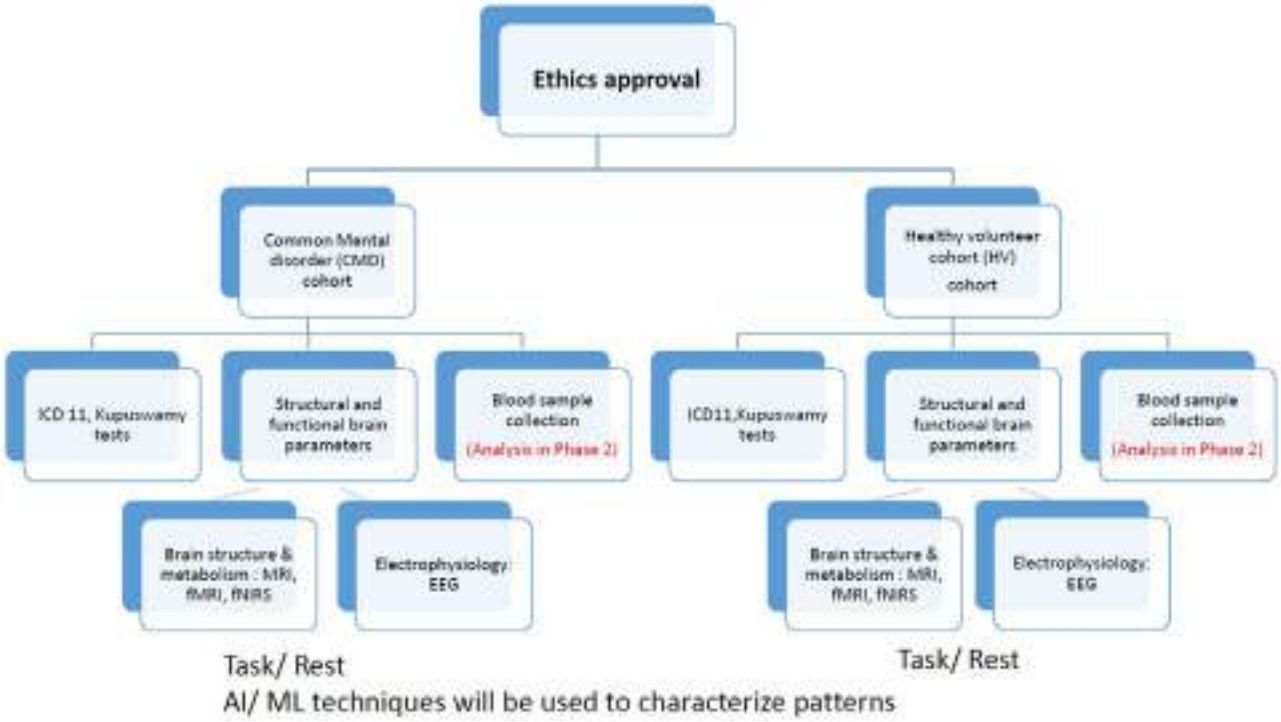
NBRC has secured funds from Department of Biotechnology in support of its flagship program for brain mapping of common mental disorders (CMD) of India. In Phase 1 the project involves collection of brain imaging and biological sample by building cohorts and identifying imaging phenotypes from anxiety, 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



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

Publications, Patents & Presentations

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2. Anindya Ghosh Roy: Wnt signaling establishes microtubule polarity in neuron through the regulation of Kinesin-13, Symposium on Chromaffin Cell Biology, ISCCB-20 at the Indian Institute of Technology, Chennai, January 2020.

3. Anindya Ghosh Roy: Regulation of functional restoration after neuronal injury by miRNA pathway, 1st International, Molecular Medicine Conference "From Bench to Bedside and Beyond" at the Amity University, Gurgaon, August 2019.

4. A Basu: Drug repositioning/repurposing: Promising strategy to develop therapy against viral infections. Ramkrishna Mission Vivekananda Centenary College, Rahara, Kolkata, 10th February, 2020.

5. A Basu: Drug repositioning/repurposing: Promising strategy to develop therapy against viral infections. Experts Opinion on Molecular Medicine, West Bengal State University, Barasat. 12th December, 2019.

6. A Basu: Drug repositioning/repurposing: Promising strategy to develop therapy against viral infections. Indo-US Symposium on New Insights into the Inflammation, Immunity, and Pathobiology of Diseases, Port Blair, Andaman Islands, 3rd-8th December, 2019.

7. A Basu: Innate Immunity in the central nervous system: Redefining the relationship between "Immune system" and "Nervous system". SNCI-Chennai Chapter, Dept. of Biochemistry, Madras University, 20-21st August, 2019.

8. A Basu: Innate Immunity in the central nervous system: Redefining the relationship between "Immune system" and "Nervous system". Department of Biochemistry, AIIMS, New Delhi, World Immunology Day, 29th April, 2019.

9. Arpan Banerjee: Introduction to Cognitive Neuroscience, Workshop on fMRI analysis at Symbiosis International University, Pune, June 2019.

10. Arpan Banerjee: Can data science lead us to the grand unified theory of brain function? NeuroAI: Aug 2019.

11. Arpan Banerjee: Can data science lead us to the grand unified theory of brain function? Invited Talk Series at IIIT Delhi, Oct 2019.

12. Arpan Banerjee: The decoherence theory of perception at Brain Modes, Pokhara, Nepal, Dec 2019.

13. Dipanjan Roy: Invited speaker International Conference Brain Modes Conference 2019 "Unified principles of Brain function" Dec 13-14, 2019 Pokhara, Nepal.

14. Dipanjan Roy: Invited talk at Neuro-AI India's first symposium at the interface of Neuroscience and Data Science "Learning subject-specific brain state transitions using big data through a unifying framework in MEG, fMRI, and computational modelling" Aug 3-4, 2019 Bangalore.

15. Elloara Sen: Targeting metabolism – inflammation link in glioma: Implications in therapy. Neuglia 19, Dept of Biochemistry, University of Madras, Chennai, August 2019

16. Elloara Sen: Epigenetic landscape and p53 mutational status: Role in SOCS1 transcriptional regulation. INDO-US 2019 New Insights into the Inflammation, Immunity, and Pathobiology of Diseases, Port Blair, Dec 2019

17. Elloara Sen: Tumor heterogeneity in glioma: Therapeutic Challenges "Experts' Opinion on Molecular Medicine" West Bengal State University, 12th Dec, 2019

18. Elloara Sen: Tension at cross-border of determinism and causality: Reconciling phenomenological philosophy with reductionist sciences. The Nalanda Dialogues, Nalanda Jan 16th 2020

19. Elloara Sen: In search of Self. International Summit on Women in STEMVisualizing the Future: New Skylines. New Delhi 22nd Jan 2020

20. Elloara Sen: Philosophy as co-traveler in the journey of Science. National Science Day, Faculty of Interdisciplinary & Allied Sciences, Delhi University, 27th February 2020

21. John Thomas, Dixit Sharma, Sounak Mohanta and Neeraj Jain 'Somatosensory Area 3b network is a composite of multiple distinct networks in macaque monkeys and humans', Neuroscience 2019, Annual Meeting of the Society for Neuroscience, USA. Oct 18-23, 2019; Chicago, USA.

22. Neeraj Jain, 'Intelligence: A neurobiologist perspective', International Workshop on Science of Intelligence, IIT Jodhpur, 18-19 January, 2020.

23. Neeraj Jain 'Spinal Cord Injuries and the Brain' Plenary Lecture at the 27th Annual Meeting of Indian Academy of Neurosciences, at AIIMS New Delhi; Nov 18-21, 2020.

24. Pankaj Seth: Invited Speaker, Molecular mechanism of HIV-1 neuropathogenesis, NCR Cluster Meeting at National Brain Research Centre, Manesar, India February 26, 2020.

25. Pankaj Seth: Guest Speaker, Molecular Mechanisms for virus induced neuronal damage, at Workshop on Molecular Neurobiology from genes, Neurons to behavior in health and disease, at Regional Centre for Biotechnology (RCB), NCR Biotech Science Cluster, Faridabad, India February 24-29, 2020.

26. Pankaj Seth: Keynote Speaker, How viruses affect human brain – finding answers, at Recent Advances in Life Sciences (RALS 2020), DPG Degree College, Gurgaon, India February 22, 2020.

27. Pankaj Seth: Guest Faculty, What we know and what we need to know about how viruses affect human brain, at Workshop on Animal Cell Culture Techniques and Applications at Department of Zoology, Miranda House, New Delhi, India, December 17-24, 2019.

28. Pankaj Seth: Invited Speaker, Novel insights into Zika virus neuropathogenesis using human neural stem cells, at the 3rd Indo-US Symposium on "New Insights into the Inflammation, Immunity, and Pathobiology of Diseases", at Sinclairs Bayview, Portblair, Andaman Islands, India, December 3-8, 2019.

29. Pankaj Seth: Invited Speaker, Friends turn Foe - Glia mediated neuronal damage in virus induced neuropathogenesis, at the 37th Annual meeting of Indian Academy of Neurosciences, at All India Institute of Medical Sciences, New Delhi, India, November 19-21, 2019.

30. Pankaj Seth: Invited Speaker, Molecular insights into zika virus induced neuropathogenesis. NeuroCON 2019 at the Maharishi Markandeshwar Medical College and University, Mullana, India, November 15-18, 2019.

31. Pankaj Seth: Guest Faculty, Molecular mechanisms of zika virus induced microcephaly. IBRO-APRC School, at Panjab University, Chandigarh, India, Nov 9-16, 2019.

32. Pankaj Seth: Guest Faculty, Novel insights into Molecular mechanisms of zika virus induced microcephaly. IBRO-APRC School, at Banaras Hindu University, India, September 1-14, 2019.

33. Pankaj Seth: Guest Lecture, Molecular insights into virus induced damage to human brain cells. Indian Institute of Science Education and Research (IISER) – Mohali, India, September 24, 2019.

34. Pankaj Seth: Invited Speaker - TEDx talk, Decoding how viruses affect human brains at Heritage Xperimental School, Gurgaon. September 28, 2019.

35. Pankaj Seth: Invited Speaker, Molecular Mechanisms of Zika Virus Induced Microcephaly – some novel insights using human neural stem cell model. Society of Neurochemistry (India), Jamia Hamdard University, New Delhi, India, October 10-12, 2019.

36. Pankaj Seth: Guest Faculty, Zika virus - what we know and want we need to know about its effects on human neural stem cells, at the University extension lecture at Interdisciplinary Brain Research Centre (IBRC), J.N. Medical College, A.M.U., Aligarh, India on May 1, 2019.

37. Pankaj Seth: Guest Speaker, Novel insights into Zika Virus induced microcephaly at IBRO-APRC School, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Kerala, India on April 26, 2019.

38. Shiv K. Sharma: Delivered a lecture on "Alzheimer's disease: Molecular and synaptic mechanisms" on World Alzheimer's day, September 21, 2019, Interdisciplinary Brain Research Centre, Aligarh Muslim University, Aligarh.

39. S. Iyengar Corvid Brain Structure,Cognition and Mirror Self-Recognition. 15th - 16th March, 2019; Invited lecture, BIOSPARKS-2019, Organized by the School of Life Sciences, JNU, New Delhi.

40. S. Iyengar Brain Structure and Behaviour in Songbirds, Abstract submitted. 22nd - 24th April, 2019; International Workshop on Social Network of Animals in Extreme Environment of Antarctica with Special Reference to Penguins including Field Studies Zoological Survey of India, MoES (Ministry of Earth Sciences), Port Blair.

41. S. Iyengar The Role of the Opioid System in Singing and Song Learning in Zebra Finches. 24th Oct, 2019; Invited lecture, Dept of Psychology, Vanderbilt University, Nashville, TN, USA.

42. Singh UA and Iyengar S (2019): "Fine-tuning birdsong: The role of delta opioid receptors in the development of song structure". # 3655, Annual Meeting of the Society for Neuroscience, 2019, Chicago, USA. **This abstract has been selected as a Neuroscience 2019 Hot Topic (Only ~100 out of the over 14,000 abstracts submitted to Neuroscience 2019 are awarded this recognition. It was shared with the media as part of Neuroscience 2019's Hot Topics book and in the Neuroscience 2019 online press room.)

43. S. Iyengar Neural Plasticity and the Development of Axonal Connections in the Human Auditory Cortex. 19th - 21st Nov, 2019; IAN 2019, All India Institute of Medical Sciences, New Delhi

44. Sourav Banerjee, Sarbani Sammadar and Balakumar Srinivasan. Mechanisms of local protein synthesis at the synapse by miRNA decay and its implications in synaptic plasticity, The Annual Meeting of the Japan Neuroscience Society and Japanese Society for Neurochemistry, July 2019.

45. Sourav Banerjee, Balakumar Srinivasan and Sarbani Samaddar. Balancing act : Mechanism of homeostatic synaptic scaling by synergistic control of protein synthesis and degradation, National Centre for Biological Sciences, September 2019

46. Sourav Banerjee, Balakumar Srinivasan and Sarbani Samaddar. RISCy Business: Regulation of homeostatic synaptic activity by remodeling of miRNA induced silencing complex, Annual meeting of Indian Academy of Neuroscience, AIIMS, New Delhi, November 2019.

47. Sahu BS Organellar proteomics reveals the crucial role of clathrin in dense-core vesicle biogenesis. M2T2-2019 – Molecular Motors, Transport and Trafficking 18-20th October 2019 at NBRC- Manesar.

48. Sahu BS TLQP-21 neuropeptide and the complement 3a receptor (C3aR1) regulate a novel calcium-dependent pro-lipolytic pathway. International Society for Chromaffin cell Biology meeting -2020 January 23-26, 2020 at IIT Madras.

49. Swagata Dey: Studying dendrite regeneration in PVD neurons of Caenorhabditis elegans. National Brain Research Centre, Manesar, India, Molecular Motors, Transport, and Trafficking Meeting. October 2019.

Externally Funded Research Projects

Externally Funded Research Projects

S. No.	Name of P.I.	Project S.No.	Name of Project	Funding Agency	Date of Sanction	Amount Recieved amount for 2019-20 (Rs. Lakh)	Sanctioned Cost (Rs. Lakh)	Date of Completion	Sanction Order No.
1	Anindya Ghosh Roy	1	Wellcom Trust/DBT Indian Alliance	D.B.T.	01.12.2013	48.90	321.93	30.11.2019	IA/I/13/1/5000874
2	Anirban Basu	2	Deciphering ANTIVIRAL Properties of Statins against Japanese Encephalitis Virus Infections	D.B.T.	26.12.2018	0.00	30.00	25.12.2020	BT/PR27796/ MED/29/1301/ 2018
		3	MicroRNA mediated regi;ation of neural stem/progenitor cell fate in neurotropic flaviviral infection	D.B.T.	29.12.2017	34.33	77.07	28.12.2020	No..BT/PR22341/ MED/122/55/2016
		4	Understanding the therapeutic role of adult stem cell derived exosome in combating virus induced neurodegenerative disease	D.B.T.	20.03.2018	8.41	25.50	19.03.2021	No.BT/PR15984/ MED/31/325/2015
		5	MicroRNAs as a potential therapeutic target in Neuro tropic viral infection (Tata Innovation fellowship)	D.B.T.	01.05.2015	8.94	45.00	31.03.2020	No.BT/HRD/ 35/01/02/2014
		6	Elucidating the role of long non coding RNAs (IncRNAs) in neuronal cell death during Japanese Encephalitis (JE)	D.B.T.	05.03.2019	14.20	19.00	04.03.2022	BT/PR26590/ MED/ 122/ 133/2017
3	Arpan Banerjee	7	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	100.00	13.02.2022	K-15015/42/2018/ SP-V
4	Ashraful Hassan	8	DBT-TWAS Fellowship	D.B.T.	11.10.2019	5.67	5.67	10.10.2020	No. DO/ CCSTDS/144/2019
5	Bhavani Shankar Sahu	9	Understanding the regulated secretory pathway and its role regulating physio-metabolic fuctions	D.B.T.	16.12.2019	21.56	_	15.12.2021	No.BT/RLF/Re-entry/38/2016
6	Dipanjan Roy	10	Oscillatory network dynamics in perceptual learning	D.S.T.	23.08.2017	10.00	50.55	22.08.2020	No.SR/ CSRI/21/2016(G)
		11	Role of default mode brain network is normal cognitive function	D.B.T.	26.05.2016	7.57	88.00	26.05.2021	No. BT/RLF/Re-entry/07/2014
		12	Dementia Science Program-Tissue MRI Studies	D.B.T.	18.12.2017	0.00	35.41	17.12.2020	No. BT/HRD/ Dementia/2017
7	Ellora Sen	13	Inflammation regulated metabolic reprogramming Implications in tumor progression (UOE)	D.B.T.	30.03.2015	16.41	172.90	29.03.2020	No.BT/MED/30/ SP11016/2015
8	Neeraj Jain	14	Mechanisms of Adult Brain Reorganization	D.B.T.	28.05.2014	0.00	89.24	25.5.2019	BT/PR7180/ MED/30/907/2012

S. No.	Name of P.I.	Project S.No.	Name of Project	Funding Agency	Date of Sanction	Amount Recieved amount for 2019-20 (Rs. Lakh)	Sanctioned Cost (Rs. Lakh)	Date of Completion	Sanction Order No.
9	Neeraj Jain Director, NBRC	15	Magentoncephalography (MEG) Resource Facility	D.B.T.	27.03.2018	32.96	1498.86	31.03.2021	BT/MED/122/ SP24580/2018
		16	Dist infromation Centre (DIC)	D.B.T.	22.12.1999	15.48	528.10	31.03.2020	BT/BI/03/012/2002
		17	Dementia Programme	D.B.T.	14.09.2007	0.00	37.50	_	No. BT/PR-NBRC/2008
		18	Delcon (E- Laibrary Consortia) Project	D.B.T.	18.03.2009	5,809.59	37123.67	31.3.2021	No. BT/ BI/12/053/2012
		19	Comparative Mapping of common mental disorders (CMD) over lifespan	D.B.T.	29.09.2019	267.35	477.05	28.09.2020	No.BT/MED/-III/ NBRC/Flagship/ program/2019
		20	Demetia Science Programme-Coordination Administration & Management setup at DBT	D.B.T.	18.12.2017	0.00	530.42	17.12.2020	No.BT/HRD/ Dementia/2017
10	Pankaj Seth	21	Differentiation of fetal neural stem cells to oligodendrocytes-a disease model to decipher the pathogenesis and devise therapeutic strategies for cerebral plasy	D.B.T.	19.03.2018	7.91	20.80	18.03.2020	No.BT/PR17581/ MED/31/333/ 2016
		22	Insights into role of a dyslexia linked long non-coding RNA(IncRNA) in human neural stem cell	D.S.T.	18.07.2017	12.00	76.97	17.07.2020	No.SR/CSRI/210/ 2016(G)
		23	Hypoxia Induced Changes in Blood Brain Barrier	D.B.T.	12.09.2018	7.00	34.66	11.09.2021	No.BT/PR23625/ MED/122/77/2017
		24	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	No.BT/PR21413/ MED/122/ 40/2016
		25	Role of Ephrins/Eph receptors in HIV mediated neuropathogensis	D.B.T.	27.06.2019	35.72	73.16	26.06.2022	No. BT/PR27512/ 122/146/2018
11	Pravat Kumar Mandal	26	Non-invasive imaging Technology Developmnet to aid Differential Diagnosis of Alzheimr, Dementia with Lewy body and parkinson Disease from Brain Glutathione Quantiation and ph Mapping(Tata Innovation Fellowship)	D.B.T.	01.04.2015	8.80	45.00	31.03.2020	No.BT/HRD/35/ 01/05/2014
		27	Construction of an indian population specific brain template	C.S.I.R.	11.05.2016	5.00	26.12	09.11.2019	No. SR/CSRI/ 229/2014(G)
		28	Unravelling the causes of stroke and cognitive decline in general population A cross-Cultural perspective (DBT Netherland Grant)	D.B.T.	21.04.2016	7.95	73.66	20.04.2022	No. BT/IN/ Netherlands/0 3/ KP/2012
		29	Novel Imaging Diagnostics for Alzheimer's Disease	D.B.T.	24.01.2018	22.37	151.26	23.01.2021	No.BT/Indo-Aus/ 10/31/2016

S. No.	Name of P.I.	Project S.No.	Name of Project	Funding Agency	Date of Sanction	Amount Recieved amount for 2019-20 (Rs. Lakh)	Sanctioned Cost (Rs. Lakh)	Date of Completion	Sanction Order No.
		30	Dementia Science Program-Imaging Studies	D.B.T.	18.12.2017	0.00	35.41	17.12.2020	No.BT/HRD/ Dementia/2017
		31	Artificial intelligence for early predictive diagnosis of alzheimer's disease using multi model imaging data	Meity	17.09.2019	31.07	59.96	16.09.2022	No. 4(5)/2019-ITEA
12	Prem Chand	32	Effect of handedness on recovery of forepaw in rats with spinal cord injury	D.S.T.	11.07.2017	8.00	17.60	10.07.2019	No. SR/CSRI/PDF-27/2016
13	Sandeep Kumar	33	Post Doctoral Fellowship	SERB	06.04.2018	9.10	19.20	05.04.2020	PDF/2017/ 001610
14	Shiv Kumar Sharma	34	Demetia Science Programme-Basic Biology Studies (i) Genetic Studies at lab	D.B.T.	18.12.2017	0.00	106.64	17.12.2020	No.BT/HRD/ Dementia/2017
15	Soibam Shayamchand	35	Post Doctoral Fellowship	SERB	03.05.2017	8.50	19.20	02.05.2019	PDF/2016/ 003188
16	Soumya Iyangar	36	Effects of the δ- opioid receptor system on singing and song learning in Zebra Finches	D.S.T. (SERB)	23.09.2016	0.00	37.43	22.09.2019	EMR/2015/ 001422
		37	The sensitive period of the human auditory cortex a neuroanatomical study	ICMR	25.09.2019	12.47	42.10	24.09.2022	No. 51/4/2019-ANA/BMS
17	Sourav Banarjee	38	CRISPRi system : A toolbox to investigate novel regulatory mechanisms of synapse formation by long non-coing RNAs"	D.B.T.	11.01.2016	0.00	74.19	10.07.2019	No. BT/PRI14071/ GET/119/36/2015
		39	Regulation of energy metabolism by miRNA-mediated control of neurogenesis	D.B.T.	21.02.2015	0.00	78.09	20.06.2019	No. BT/PR8793/ AGR/36/749/2013
		40	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	0.00	52.39	24.03.2022	No. SERB/F/ 12655/2018-19
		41	CRISPR-Cas13- mediated engineering of endogenous long non-coding RNAs for fluorenscent tagging to study RNA dynamics	D.B.T.	29.02.2020	35.81	72.00	28.02.2023	No.BT/RLF/ PR31811/ GET/119/285/2019
18	Subham Kumar	42	EEG correlates of 'insight' and its facilitating through emotional priming	D.S.T	08.05.2019	9.46	18.92	07.05.2021	DST/CSRI/PDF-14/2018
19	Swagata Dey	43	Insprite Faculty fellowship 2019	D.S.T.	11.02.2019	22.00	112.40	31.12.2019	DST/Inspire Faculty/ Batch-15/2019
		44	Wellcom Trust/DBT Indian Alliance	D.B.T.	01.01.2020	13.34	167.73	31.12.2025	No.IA/E/18/ 1/504331
20	Yogita K Adlakha	45	Innovation in science pursuit for inspired Research(INSPIRE)	D.S.T.	01.07.2014	14.25	86.27	31.06.2019	No. DST/INSPIRE faculty Award/2014/ DST/INSPIRE/04/ 2013/001157

Distinctions, Honours & Awards

Distinctions, Honours and Awards

Faculty

Prof Neeraj Jain: Haryana Vigyan Ratna Award

Dr. Sourav Banerjee: Global Research Partnership Award, University of Iowa, USA to conduct joint research programme with Prof. Ted Abel.

Faculty Fellow

Dr. Swagata Day: DBT/Wellcome Trust India Alliance Early Career Fellowship (2019)

Students

Atrayee Basu: Travel Award for attending 22nd International C. elegans conference, UCLA, CA from SERB and Genetics Society of America (GSA

Hriday S Pandey - Awarded International Travel Grant from International, Society for Neurochemistry (ISN) for presenting a poster in the "2019, ISN-ASN Meeting" held at Montreal, Canada from August 4-8, 2019.

Course-Work

M.Sc. 2018

Ms. Surbhi

M.Sc. student, has been awarded first rank upon completion of Course-Work during the year 2018-19 and a certificate was given to her on the 16th Foundation Day, the 16th December 2019.

Mr. Thakar Darshit Mahesh

M.Sc. student, has been awarded second rank upon completion of Course-Work during the year 2018-19 and a certificate was given to him on the 16th Foundation Day, the 16th December 2019.

Ph.D. 2018

Ms. Roopashi Saxena

Ph.D. student, has been awarded first rank upon completion of Course-Work during the year 2018-19 and a certificate was given to her on the 16th Foundation Day, the 16th December 2019.

Ms. Khushboo Vinod Punjabi

Ph.D. student, has been awarded second rank upon completion of Course-Work during the year 2018-19 and a certificate was given to her on the 16th Foundation Day, the 16th December 2019.

Ph.D. Degrees Awarded

S/No	Name of the Student
1	Dr. Reshma Bhagat
2	Dr. G.Vinodh Kumar
3	Dr. Bharat Prajapati
4	Dr. Naman Vatsa

M.Sc. Degrees Awarded

S/No	Name of the Student
1	Ms. Shelly Pal
2	Mr. Azman Akhter
3	Ms. Guneet Kaur
4	Ms. Kirti Saluja
5	Mr. Masood Ahmad Wani
6	Ms. Pallavi Singh
7	Mr. Ranjit Pradhan

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.


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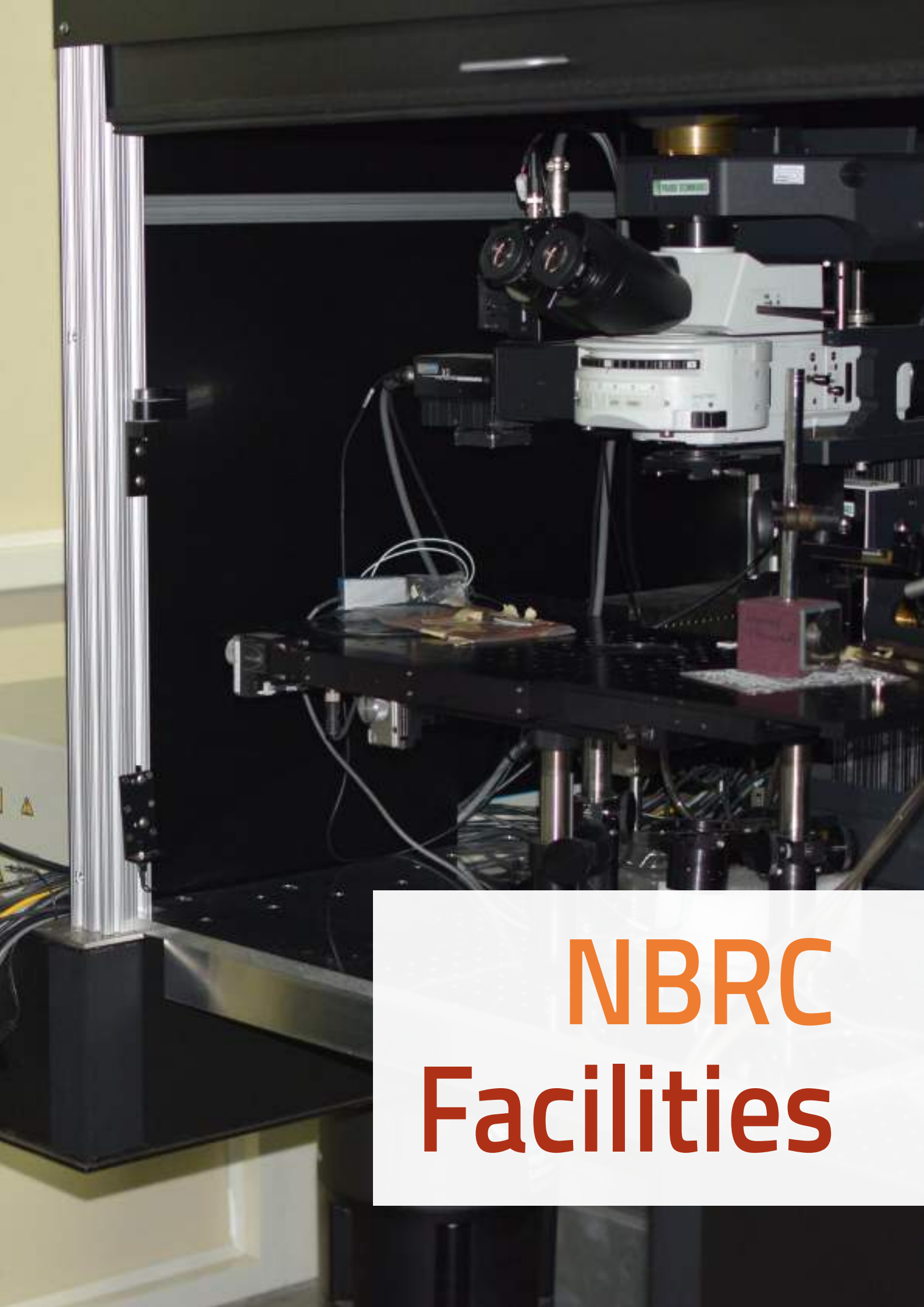


NBRC Facilities

INFORMATION TECHNOLOGY COMMUNICATIONS CELL

The Information Technology and Communications Cell (ITCC) of National Brain Research Centre manages the overall Information and Communications infrastructure of the Institute apart from aiding in R&D activities. Previously, ITCC functioned as Distributed Informatics Centre (DIC) under the BTISNET initiative of Department of Biotechnology. ITCC 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 campus wide Local Area Network running on 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 is built in the network architecture. The network is supplemented with 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 a IPv6 compliant and IPv6 services are functional in 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 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 NBRC-AIIMS data pipeline for MEG as part of 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 tele-communication 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 institute's datacenter. 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 end-points.

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

a. Web-servers for the institute and various web-servers related to ongoing computational projects and applications of various scientific groups . The primary webserver for official website - running from VM's installed on NIC cloud.

b. 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, project personnel for broadcast and academic purpose.

c. DNS servers for the official and hosted domains which are running from NBRC datacenter as well as VM's hosted on NIC cloud.

d. Virtualization servers for providing virtualized hardware to run various applications and service in a more systematic manner and to consolidate and utilize the existing physical server infrastructure.

e. New Central Storage servers of 400TB has 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.

f. Radius and authentication servers for access, accounting and authorization of computing resources

g. License management servers for managing institutional site/network/concurrent licenses.

h. 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.

i. Antivirus and security servers for providing protection to user end-points across the campus.

D. Other Facilities & Services

a. NIC Cloud and Email Services : The DIC unit 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.

b. Central Documentation Facility: The central documentation facility provides round the clock availability to users for various computational needs like facility for printing, scanning, poster-printing etc. apart from providing data-processing computational nodes.

c. 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's etc. An online support ticketing system with automated workflow management is functional for support activities.

d. CCTV Monitoring and Management: The DIC has also installed IP-Cameras connected to the core network which has enhanced the security and monitoring of the campus. Most entry/exit points of the buildings are covered with the Central CCTV system.

e. Software Development: The computing facility also undertakes software development activities in line with the institute requirements, several scientific and e-Governance applications have been developed in-house.

f. 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.

g. Video-conferencing: Management of video-conferencing for official meetings, interviews and academic activities.

ANIMAL FACILITY

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 Environment and Forests, 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.

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 the 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 is 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

Knock Out Mice

- UBE3A null mice (Angelman syndrome model)

Mutant Mice

- CBA/J mice (Retinal degeneration model)

Rat Strains

- Long Evans
- Sprague Dawley

Non-human primates

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

Birds

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

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.

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 1000+ online journals through the DBT e-Library Consortium (DeLCON), 5 specialized journals, and 119 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 440 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 1000+ 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. 3. National Institute of Plant Genome Research (NIPGR), New Delhi
4. 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. 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 Advancement of Science(AAAS)→ http://www.sciencemag.org → 3 Journals
- American Association for Cancer Research (AACR) → http://www.aacr.org → 8 Journals
- American Society for Biochemistry and Molecular Biology (ASBMB)→ http://www.jbc.org → 2 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
- American Society for Hematology (ASH) → http:// bloodjournals.hematologylibrary.org → 1 Journal
- Wiley-Blackwell → http:// www3.interscience.wiley. com/cgi-bin/home → 86 Journals
- Elsevier Science (ScienceDirect) → http:// www. sciencedirect.com → 433 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 Journal (Only Archives from 2009-2018)

- American Society of Plant Biologists (ASPB) → http://www.aspb.org/→ 2 Journals (Only Archives from 2009-2018)

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): 64-channel Synamps 2 EEG system, Compumedics Neuroscan, Inc
3. Transcranial magnetic stimulation (TMS): Magventure MagPro

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 studies. 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 in 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 magnetic field. These 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 2019-March 2020.

Publications

1. Ray, D., Hajare, N., Roy, D., Banerjee, A. (2020) Large-scale Functional Integration, Rather than Functional Dissociation along Dorsal and Ventral Streams, Underlies Visual Perception and Action. *Journal of Cognitive Neuroscience* 32:5, 847-861.
2. Pal A.K., Roy, D., Kumar, V. G., Chatterjee, B., Sharma, L. N., Banerjee, A., & Gupta, C. N. (2020) Empirical Mode Decomposition Algorithms for Classification of Single-Channel EEG Manifesting McGurk Effect. *In: Tiwary U., Chaudhury S. (eds) Intelligent Human Computer Interaction. IHCI 2019. Lecture Notes in Computer Science, vol 11886. Springer, Cham.*
3. Halder, T., Talwar, S., Jaiswal, A. K., & Banerjee, A. (2019): Quantitative evaluation in estimating

sources underlying brain oscillations using current source density methods and beamformer approaches. *eNeuro* DOI: https://doi.org/10.1523/ENEURO.0170-19.2019.

4. Sumathi T. A., O. Spinola., N Chatterjee Singh, B. Chakrabarti (2020). Perceived Closeness and Autistic Traits Modulate Interpersonal Vocal Communication. *Frontiers in Psychiatry*, 11, 50. https://doi.org/10.3389/fpsyt.2020.00050.

5. Midya V., Valla J., Balasubramanian H., Mathur A. and Singh N. C. (2019). Cultural Differences in the Use of Acoustic Cues for Musical Emotion Experience. *PLoS One*, 14(9), e0222380.

6. Rajan A., Valla J. M., Alappatt J. A., Sharda M., Shah A., Ingalhalikar M. and Singh N. C. (2019). Wired for Musical Rhythm? A Diffusion MRI-Based Study of Individual Differences in Music Perception,. *Brain Struct Funct,* 224(5), 1711-1722. https://doi.org/10.1007/s00429-019-01868-y.

7. D Divya, M Kanu, M Ritwick, PK Mandal (2020) Glutathione in Brain: Overview of Its Conformations, Functions, Biochemical Characteristics, Quantitation and Potential Therapeutic Role in Brain Disorders. *Neurochemical Research* 45 (7), 1-22.

8. PK Mandal, D Shukla (2020) KALPANA: Advanced Spectroscopic Signal Processing Platform for Improved Accuracy to Aid in Early Diagnosis of Brain Disorders in Clinical Setting *Journal of Alzheimer's Disease* 72 (Preprint), 1-6 .

9. Praful Pai, Pravat K Mandal*, Khushboo Punjabi, Deepika Shukla, Anshika Goel (2020) BRAHMA: Population Specific T1, T2, and FLAIR weighted Brain Templates and their impact in Structural and Functional Imaging Studies Journal: Magnetic Resonance Imaging *Journal of Magnetic Resonance Imaging* 70, 5-21.

10. D Shukla, PK Mandal*, M Tripathi, G Vishwakarma, R Mishra, K Sandal (2020) Quantitation of in vivo brain glutathione conformers in cingulate cortex among age - matched control, MCI, and AD patients using MEGA - PRESS. *Human Brain Mapping* 41 (1), 194-217.

TRANSLATIONAL & CLINICAL NEUROSCIENCE UNIT

The National Brain Research Centre (NBRC) has always been on the forefront when it comes to helping the nation to reduce the burden of neurological disorders in our country. Realizing the social responsibility and the need for serious efforts to address the growing cases of neurological diseases in our country, the National Brain Research Centre extended its expertise and support to the Government General Hospital (GGH), Gurgaon more than a decade ago. As the Government General Hospital, lacked the expertise of a neurologist and did not have a neurology department, the needy patients coming from Gurgaon neighboring districts and villages were turned away or refereed to other hospitals. We established the Translational and Clinical Neuroscience Unit and provided a neurology outpatient department to the government hospital to help the citizens and also assess the occurrence of neurological cases in this region.

The Translational and Clinical Neuroscience Unit initially started from room number 7 of the Government General Hospital, Gurgaon near that city bus stand in heart of the city. In 2019, as the GGH was shifted to Sector 10A in Gurgaon, and the unit was also transferred. We continue to cater the service to the needy citizens of state of Haryana.

Investigation facilities:

As the unit is established at the hospital, the patients visiting the unit, 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 unit has highly qualified consultants and a support team of following personnel:

- Consultant Clinical Professor, Neurology: Dr Rajnish Kumar
- Consultant Clinical Professor, Pediatric Neurology, Dr. Rakesh Jain
- Clinical Psychologist: Priyanka Kaushik
- Clinic Assistant: Hanuman Singh

It is mandatory to understand the mechanisms of diseases through a clear understanding the sequence of events that underlie any disease pathogenesis. This can be achieved only through a close collaboration of basic researchers and clinicians that have to work together with a common aim to reduce the suffering of patients and minimizing their hospital stay and visits. The translational and clinical neuroscience unit of NBRC is working towards that goal and has made a good progress. The neurologists at the unit have not only attended to the neurological patients that visit GGH, but have also build strong ties with the basic researchers at NBRC. Before this unit was established, the patients often relied upon unqualified quacks and believed in non-scientific superstitious practices. This has been reduced to a great significance and the population is relatively more aware of the neurological disorders and getting the proper treatment. As the the Clinical Research Unit of NBRC is established within the Hospital the patients also have access to a variety of services such as - Neurology, Neuropsychology, Neuropsychiatry, Behavioral therapy, Psychology, and Psychometry.

The outpatient department of this unit at the Government General Hospital, is supported by highly qualified and accomplished consultants, including a Pediatric neurologist and a DM in Neurology. These neurologists offer their services on one of the designated days of the week. Last year, we had added a Pedaitric Neurologist, Dr. Rakesh Jain, to the list of consultants of the unit. This has been a great help for the visiting patients and the hospital as we had a significant number of neurological patients of pediatric age group. We are noticed that the

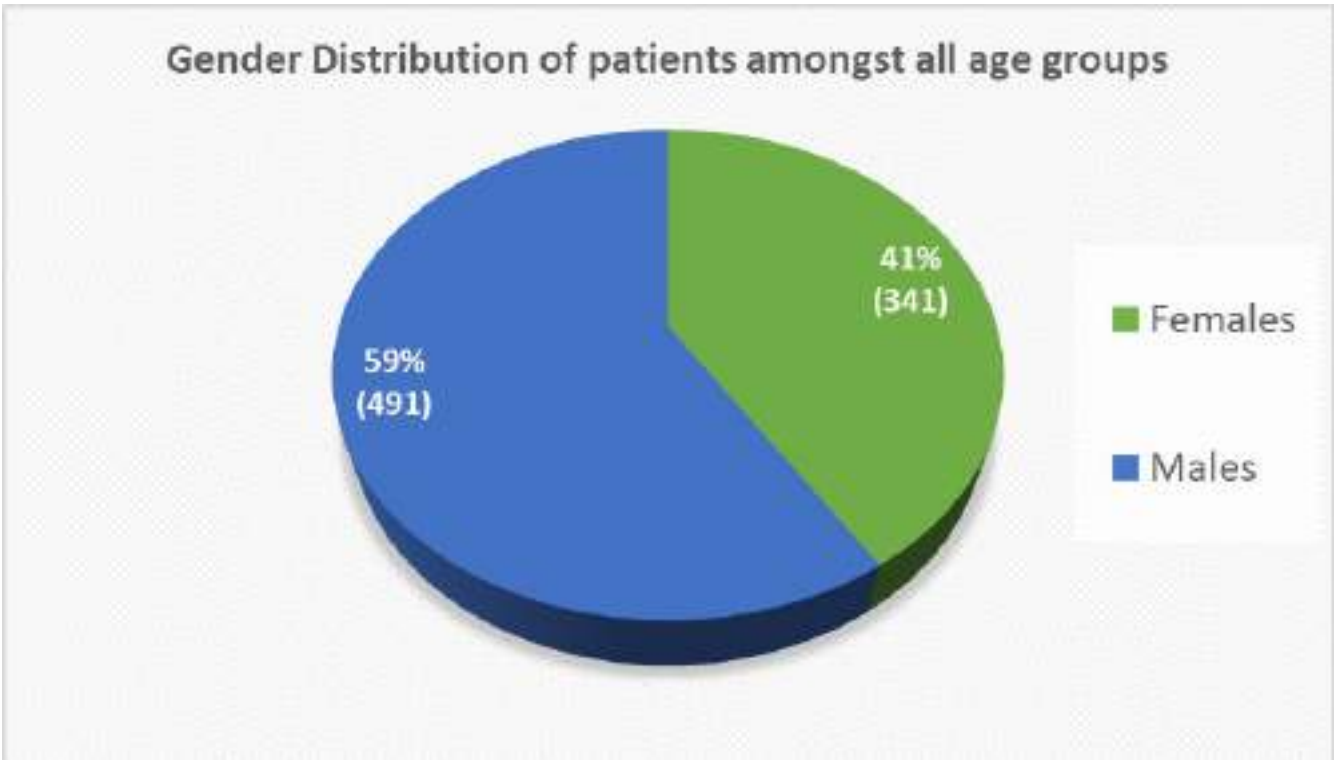
NBRC Unit has registered an increase in number of referrals of such cases by the pediatric department and relief to the needy patients.

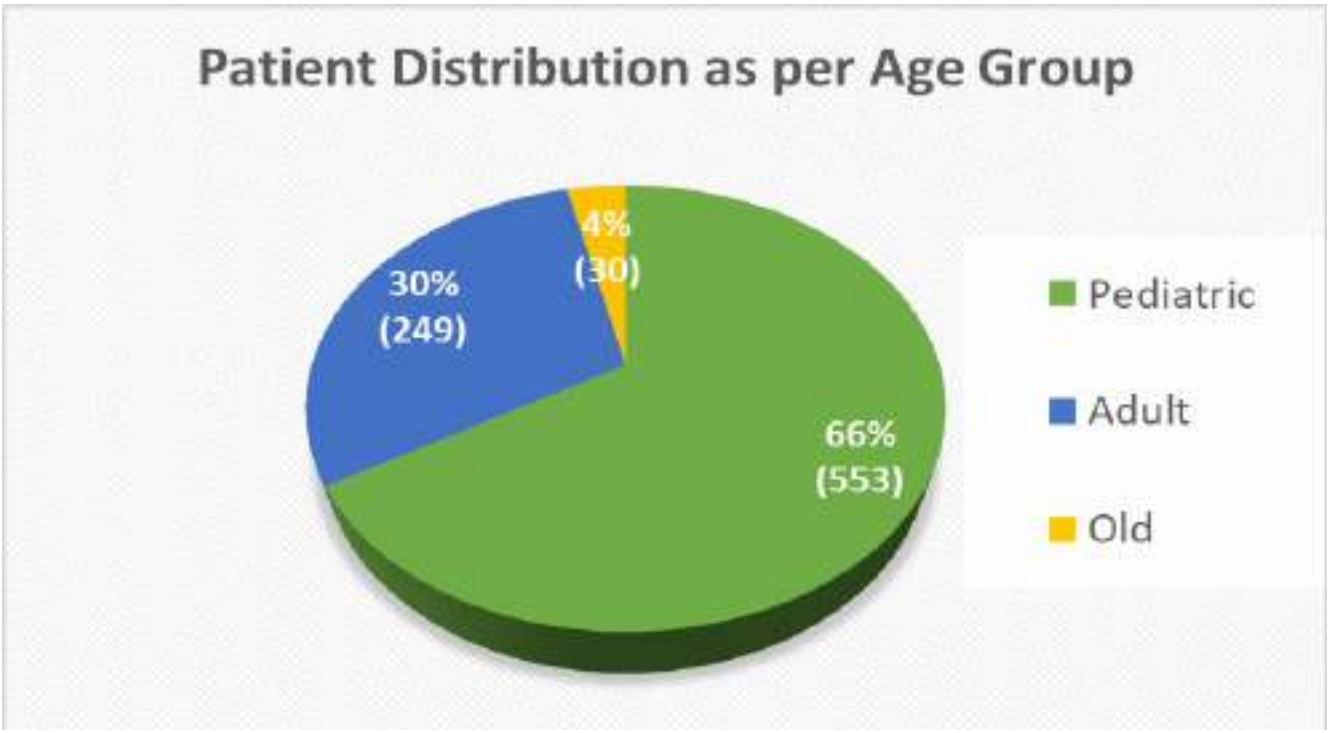
The out-patient facility is visited by patients not only from Gurgaon but from the neighbouring districts as well, due to which the number of patients continues to be high. The clinical facility also maintains a good follow up rate of patients, and a large number of the patients rely on the clinics for follow-ups. Out of all the patients attending neurology OPD, the percentage of male patients was 59% while the same for female was 41% as shown in the pie chart. Patients visiting the NBRC unit are of different age groups ranging from pediatric (66%) to adult 30% and elderly (4%) patients. The Elderly or Geriatric patients mostly come for the Movement Disorders, dementia, where as that 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.

It was also observed that the footfall of patients in the OPD at GGH is from old Gurgaon township and from the villages and towns in the surrounding districts of Haryana. 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.

We are in process of creating a database of all the patients that visit the neurology OPD, and wish to create a computer database with relevant patient data along with any planned imaging/molecular/neurophysiological studies at the NBRC laboratories. This would help in creating a well documented "clinical window" for NBRC and the neuroscience research community. In this effort to narrow the gap between Basic Neuroscience and Applied Neuroscience, an ethics committee has been formulated jointly with the Government General Hospital/Government of Haryana.

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.




Patient Distribution as per Age Group
4%
(30)
30%
(249)
66%
(553)
Pediatric
Adult
Old

Magnetoencephalography (MEG) Resource Facility

(Funded by Department of Biotechnology, Govt. of India)

Investigators from AIIMS

Prof. P Sarat Chandra

Prof. Manjari Tripathi

Dr. Jyotirmoy Banerjee

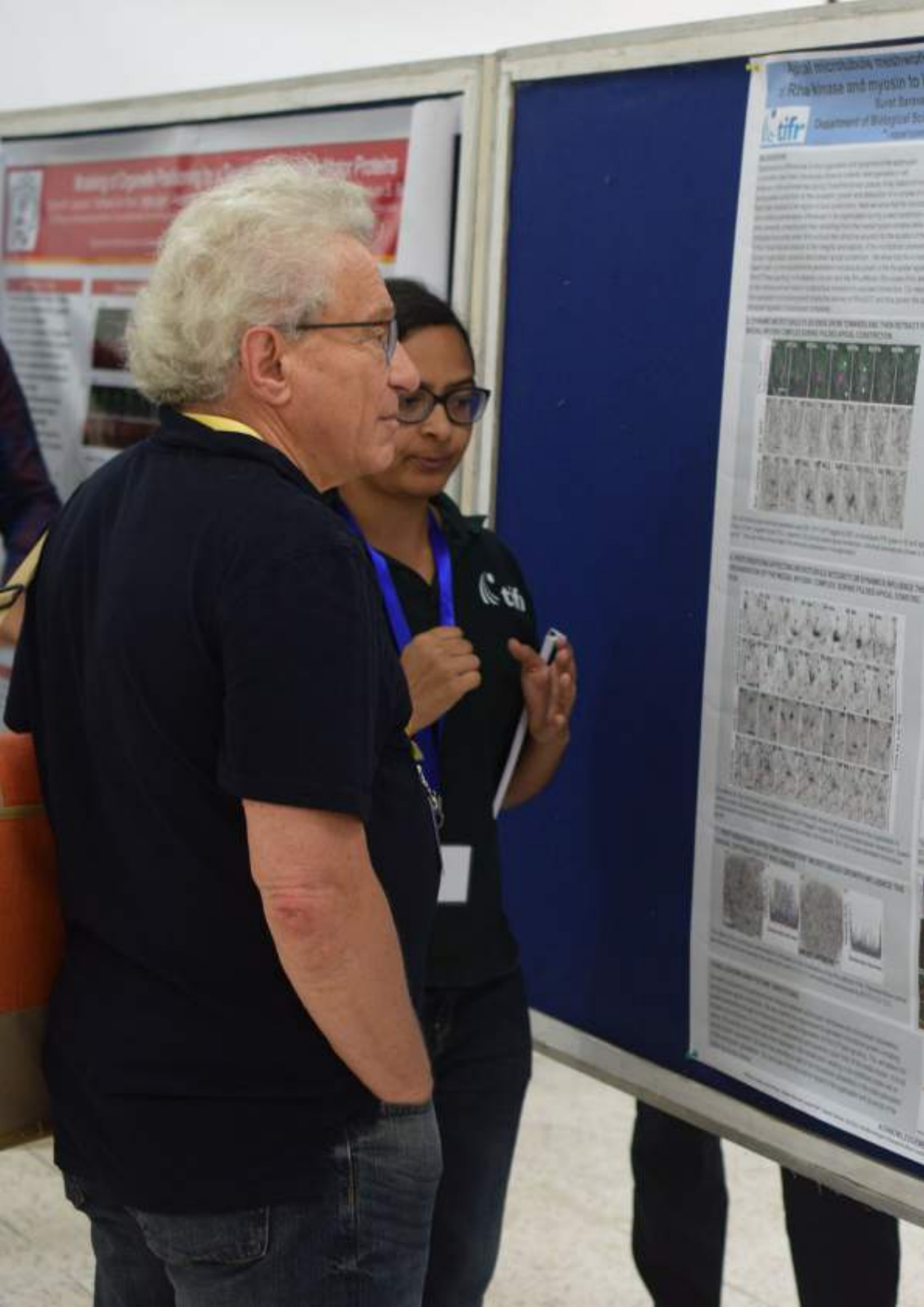
Investigators from NBRC

Prof. Neeraj Jain, Director

Investigator from ACBR

Dr. Aparna Dixit

Magnetoencephalography (MEG) Resource Facility is jointly run by National Brain Research Centre (NBRC) and All India Institute of Medical Sciences (AIIMS) established under the aegis of Department of Biotechnology (Government of India).



Lectures, Meetings & Workshops

INVITED SPEAKERS AT NBRC

Sr. No.	Name of the Speaker	Title of the Talk	Date	Host Faculty
1	Dr. Vimilesh Kumar IISER, Bhopal	Endocytosis-dependent regulation of synaptic morphogenesis	08.05.2019	Dr. Anindya Roy Ghosh
2	Prof. Krishna Menon, Dean School of Human Studies, Ambedkar University, Delhi	Women at Work - The Pursuit of Dignity and Freedom	22.05.2019	Administration Department, NBRC
3	Dr. Bhavani Shankar Sahu MS University, Baroda	Bio genesis of Dense core vesicles and their role in regulating physiological functions	18.06.2019	Prof. Anirban Basu
4	Dr. Abhishek Bhattacharya HHMI Columbia University, New York	Molecular identity of the electrical synapse connectome and its plasticity	09.07.2019	Dr. Anindya Ghosh Roy
5	Dr. Urmi Bandyopadhyay Memorial Sloan Kettering Cancer Centre, New York	Lysosome in novel nutrient homeostasis: from Degradation to disorder"	10.07.2019	Dr. Anindya Ghosh Roy
6	Dr. Tamalika Chaira IIT Delhi	Intuitionistic fuzzy/Type II Fuzzy Set Theoretic Approach for Medical Image Processing	24.07.2019	Dr. Dipanjan Roy
7	Dr. Anand Kumar Singh Postdoc fellow from School of Biosciences, University of Birmingham, UK	Cytoplasmic surveillance machinery regulates mRN within nucleus : Footprints of nuclear-translation in eukaryotes	25.07.2019	Dr. Anindya Ghosh Roy
8	Dr. Pradeep Punnakkal Molecular medicine, BMT wing Sree Chitra Tirunal Institute for Medical Sciences and Technology Poojapura, Thiruvananthapuram 12 Kerala India	NMDA Receptor subtypes and synaptic plasticity in the epileptic rat brain	5.08.2019	Prof. Anirban Basu
9	Dr. Jogender Singh, Postdoctoral Scholar The Aballay Lab 6351 Richard Jones Hall Department of Molecular Microbiology & Immunology Oregon Health & Science University, Portland 97239, OR, USA	Intestinal infection regulates immunity, behavior and learning in C. elegans	9.08.2019	Prof. Anirban Basu
10	Dr. Deepika Kandilya Department of Anatomy, Yong Loo Lin School of Medicine, National University of Singapore	Zika virus alters DNA methylation status of genes invoved in Hippo signalling pathway in human neural progenitor cells	19.08.2019	Prof. Pankaj Seth
11	Dr. Jyoti Kapoor PARAS Hospital, Gurugram	Introduction to stress and its management	04.09.2019	Prof. Ellora Sen
12	Dr. Durgesh Singh from Bio-Rad Laboratories (India) Pvt Ltd.	Multiplex fluorescence western blotting & introducing total protein Normalization	16.09.2019	
13	Dr Sanhita Sinha Ray Faculty Research Instructor at Cancer Systems Imaging, Univ of Texas MD Anderson Cancer Center, TX, USA.	Picturing the future of healthcare through molecular imaging	17.09.2019	Dr. Arpan Banerjee
14	Dr. Suresh Kumar University of Mexico, Albuquerque	Autophagy recognition particle : its mechanism of action; function; and physiological relevance	25.09.2019	Prof. Anirban Basu

Sr. No.	Name of the Speaker	Title of the Talk	Date	Host Faculty
15	Dr. Bhavna Tiwari Department of Cell Biology, UT Southwestern Medical Center, Texas	Transposons: New p53 targets in genomic stability	27.09.2019	Prof. Anirban Basu
16	Dr. Mike Lucero Vice President Product Strategy from 10X Genomics, USA	Accelerating biology: 10X Genomics products and vision	04.10.2019	Dr. Yogita K. Adlakha/Prof. Pankaj Seth
17	Dr. Shadab Raza Era Medical University, Lucknow	Possible reasons failure of stem cell therapy in ischemic stroke: An /in vitro / study on dental and adipose-derived human mesenchymal stem cells	10.10.2019	Prof. Pankaj Seth
18	Prof. Merav Ahisaar Hebrew National University, Jerusalem	Autism versus dyslexia – different time windows of perceptual inference	17.10.2019	Dr. Arpan Banerjee
19	Dr. Sajikumar S National University of Singapore, Singapore	The p75 neurotrophin receptor is an essential mediator of impairments in hippocampal-dependent associative plasticity and memory induced by sleep deprivation	17.10.2019	Prof. Pankaj Seth
20	Dr. Ravi Muddashetty inStem, Bangalore	Dysregulated translation at the centre of synapse pathology in Alzheimer's disease	20.11.2019	Dr. Sourav Banerjee
21	Prof. Siyaram Pandey, Professor, Department of Chemistry and Biochemistry, University of Windsor	Targeting mitochondrial dysfunction, oxidative stress, inflammation and autophagy impairment to halt progression of neurodegenerative diseases using Ubisol Q10 and natural extracts	20.11.2019	Prof. Neeraj Jain
22	Dr. Aditi Bhattacharya Centre for Nuerodevelopmental Synaptopathies (CNS), Institute of Stem Cell Science and Regenerative Medicine (inStem) , Bengaluru	Novel roles of Neurologin3 activity-mediated translation control and cell fate specification	21.11.2019	Dr. Sourav Banerjee
23	Prof. Sukesh Ranjan Bhaumik Southern Illinois University, USA	Fine tuning of an evolutionary conserved chromatin remodelling factor FACT, in orchestrating transcriptional elongation coupled DNA repair	27.11.2019	Prof. Ellora Sen
24	Prof. Nicola S Clayton, FRS Professor of Comparative Cognition, Department of Psychology, University of Cambridge, UK and Rambert's Scientist in Residence	Ways of Thinking: From Crows to Children and back Again	13.12.2019	Prof. Neeraj Jain
25	Prof. Clive Wilkins, MMC Artist in Residence in the Department of Psychology University of Cambridge, UK and Member of the Magician Circle	The Long March to the Mountain	13.12.2019	Prof. Neeraj Jain
26	Dr. Abhishek Bhardwaj Sharma Luxembourg Institute of Health	Understanding the Temozolomide Induced DNA Break Repair in Glioblastoma Brain Cancer-The story of XAB2	20.12.2019	Dr. Anindya Ghosh Roy
27	Dr. Srinivasa Prasad Kommajosyula SIU Medicine, Springfield, IL, 62702, USA	Blockade of Corticothalamic Projections Alters Coding in Medical Geniculate Body to Less Salient Modulated Stimuli	27.12.2019	Dr. Bhavani Shankar Sahu

Sr. No.	Name of the Speaker	Title of the Talk	Date	Host Faculty
28	Prof. Mriganka Sur Newton Professor of Neuroscience Director, Simons Centre Massachusetts University of Technology	Mechanisms of Cortical Plasticity	09.01.2020	Prof. Neeraj Jain
29	Dr. Shalley Kant Gupta Executive Scientific Manager and Regional Director, Medical Affairs - Astellas	A Career in Research and Drug Discovery- Insights from a Personal Journey	15.01.2020	Prof. Neeraj Jain
30	Dr. Mark Hallett Chief Human Motor Control Section, NINDS NIH, USA	Oscillations: Good and Bad	29.01.2020	Prof. Neeraj Jain
31	Dr. Shovan Naskar Unit of Foundation Neuronal Circuits, NIMH, NIH, Bethesda, USA	Functional connectivity of diverse long-range inputs to the primary somatosensory cortex	05.02.2020	Dr. Sourav Banerjee
32	Prof. Ashley Bush, *MBBS, DPM, Phd, FTSE Director, Melbourne Dementia Research Centre Florey Institute of Neuroscience and Mental Health Melbourne, Australia	Iron and Glutathione in aging & Brain Disease	10.02.2020	Prof. Pravat K. Mandal
33	Dr. Amitiva Majumder National Center for Cell Sciences, Pune	A role of cellular translation regulation associated with toxic huntingtin protein	25.02.2020	Dr. Sourav Banerjee
34	Dr. Gaurav Goyal Institute for Medical Genetics, Medical University of Vienna	Segregating proteins during neuronal development: the lipidic way	27.02.2020	Dr. Anindya Ghosh Roy
35	Dr. Niranjan Kambi Department of Psychology, University of Wisconsin-Madison	Neural basis of Memory	02.03.2020	Prof. Soumya Iyengar
36	Dr. Prakash Devaraju Post-Doctoral Fellow from Department of Developmental Neurobiology, St. Jude Children's Research Hospital	Neural Circuits, Mitochondria and Beyond	05.03.2020	Dr. Anindya Ghosh Roy

The Molecular Motors, Transport and Trafficking Meeting 2019 (18th to 20th October)

Cell biologists from India, USA and UK gathered in National Brain Research Centre (NBRC), Gurugram, India on October 18th to 20th 2019 to discuss recent developments in the field of cytoskeleton, molecular motors and membrane trafficking. The Molecular motors, transport and trafficking (M2T2) meeting was organized by Anindya Ghosh Roy, NBRC and co-organized by Mahak Sharma from Indian Institute of Science Education and Research (IISER), Mohali, India. The speakers were highly successful in stimulating scientific discussions on the topic of interest, moreover the confluence of researchers in the field of cellular transport led to initiation of new collaborations. This was the sixth in the M2T2 meeting series, the concept of which was initiated by researchers at Tata Institute of Fundamental Research (TIFR), Mumbai and the meeting had always been traditionally organized at TIFR. The format of this meeting is such that the participant number is small and sufficient time is given for in-depth discussion on the different topics covered at the meeting. In this report, I am highlighting and summarizing the scientific sessions of the meeting.

There were total 21 national and 4 international invited speakers attended this event. Similarly, 32 national and 2 international student/post-doc participants attended the meeting. There were total of nine scientific sessions and nine speakers for each of the three days of the meeting. The meeting began on the morning of October 18th (Friday) with an introduction about the history of the M2T2 meetings by Anindya Ghosh-Roy. The first day of the meeting had three sessions on the topic of cytoskeletal organization and organelle positioning in neurons, microtubule dynamics and role of motors in spindle organization during mitosis and the different modes of regulation of microtubule-motor interactions. Each of the three sessions also had few short talks by students and postdocs. Similar to earlier M2T2 meetings, there were several interesting and relevant questions from the audience including several questions from the students. The highlights of the day 1 were on the role of posttranslational modifications (PTMs) of microtubules in organelle transport and a biological sensor to detect these PTMs. There were also fascinating talks on the mechanisms regulating microtubule and actin organization in neuronal dendrites and axons.

The second day of the meeting had three sessions on the topic of cargo positioning by Motors, and mechanistic insights into regulation of dynein motor as well as a breakout topic on how mechanical forces regulate axonal morphology and collective cell migration. The second day generated a lot of enthusiasm in its first session with stunning live imaging videos of cytoplasmic streaming in drosophila oocyte. The session also addressed a novel role of how hormones such as insulin regulate lipid composition of organelles that further controls association of motor and motor adaptors with the organelle membrane. The second day of the meeting also had talks by theoretical biologists on the behavior of motor proteins and debating the various models of in vivo motor competition. The day ended with a panel discussion on upcoming trends in scientific publishing and peer review process by five experts including, Mohan Balasubramanian, Vladimir Gelfand, Roop Mallik, Vaishnavi Ananthanarayanan, Melissa Rolls.

The third day of the meeting had three sessions on the topic of Mechanism of Cytokinesis and two sessions on first time introduced topic in an M2T2 meeting of Cell Biology of Pathogens and their hosts. The talks in the first session revealed the mechanistic requirements for assembly of the cytokinetic ring. The following sessions on host pathogen interactions were all by first time speakers on the M2T2 platform where diverse pathogens such as Candida, Mycobacterium, Encephalitis virus and Plasmodium were introduced to the audience and insights into their intracellular lifestyles were discussed. The aim of these new sessions with new speakers was to provide an opportunity where collaborations between the pathogen community and motor and transport community could be initiated.

Overall, the M2T2 2019 was another successful meeting in this series where several young scientists who have recently started their academic career presented their work. The tracks, motor and cellular trafficking community is growing by leaps and bounds in India and there is critical mass in this subject area for fruitful collaborations. There is no doubt that the M2T2 meeting series will continue to be a very relevant and exciting platform to discuss the research for this community in coming years.

NBRC 16th Foundation Day- 16th December, 2019

The National Brain Research Centre celebrated its 16th foundation day with pomp and gaiety on 16th December 2019. The events were kicked off with an open day that saw participation of school children from various schools around NCR. The children were taken around labs in NBRC to give them a feel for neuroscience research. Student volunteers gave broad overviews of their respective labs with a view to instil scientific temper in the young children. The natural curiosity of children was on display as a lot of them posed probing questions to the student volunteers. This was followed by a science quiz which was hosted by NBRC students for the visiting schools which saw the director, faculty and the chief guest in attendance. The quiz was followed by a grand lunch for the students, staff, faculty and visiting school children.

In the evening, a public lecture was delivered by Prof Nicola Clayton, FRS, of University of Cambridge, and Prof Clive Wilkins Artist in Residence, University of Cambridge and a Member of the Magic Circle. The title of his public lecture was 'Seven Myths of Memory'. In this lecture the speakers explored the complex relationship between episodic memory, and our ability to travel backwards and forwards mentally (mental time travel), including a discussion of Prof. Nicky's research on corvids and children, and Clive's published work 'The Moustachio Quartet', a series of novels. In this lecture, they incorporated various aspects of science, art. They also performed arts to explore the nature of memory and mental time travel. This gave insights into the subjective nature of memory in which we differentiate time and space in the mind's eye. This was a unique opportunity to appreciate why memories are not only about the past, -- they allow the strategies to define the future. The lecture was followed by an equally provocative question-answer session.

The lecture was preceded by a prize distribution ceremony where the class toppers from the MSc. and PhD programme were felicitated for meritorious performance in course work. The ceremony was closed after a brief address by the president of NBRC society, Dr. P.N Tandon.

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. The officer is also responsible for the administration of DIC project personnel.

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, Hindi Week, Vigilance Awareness week, International Yoga Day etc. The Administration achieved excellence in execution of the following activities at NBRC:

- The annual cultural festival of NBRC, 'TANTRIKA 2019' 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 talk by Dr. Ahmad Sohaib, Assistant Professor, Jamia Millia Islamia, New Delhi was organized on 17th September 2019.

- A talk on "Religion as a social protest: the case of early Buddhism." by Dr. Annapurna Vancheswaran, Senior Director, Communications Outreach and Advocacy Unit, TERI was organized on 16th September 2019.

- 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 16th Foundation Day of NBRC was held on 16th day of December, 2019. On this occasion, several programmes were organized within and outside the campus. The daylong celebrations included the poster presentations on ongoing research activities of NBRC. Students from various schools were invited to interact with NBRC scientists and they visited the laboratories. A quiz programme for students from local schools was also organized on this occasion. On this august occasion, **Prof. Nicola S Clayton and Prof. Clive Wilkins** of University of Cambridge, UK delivered the lecture to the students and scientific community at India International Centre, New Delhi.

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 2019-20 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 can 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, and in the matter of students' admissions, the provision of exemption as provided in Gazette Notification No. 5 dated 4th January, 2007 is 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 Chief Vigilance Officer of the Centre.

Institutional Governance Structure & People at NBRC

Members of The General Body of NBRC Society

1 **Prof. P.N. Tandon** (President)
No. 1, Jagriti Enclave,
Vikas Marg,
New Delhi – 110 092

2 **Dr. Renu Swarup**
Secretary
Department of Biotechnology,
C.G.O Complex,
New Delhi – 110 003

3 **Prof. Ashutosh Sharma**
Secretary
Department of Science & Technology,
New Delhi – 110 016

4 **Prof. Balram Bhargava**
Director-General
Indian Council of Medical Research,
New Delhi – 110 029

5 **Dr. Sandip K. Basu**
JC Bose Chair Professor,
FD 426, Sector 3, Bidhannagar,
Kolkata 700106

6 **Director**
National Centre for Biological Sciences
GKVK Campus, GKVK P.O.,
Bangalore – 560 065

7. **Dr. Shekhar Mande**
Director General, CSIR and Secretary, DSIR
Anusandhan Bhavan, 2, Rafi Marg
New Delhi-110001 (India).

8 **Joint Secretary** (Financial Advisor)
Department of Biotechnology,
Lodhi Road, CGO Complex,
New Delhi – 110003

9 **Dr. M. Gourie Devi**
Director (Retd.),
Flat –9, Doctors Apartments,
Vasundhara Enclave,
Delhi – 110 096

10 **Dr. L. M. Patnaik**
CSA Department
Indian Institute of Science
Bangalore - 560012

11 **Dr. Kalluri Subba Rao**
(INSA Hon. Scientist & Professor)
School of Medical Sciences
University of Hyderabad
Hyderabad – 500 046

12 **Prof. Gomathy Gopinath**
Flat # 001, Kanchanjunga Apartments, 122/2,
Nagavarapalaya, Varthur Road,
Bangalore – 560093

13 **Dr. Sundeep Sarin**
Advisor
Department of Biotechnology,
New Delhi

14 **Prof. Neeraj Jain**
Director
National Brain Research Centre
Manesar – 122052, Haryana

Members of The Governing Council

Dr. Renu Swarup
(Ex Officio, Chairperson)
Secretary
Department of Biotechnology, Lodhi Road,
CGO Complex,
New Delhi – 110 003.

Prof. Upinder S. Bhalla,
Scientist,
National Centre for Biological Sciences, NCBS,
Bellary Road,
Bangalore- 560 065

Dr. A. K. Agarwal
Dean, Director, Professor & HOD (Retd.)
N-9, Green Park Main
New Delhi

Dr. Chitra Sarkar
Department of Pathology,
All India Institute of Medical Sciences,
Ansari Nagar,
New Delhi – 110 029.

Mr. B. Anand (Ex-Officio)
Additional Secretary & Financial Advisor
Department of Biotechnology,
New Delhi – 110003

Prof. Ashutosh Sharma (Ex-Officio)
Secretary
Department of Science & Technology, Technology Bhawan, New Mehrauli Road,
New Delhi – 110 016

Nominee of UGC (Ex-Officio)

Prof. Neeraj Jain
Director
National Brain Research Centre
Manesar -122052
Haryana

Prof. P.N. Tandon
(Ex-Officio)
No. 1, Jagriti Enclave,
Vikas Marg
Delhi – 110 092.

Prof. Dinakar M. Salunke
Director
International Centre for Genetic Engineering and Biotechnology,
Aruna Asaf Ali Marg,
New Delhi – 110 067

Prof. G. Mehta, *FNA, FRS*
Bhartia Chair School of Chemistry,
University of Hyderabad
Hyderabad 500046

Prof. Seyed E. Hasnain
Vice Chancellor
Jamia Hamdard University
Mehrauli - Badarpur Road,
Near Batra Hospital,
Hamdard Nagar,
Delhi 110062

Prof. Balram Bhargava (Ex-Officio)
Director General
Indian Council for Medical Research,
V. Ramalingaswamy Bhawan,
Ansari Nagar, New Delhi – 110 029

Dr. Sanjeev Jain
Head of the Department,
Department of Psychiatry, NIMHANS, Bangalore

Mr. C. P. Goyal (Ex-Officio)
Joint Secretary (Admin),
Department of Biotechnology
New Delhi – 110 003

Members of The Finance Committee

Mr. B. Anand (Chairman, Ex-Officio)
Additional Secretary & Financial Advisor
Department of Biotechnology
New Delhi

Dr. Sundeep Sarin (Ex-officio)
Scientific Coordinator of NBRC
Advisor, Department of Biotechnology,
New Delhi - 110003

Prof. Dinakar M. Salunke
Director
International Centre for Genetic Engineering and Biotechnology,
Aruna Asaf Ali Marg, New Delhi – 110 067

Prof. Seyed E. Hasnain
Vice Chancellor
Jamia Hamdard University
Mehrauli - Badarpur Road, Near Batra Hospital,
Hamdard Nagar, Delhi 110062

Prof. Neeraj Jain (Ex-Officio)
Director
National Brain Research Centre
Nainwal More, Manesar – 122 052
Haryana

F&AO (Ex-officio)
National Brain Research Centre
Manesar-122052, Haryana

Members of The Building Committee

Prof. Dinakar M. Salunke (Chairperson)
Director
International Centre for Genetic Engineering and Biotechnology
Aruna Asaf Ali Marg,
New Delhi – 110 067

Dr. Amulya K. Panda
Director
National Institute of Immunology (NII),
New Delhi – 110067

Dr. S. K. Gupta
Deputy Director (Retired) &
Emeritus Scientist
National Institute of Immunology (NII),
New Delhi.

Sh. V. H. Rao
Senior Consultant Engineering,
Mehrauli - Badarpur Road,
Near Batra Hospital, Hamdard Nagar,
New Delhi – 110062

Mr. M. K. Gupta
Engineer-In-Charge (Civil),
IUAC, New Delhi

Prof. Sidhartha Satpathy
HOD Hospital Administration
AIIMS, New Delhi

Prof. Neeraj Jain (Ex-Officio)
Director
National Brain Research Centre
Manesar - 122052

Members of The Scientific Advisory Committee

Prof. P. N. Tandon (Chairperson)
President, NBRC Society
H.No. 1, Jagriti Enclave Delhi

Prof. Upinder S. Bhalla
(Co-Chairperson)
Scientist
National Centre for Biological Sciences (NCBS)
Bangalore - 560 065

Prof. N.R. Jagannathan
Head of the Department of NMR and MRI Facility
All India Institute of Medical Sciences (AIIMS)
New Delhi – 110 029

Prof. Vijayalakshmi Ravindranath
Chairperson
Centre for Neuroscience, Indian Institute of Sciences (IISc)
Bangalore – 560 012

Prof. Amitabha Chattopadhyay
Scientist,
Centre for Cellular and Molecular Biology (CCMB)
Hyderabad

Dr. Ayub Qadri
Scientist,
National Institute of Immunology (NII)
New Delhi – 110 067

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

Prof. Siddhartha Roy
Director
Indian Institute of Chemical Biology (IICB)
Kolkata-700 032

Prof. Jyotsna Dhawan
Scientist,
CSIR Centre for Cellular and Molecular Biology
Hyderabad.

Prof. Rohit Manchanda,
Biomedical Engineering Group,
School of Biosciences and Bioengineering
IIT Bombay
Mumbai-400076

Prof. B. N. Mallick
Professor
Department of Life Sciences
Jawaharlal Nehru University, New Delhi

Dr. V. Rajshekhar
Department of Neurological Sciences
Christian Medical College Hospital (CMC)
Vellore- 632 004

Dr. Sanjeev Jain
Head of the Department
Department of Psychiatry, NIMHANS
Bangalore

Prof. Sudipta Maiti
Dept. of Chemical Sciences, TIFR
Homi Bhabha Road, Colaba,
Mumbai - 400 005

Prof. Ajoy Ray
Vice-Chancellor
Bengal Engineering & Science University
Howrah-711103, West Bengal,

Dr. Chitra Sarkar
Department of Pathology,
All India Institute of Medical Sciences,
Ansari Nagar, New Delhi– 110 029

Dr. Sundeep Sarin
Scientific Coordinator for NBRC
Advisor
Department of Biotechnology
New Delhi

Prof Neeraj Jain (Ex Officio)
Director
National Brain Research Centre
Manesar 122052

International Members

Prof. Ariel Ruiz I Altaba
Professor,
Faculty of Medicine, University of Geneva,
Department of Medicinal Genetics, 8242 CMU,
1 rule Michel Servet, CH-1211, Geneva 4,
Switzerland

Prof. Thomas D. Albright
Professor,
The Salk Institute for Biological Studies,
La Jolla, California, USA 92037

Prof. Baroness Susan Greenfield
Professor,
Department of Pharmacology, Lincoln College,
Oxford University, UK

Michael W. Weiner
MD, Director of the Center for Imaging of
Neurodegenerative Diseases,
SFVAMC, Professor of Radiology,
Medicine, Psychiatry and Neurology, UCSF

Members of Academic Council

Prof. Neeraj Jain (Chairperson)
Director & Vice Chancellor
NBRC, Manesar

Prof. Krishnamurthy Natarajan
Professor
Dr. B.R. Ambedkar Center for Biomedical Research
University of Delhi,
Delhi - 110 007

Prof. James Gomes
Professor
School of Biological Sciences
Indian Institute of Technology
Hauz Khas, New Delhi- 110 016

Prof. Chinmay K. Mukhopadhyay
Professor
Special Centre for Molecular Medicine
Jawaharlal Nehru University
New Delhi 110 067

Prof. Pravat Mandal
Scientist VII
NBRC, Manesar

Prof. Pankaj Seth
Scientist VII
NBRC, Manesar

Dr. Soumya Iyengar
Scientist VI
NBRC, Manesar

Dr. Anirban Basu
Scientist VI
NBRC, Manesar

Dr. Shiv Kumar Sharma
Scientist VI
NBRC, Manesar

Dr. Ellora Sen
Scientist VI
NBRC, Manesar

Dr. Arpan Banerjee
Scientist V
NBRC, Manesar

Offg. Registrar
NBRC, Manesar

Members of Board of Studies

Prof. Neeraj Jain (Chairperson)
Director,
National Brain Research Centre
Manesar, Haryana

Prof. Kunzang Chosdol
Department of Biochemistry,
All India Institute of Medical Sciences,
New Delhi

Dr. Sushil Kumar Jha
Associate Professor,
Jawaharlal Nehru University,
New Delhi

Prof. Soumya Iyengar
National Brain Research Centre
Manesar, Haryana

Prof. Ellora Sen
National Brain Research Centre
Manesar, Haryana

Prof. Ranjit K. Giri
National Brain Research Centre
Manesar, Haryana

Dr. Anindya Ghosh Roy
National Brain Research Centre
Manesar, Haryana

Dr. Arpan Banerjee
National Brain Research Centre
Manesar, Haryana

Dr. Dipanjan Roy
National Brain Research Centre
Manesar, Haryana

Offg. Registrar
National Brain Research Centre
Manesar, Haryana

DST-INSPIRE Faculty

1	Dr. Yogita Kapil Adlakha
2	Dr. Swagata Dey (Till 31/12/2019)

Wellcome Trust India Alliance / DBT India Alliance Early Career Fellow

1	Dr. Swagata Dey

Ph.D. Students

1	Mr. Apoorv Sharma
2	Mr. Sandeep Kumar
3	Mr. Bharat Prajapati (Till 22/01/2020)
4	Mr. John Thomas
5	Mr. Kautuk Kamboj
6	Mr. Biswaranjan Sahoo
7	Mr. Indrajith R. Nair
8	Mr. Shashi Shekhar Kumar (Till 31/07/2019)
9	Mr. Touseef Ahmad Sheikh
10	Mr. Tushar Arora
11	Mr. S Balakumar
12	Ms. Arti Kumari
13	Mr. Dharmendra Puri
14	Ms. Mukta Kumari
15	Mr. Raghav Shankar
16	Md. Tipu Khan
17	Ms. Priyanka Ghosh
18	Ms. Sarbani Samaddar
19	Ms. Shruti Patrick
20	Mr. Surajit Chakraborty
21	Ms. Bindu
22	Mr. Shiladitya Laskar
23	Mr. Sibaram Behera
24	Ms. Tripti Joshi
25	Mr. Abhishek Singh Narvaria
26	Ms. Deepti Dama
27	Mr. Karthick R
28	Ms. Nisha Chetana Sastry
29	Ms. Shivangi Sharma
30	Ms. Sunanda Sharma
31	Ms. Vanshika Singh
32	Ms. Himali Arora
33	Ms. Meenakshi Bhaskar
34	Mr. Neeraj Kumar
35	Ms. Dipanjana Banerjee
36	Ms. Gargi Majumdar
37	Ms. Kamakshi Garg
38	Ms. Khushboo Vinod Punjabi
39	Ms. Partika
40	Ms. Roopashi Saxena
41	Ms. Shalini Sharma
42	Ms. Stuti Mohapatra
43	Mr. Anagh Pathak
44	Ms. Kirti
45	Ms. Ritu Moni Borah
46	Ms. Anjali
47	Ms. Archana Mehta
48	Mr. Chandramouli Mukherjee
49	Ms. Sakshi Shukla
50	Ms. Sonia Balahun Umdor

Integrated Ph.D. Students

1	Mr. Shubham Krishna
2	Ms. Guncha Bhasin
3	Ms. Shankhamala Sen
4	Ms. Uzma Din
5	Ms. Chitra Mohinder Singh Singal
6	Ms. Utkarsha A Singh
7	Ms. Pooja Parishar
8	Mr. Apurva Agrawal
9	Mr. Atanu Datta
10	Mr. Naman Vatsa (Till 04/04/2019)
11	Mr. Hriday Shanker Pandey
12	Mr. Vikas Pareek
13	Ms. Reshma Bhagat (Till 11/09/2019)
14	Mr. Vipendra Kumar
15	Ms. Atrayee Basu
16	Ms. Priyanka
17	Mr. Gourav Sharma
18	Ms. Harjot Kaur
19	Mr. Pruthvi S.G
20	Ms. Shelly Pal (Till 31/07/2019)

M.Sc. Students

1	Mr. Azman Akhter
2	Ms. Guneet Kaur
3	Ms. Kirti Saluja
4	Mr. Masood Ahmad Wani (Till 29/07/2019)
5	Ms. Pallavi Singh
6	Mr. Ranjit Pradhan (Till 15/07/2019)
7	Ms. Akanksha Goyal
8	Ms. Akanksha Gupta
9	Mr. Ankit Dhoundiyal
10	Mr. Thakar Darshit Mahesh
11	Mr. Mantosh Patnaik
12	Ms. Mishaben Parmar
13	Mr. Nitish Kumar
14	Ms. Pratibha Ahirwal
15	Ms. Rekha Singh
16	Ms. Rishika Tiwari
17	Ms. S Indira Priya
18	Ms. Sharmistha Panda
19	Ms. Shashwati Tripathi
20	Ms. Surbhi
21	Ms. Vinsea A V Singh
22	Ms. Aamna Jain
23	Mr. Ankit Kumar Shah
24	Ms. Anwesha Das
25	Ms. Bhanumita Agrawal
26	Ms. Debapriya Roy
27	Ms. Bapat Ojasee Ajinkya
28	Ms. Pooja Kri Gupta
29	Mr. Rudradeep Mukherjee
30	Mr. Akshay Kumar Tiwari

Project Assistant

1	Ms. Keerthana. P
2	Mr. Subhajit Jana (Till 07/10/2019)
3	Mr. Utsav Mukherjee (Till 19/07/2019)
4	Dr. Fahd M Yasin
5	Ms. Ritu Nayak (Till 10/01/2020)
6	Dr. Bahaar Meera Jain (Till 22/04/2019)
7	Ms. Divya Dwivedi (Till 21/11/2019)
8	Ms. Fathima Murshida P (Till 18/04/2019)
9	Ms. Priya Maddhesiya (Till 30/04/2019)
10	Mr. Vivek Sharma
11	Ms. Karnika Gupta (Till 16/08/2019)
12	Ms. Smriti Bhardwaj
13	Mr. Devashish Arvind Pande
14	Mr. Paritosh Jaiswal
15	Mr. Sharan G (Till 30/09/2019)
16	Mr. Rishabh Kapoor
17	Ms. Sigar Priyanka Jaipal
18	Ms. Reshma Raj
19	Mr. Varun Madan Mohan
20	Ms. Bhavya Gohil
21	Mr. Shubham Singhal
22	Ms. Kulshrestha Shruti
23	Mr. Mainak Ghosh

Research Associates

1	Dr. Chetan Kumar Yadav, Research Associate-3 (Till 30/04/2019)
2	Dr. D. Subhashree, Research Associate-2 (Till 31/05/2019)
3	Dr. Dipanjan Ray, Research Associate-3 (Till 10/12/2019)
4	Ms. Deepali Singh, Research Associate-2
5	Dr. Navinder Kumar, Research Associate-1 (Till 30/04/2019)
6	Dr. Moumita Das, Research Associate-2 (Till 06/12/2019)
7	Mr. M. Gopi, Research Associate-1 (Till 06/01/2020)
8	Dr. Kanu Megha, Research Associate-1
9	Dr. Sonika, Research Associate-2
10	Dr. Sandeep Kumar, Research Associate-3
11	Dr. Soibam Shyamchand Singh, Research Associate-3
12	Ms. Sriparna Mukherjee, Research Associate-1 (Till 29/11/2019)
13	Dr. Karthick C

Research Associate (Project)

1	Dr. Prem Chand (Till 17/10/2019)
2	Dr. Bibhabasu Hazra (Till 26/09/2019)
3	Dr. Amit Naskar
4	Dr. Shubham Kumar (Till 22/05/2019)
5	Dr. Rituparna Chaudhuri
6	Dr. Jasleen Gund
7	Dr. Md. Ashraful Hasan, DBT-TWAS Postdoctoral Fellowship

SERB-National Post Doctoral Fellowship

1	Dr. Soibam Shyamchand Singh (Till 02/05/2019)
2	Dr. Sandeep Kumar (Till 05/04/2020)

Research Fellows

1	Ms. Reshma Bhagat (From 30/04/2019 till 29/10/2019)
2	Mr. G. Vinodh Kumar (From 01/02/2019 till 31/07/2019)
3	Mr. Vikas Pareek
4	Mr. Touseef Ahmad Sheikh

Project Employees

1	Ms. T. Ammaponnu Sumathi, R&D Engineer (Till 21/06/2019)
2	Mr. Manjit, Lab Attendant (MEG)
3	Mr. Rakesh Yadav, Nursing Orderly (MEG)
4	Mr. Ashok Kumar, Nurse (MEG)
5	Mr. Gaurav Singh, Technician (MEG) (Till 25/06/2019)
6	Mr. Vivek Singh, Technician (MEG)
7	Mr. Om Prakash Jakhar, Nurse (MEG)
8	Mr. Arun E V R, Senior Research Fellow
9	Mr. Sukhvir Singh Pundir, Technical Associate (Computer / IT)
10	Ms. Deepika Shukla, Research Scientist
11	Mr. Krishan Sharma, Technician A (Till 22/09/2019)
12	Mr. Dixit Sharma, Junior Research Fellow (Till 15/07/2019)
13	Ms. Teesta Naskar, ICMR-SRF (Till 16/09/2019)
14	Ms. Sriparna Mukherjee, DST-INSPIRE Fellow Senior Research Fellow (Till 30/04/2019)
15	Mr. Prasann Jeet, Lab Attendant (Till 30/11/2019)
16	Ms. Shallu, Neuropsychologist
17	Ms. Anshika Goel, Senior R&D Engineer
18	Mr. Praful P Pai, R&D Engineer-1 (Till 21/08/2019)
19	Ms. Kanika Sandal, Research Manager (Till 27/09/2019)
20	Mr. Saurav Roy, R&D Engineer
21	Mr. Chen Chongtham, Research Assistant (Till 26/06/2019)
22	Mr. Jayakrishnan U, R&D Engineer (Till 22/03/2019)
23	Mr. Ritwick Mishra, Clinical Coordinator
24	Ms. Radhika Shivhare, Senior R&D Engineer (Project) (Till 11/03/2020)
25	Ms. Avinash Kalyani, R&D Engineer (Till 08/11/2019)
26	Mr. Prem Chand, Manager
27	Mr. Jatin Rathore, Technologist (Till 31/07/2019)
28	Ms. Priya Shrivastav, Nurse
29	Ms. Ruchika Mittal, Programmer (Till 12/02/2020)
30	Mr. Rajnish Kumar, Technical Assistant (Till 31/01/2020)
31	Mr. Praful P Pai, Research Scientist (Till 25/10/2019)
32	Ms. Kanika Sandal, R&D Engineer-1
33	Ms. Shalini, Technical Assistant
34	Mr. Neeraj Kasana, Technical Assistant
35	Mr. Gaurav Singh, Technologist (MEG)
36	Mr. Vishnu Singh, Nurse (MEG)
37	Mr. Dharmendra Jakhar, Technical Assistant (MEG)
38	Mr. Kuldeep Singh, R&D Engineer
39	Dr. Rini Dhawan, Scientist "B"
40	Dr. Deepak Sharma, Casualty Medical Officer (Till 17/12/2019)
41	Ms. Sunita Kumawat, Nursing Orderly (MEG)
42	Ms. Srimathi P, Technician (MEG)
43	Mr. Sachin Kumar, Lab Attendant (MEG)
44	Ms. Kirandeep Kaur, Technologist (MEG)
45	Mr. Deepak Kumar, Nursing Orderly (MEG)
46	Ms. Meenu Yadav, Technician (MEG)
47	Ms. Anupam Das, Junior Research Fellow
48	Mr. Saurav Roy, R&D Engineer
49	Ms. Divya Dwivedi, R&D Engineer
50	Ms. Shallu, Research Scientist
51	Ms. Apoorva Misra, Research Manager
52	Dr. Rini Dhawan, Project Coordinator-1

Scientist Staff

1. Prof. Neeraj Jain, Director
2. Prof. Pravat Kumar Mandal, Scientist – VII
3. Prof. Pankaj Seth, Scientist – VII
4. Prof. Shiv Kumar Sharma, Scientist – VI
5. Prof. Nandini C. Singh, Scientist-VI (Working at UNESCO, New Delhi on deputation basis)
6. Dr. Ellora Sen, Scientist – VI
7. Prof. Soumya Iyengar, Scientist – VI
8. Prof. Anirban Basu, Scientist – VI
9. Dr. Ranjit Kumar Giri, Scientist – VI
10. Dr. Sourav Banerjee, Scientist – V
11. Dr. Arpan Banerjee, Scientist – V
12. Dr. Anindya Roy Ghosh, Scientist – V
13. Dr. Dipanjan Roy, Scientist - IV
14. Mr. Mahender Kumar Singh, Information Scientist
15. Dr. Bhavani Shankar Sahu, Ramalingaswamy Fellow

Technical Staff

1. Mr. Rajbir Singh, Superintending Engineer (Relieved on 02.09.2019)
2. Mr. Sanjeev Kumar Choudhary, Assistant Engineer
3. Dr. D.D. Lal, Technical Officer
4. Mr. Jitender Ahlawat, Technical Officer – B
5. Mr. Arvind Singh Pundir, Technical Officer – B
6. Dr. Inderjeet Yadav, Veterinarian
7. Mr. Kedar Singh Bajetha, Computer Operator
8. Ms. Seepika, Computer Operator
9. Mr. Sachin Kumar, Computer Operator
10. Ms. Tarnnum Mansoori, Computer Operator
11. Mr. Sanjeev Bhardwaj, Computer Operator
12. Mr. Kanhaiya Lal Kumawat, Technician-C
13. Mr. Shankar Dutt Joshi, Technician-C
14. Mr. Sumit Kumar Sinha Mahapatra, Technician-C
15. Mr. D. Narender, Technician-C
16. Mr. Sanjay Kumar, Technician-B
17. Mr. Mithlesh Kumar Singh, Technician-B
18. Mr. Ankit Sharma, Technician-B
19. Mr. Yunis Khan, Technician-B
20. Mr. Durga Lal Meena, Technician-B
21. Md. Irshad Alam, Technician-B
22. Mr. Manish Kumar, Technician-B
23. Mr. P. Manish, Technician-B
24. Mr. Dil Bahadur Karki, Technician-A

25. Mr. Rammehar, Technician-A
26. Mr. Hari Shankar, Technician-A
27. Mr. Mahendra Singh, Technician-A
28. Mr. Sanjay Kumar Singh, Technician-A

Administrative Staff

1. Mr. Tanmoy Bhattacharyya, Chief Administrative Officer
2. Mr. Santosh Kumar Choudhary, Deputy Finance Officer
3. Mrs. Pooja Gosain, Administrative Officer
4. Mr. Ravinder Pal, Stores & Purchase Officer
5. Sanjay Kumar Gupta, Office Assistant
6. Mr. Suraj Bhan, Office Assistant
7. Mr. Rakesh Kumar Yadav, Office Assistant
8. Mr. Himanshu Mal, Office Assistant (Working at ICSSR, New Delhi on deputation basis)
9. Mr. Ajay Kumar Dehariya, Office Assistant (Working at DTU, New Delhi on deputation basis)
10. Mr. Parmander Singh Rawat, Office Assistant
11. Mr. Jitendra Kumar Meena, Office Assistant
12. Mr. Bhupender Pal Sharma, Driver Grade-I
13. Mr. Satish Kumar, Driver Grade-II

DIC Project

1. Ms. Reema Saxena, Computer Operator
2. Ms. Sunita Yadav, Computer Operator
3. Mr. Amit Kumar, Computer Operator
4. Mr. R. Ganesh Gurumoorthy, Computer Operator

Contract Employees

1. Dr. Rema Velayudhan, Sr. Consultant
2. Dr. P. Raghunathan, Consultant

Annual Financial Statements

INDEPENDENT AUDITOR'S REPORT

Report on the Financial Statements

1. We have audited the accompanying financial statements of **M/S NATIONAL BRAIN RESEARCH CENTRE** ("the Institute"), which comprise the Balance Sheet as at March 31, 2020, the Statement of Income & Expenditure A/c for the year then ended, and a summary of the significant accounting policies and other explanatory information, which we have signed under reference to this report.

Management's Responsibility for the Financial Statements

2. The Institute's Management is responsible for the matters with respect to the preparation of these financial statements that give a true and fair view of the financial position and financial performance of the Institute in accordance with the accounting principles generally accepted in India, including the Accounting Standards specified. This responsibility also includes the maintenance of adequate accounting records for safeguarding of the assets of the Institute and for preventing and detecting the frauds and other irregularities; selection and application of appropriate accounting policies; making judgments and estimates that are reasonable and prudent; and design, implementation and maintenance of 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.

Auditor's Responsibility

3. Our responsibility is to express an opinion on these financial statements based on our audit. We conducted our audit in accordance with the Standards on Auditing issued by the Institute of Chartered Accountants of India and in accordance with the Standards on Auditing specified. Those Standards require that we comply with ethical requirements and plan and perform the audit to obtain reasonable assurance about whether the financial statements are free from material misstatement.

4. An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the financial statements. The procedures selected depend on the auditor's judgment, including the assessment of the risks of material misstatement of the financial statements, whether due to fraud or error. In making those risk assessments, the auditor considers internal control relevant to the Institute's preparation and fair presentation of the financial statements in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Institute's internal control. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of the accounting estimates made by management, as well as evaluating the overall presentation of the financial statements.

5. We believe that the Audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

Opinion

6. In our opinion and to the best of our information and according to the explanations given to us, the aforesaid financial statements give the information, in the manner so required and give a true and fair view in conformity with the accounting principles generally accepted in India:

a) In the case of the Balance Sheet, of the state of affairs of the Institute as at March 31, 2020;

b) In the case of the Statement of Income & Expenditure A/c of the Institute for the year ended on that date.

7. *Report on Other Legal and Regulatory Requirements*

1) As required, we report that:

a) We have 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 Institute so far as it appears from our examination of those books;

c) The Balance Sheet and Statement of Income & Expenditure A/c dealt with by this Report are in agreement with the books of account;

d) In our opinion, the Balance Sheet, Statement of Income & Expenditure A/c, Receipt & Payment A/c comply with the Accounting Standards;

e) In our opinion and to the best of our information and according to the explanations given to us, we report as under with respect to other matters to be included in the Auditor's Report:

i) The Institute does not have any pending litigations which would impact its financial position, except one case which is pending.

ii) There are some payables pending since last 3 years.

iii) Donation Received should be transferred to indirect income.

iv)TDS should be deducted on due basis.

v) The Institute did not have any long term contracts including derivative contracts; as such the question of commenting on any material foreseeable losses thereon does not arise.

FOR MAHESHWARI P A AND ASSOCIATES
(Chartered Accountants)

(PARTNER)
CA ABHISHEK GOEL
M. NO. 412467

Date: 11th September, 2020
Place: Meerut
UDIN:20412467AAAAEL3817

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGRAM, HARYANA
BALANCE SHEET AS AT MARCH 31,2020

(Amount-Rs.)

CORPUS / CAPITAL FUND AND LIABILITIES	Schedule	Current Year	Previous Year
Corpus/Capital Fund	1	1,373,502,000.00	1,373,502,000.00
Reserve and Surplus	2		
		(111,840,570.41)	(79,172,116.60)
Earmarked/Endowment Funds	3	836,824,080.29	911,744,376.60
Secured Loans and Borrowings	4	0.00	0.00
Unsecured Loans and Borrowings	5	0.00	0.00
Deferred Credit Liabilities	6	0.00	0.00
Current Liabilities and Provisions	7	48,550,775.64	43,017,897.24
Total (Liabilities)		**2,147,036,285.52**	**2,249,092,157.24**
ASSETS			
Fixed Assets	8	1,092,158,034.51	1,172,321,456.15
Investments - From Earmarked/Endowment Funds	9	0.00	0.00
Investments-Others	10	25,108,109.99	29,112,172.79
Current Assets, Loans, Advances etc.	11	1,029,770,141.02	1,047,658,528.30
Miscellaneous Expenditure		0.00	0.00
(to the extent not written off or adjusted)			
Total (Assets)		**2,147,036,285.52**	**2,249,092,157.24**
Significant Accounting Policies	24		
Contingent Liabilites and Notes on Accounts	24		

O.P NAGAR
INCHARGE FINANCE OFFICER
NBRC

PROF. NEERAJ JAIN
DIRECTOR
NBRC

As per our separate report of even date attached

For Maheshwari PA & Associates
Chartered Accountants
(FRN-012023C)

ABHISHEK GOEL
PARTNER
Membership No. 412467
Date: 11.09.2020
Meerut

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGRAM, HARYANA
INCOME AND EXPENDITURE ACCOUNT FOR THE YEAR ENDED March 31, 2020

(Amount-Rs.)

INCOME	Schedule	Current Year	Previous Year
Income from Sales/Services	12	0.00	0.00
Grants/ Subsidies (Revenue) from DBT	13	291,300,000.00	320,000,000.00
Fees/Subscriptions	14	1,160,404.00	3,316,303.00
Income from Investments (Income on Invest. From earmarked/endow. Funds transferred to funds)	15	6,029,338.92	939,240.00
Income from Royality, Publication etc.	16	0.00	0.00
Interest Earned	17	38,984,253.22	20,982,261.64
Other Income	18	2,041,033.00	4,701,483.00
Increase/(decrease) in stock of Finished goods and work-in-progress	19	0.00	0.00
Total Income (A)		**339,515,029.14**	**349,939,287.64**
EXPENDITURE			
Establishment Expenses	20	89,529,003.00	86,294,023.00
Other Administrative etc.	21	169,376,010.40	189,055,416.22
Expenditure on Grants, Subsidies etc.	22	0.00	0.00
Interest Paid	23	0.00	0.00
Depreciation (Net Total at the year-end-corresponding to Schedule 8)		99,257,469.55	32,446,934.00
Total Expenditure (B)		**358,162,482.95**	**307,796,373.22**
Balance being excess of Income over Expenditure (A-B)		-18,647,453.81	42,142,914.42
Transfer to Special Reserve (Specify each)		0.00	0.00
Transfer to /from General Reserve		0.00	0.00
Balance Being Surplus/(Deficit) carried to Corpus/ Capital Fund		**-18,647,453.81**	**42,142,914.42**
Significant Accounting Policies	24		
Contingent Liabilites and Notes on Accounts	24		

O.P NAGAR
INCHARGE FINANCE OFFICER
NBRC

PROF. NEERAJ JAIN
DIRECTOR
NBRC

As per our separate report of even date attached

For Maheshwari PA & Associates
Chartered Accountants
(FRN-012023C)

ABHISHEK GOEL
PARTNER
Membership No. 412467
Date: 11.09.2020
Meerut

NATIONAL BRAIN RESEARCH CENTRE, MANESAR
NH-8, NAINWAL MORE, MANESAR, GURGAON, HARYANA
RECEIPTS AND PAYMENTS FOR THE YEAR ENDED March 31, 2020

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	148,195.00	273,188.00		i)	Establishment Expenses	10,047,485.00	10,418,602.00
	b)	Bank Balances				ii)	Administrative Expenses	2,731,821.47	2,972,287.21
		i) In Deposit Accounts	-	-	II.	**Payment Made Against Funds For Various Projects**			
		ii) Saving Accounts	557,226,483.43	1,083,725,273.34		i)	Recurring /Capital expenditure	13,576,622.58	91,895,138.46
		iii) CPF Investments	9,112,172.79	31,526,119.18		ii)	Capital Grant Refunded to DBT	-	
II.	**Grants Received**					iii)	Refund to RCGB	-	
	a)	From Government of India				iv)	Refund of Interest	14,021,000.00	26,633,897.00
		Plan				v)	Bank Deposits	1,010,000,000.00	719,100,000.00
		i) Recurring Income	291,300,000.00	320,000,000.00	III.	**Maintenance Cost**			
		ii) Non-Recurring Income	-	130,000,000.00		i)	Lab Maintenance Expenses	3,138,234.93	24,885,124.56
		Plan (Recurring)				ii)	Office Maintenance	35,092,734.00	44,280,071.00
	b)	Fellowship Grant	270,501.00	2,346,598.00		iii)	Vehicle Running & Maintenance	719,199.00	689,915.00
	c)	Delcon Projects (Including Interest)	587,193,205.00	477,350,987.00	IV.	**Investment and Deposit Made**			
III.	**Receipt made against funds for various projects**					i)	Out of Earkmarked/ Endowment funds	26,918,669.00	37,253,214.00
	i)	Recurring Receipt/ Capital Grant	89,393,279.14	45,566,732.16	V.	**Expenditure of Fixed Assets & Capital Work-in-progress**			
		(Including Interest)				i)	Purchase of Fixed Assets	4,677,725.69	9,587,767.99
	ii)	Bank Deposits	688,118,520.00	269,250,000.00	VI.	**Training Expenses**		3,224,477.82	2,861,644.82
IV.	**Interest Received**				VII.	**Other Payments(Specify)**			
	i)	On Bank Deposits				i)	Advances to Supplier	28,472,772.96	13,005,547.75
	ii)	Savings Account	8,601,651.06	12,652,633.10		ii)	Advances to Staff	3,186,169.00	3,733,709.87
	iii)	On CPF Fund	20,785,226.00	7,298,493.41		iii)	Leave Encashment/ LTC/ Bonus	379,046.00	676,169.00
	iv)	Other Interest	226,185.00	140,382.00		iv)	Security Deposit Paid	2,231,336.00	378,656.00
V.	**Any Other Receipt**					v)	EMD Refunded	2,656,439.00	2,883,827.00
	Indirect Income					vi)	TDS Paid	67,193,163.56	60,056,240.00
	i)	Advance to Supplier Received	700,228.00	219,668.00		vii)	Imprest	195,578.00	181,991.00
	ii)	Advance to Staff Received	1,698,360.00	1,194,170.00		viii)	Payment of Current Liabilities	852,562,364.38	789,065,434.17
	iii)	Sale of Tender Documents	43,100.00	404,771.00		ix)	Prepaid Insurance	-	296,064.00
	iv)	Misc. Receipts.	497,581.00	1,471,729.00	VIII.	**Closing balances**			
	v)	Earnest Money Deposit Received	3,385,139.00	1,673,964.00		a)	Cash in Hand	262,526.00	148,195.00
	vi)	Sale of Scrap	112,731.00	2,000.00		b)	Bank Balance		
	vii)	Guest House Charges	224,150.00	289,650.00			i) In Deposit Accounts	-	-
	viii)	Hostel Deposit	339,000.00	446,000.00			ii) Saving Accounts	198,080,018.04	557,226,483.43
	ix)	CPF Fund Received	16,410,480.00	12,750,556.00			iii) CPF Investments	231,321.99	9,112,172.79
	x)	Library Deposit	116,000.00	140,000.00					
	xi)	Current Liabilities Rec.	3,634,115.00	8,555,587.86					
	xii)	Other Receipts	62,402.00	63,650.00					
		TOTAL	**2,279,598,704.42**	**2,407,342,152.05**			**TOTAL**	**2,279,598,704.42**	**2,407,342,152.05**

O.P NAGAR
INCHARGE FINANCE OFFICER
NBRC

PROF. NEERAJ JAIN
DIRECTOR
NBRC

As per our separate report of even date attached
For Maheshwari PA & Associates
Chartered Accountants
(FRN-012023C)

ABHISHEK GOEL
PARTNER
Membership No. 412467
Date: 11.09.2020
Meerut

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGRAM
SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2020

(Amount-Rs.)

SCHEDULE 1-CORPUS/CAPITAL FUND:				
	Current Year		**Previous Year**	
1 Grant-in-Aid - Balance as at the beginning of the year		1,373,502,000.00		1,243,502,000.00
Add: Contribution towards Corpus/Capital Fund	0.00		130,000,000.00	
Add/(Deduct): Balance of net income/ (expenditure) transferred from the Income and Expenditure Account		0.00		130,000,000.00
Balance as at the year end		**1,373,502,000.00**		**1,373,502,000.00**

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(Amount-Rs.)

SCHEDULE 2 - RESERVES AND SURPLUS:				
	Current Year		**Previous Year**	
1 **Capital Reserve:**				
As per last Account	0.00		0.00	
Addition during the Year	0.00		0.00	
Less : Deductions during the year (deficit)	0.00	0.00	0.00	0.00
2 **Revaluation Reserve:**				
As per last Account	0.00		0.00	
Addition during the Year	0.00		0.00	
Less : Deductions during the year (deficit)	0.00	0.00	0.00	0.00
3 **Special Researve:**				
As per last Account	0.00		0.00	
Addition during the Year	0.00		0.00	
Less : Deductions during the year (deficit)	0.00	0.00	0.00	0.00
4 **General Reserve**				
As per last Account	(79,172,116.60)		(114,354,308.02)	
Addition during the Year	-			
Surplus during the yar (as per I&E A/c)	(18,647,453.81)		42,142,914.42	
Less : Deductions during the year (deficit)	14,021,000.00	(111,840,570.41)	6,960,723.00	(79,172,116.60)
Balance as at the year end		**(111,840,570.41)**		**(79,172,116.60)**

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SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2020

Amount in (Rs.)

SCHEDULE 3 - EARMARKED/ENDOWMENT FUNDS	FUND-WISE BREAK UP							
	Project Fund		Fixed Assets Fund (Project)		Contributory Provident Fund		DeLcon E-library Consortium	
a) Opening Balance of Project Fund		157,864,038.10		299,783,144.14		14,263,835.00		437,201,571.36
b) Additions to the Funds:								
i. Donations/grants/Additions to Fund	85,575,722.20		24,663,489.18		1,410,480.00		580,959,268.00	
ii. Income from investments made on account of funds	0.00		0.00		0.00		0.00	
iii. Other additions (Interest Earned)	3,762,812.94	89,338,535.14	0.00	24,663,489.18	513,090.00	1,923,570.00	6,233,937.00	587,193,205.00
Total (a+b)		**247,202,573.24**		**324,446,633.32**		**16,187,405.00**		**1,024,394,776.36**
c) Utilisation/Expenditure towards objectives of funds								
i. Capital Expenditure								
Fixed Assets (net)	24,554,347.18		0.00		0.00		109,142.00	
Others	0.00		0.00		0.00		0.00	
Total		**24,554,347.18**		**0.00**		**0.00**		**109,142.00**
ii. Revenue Expenditure								
-Salaries, Wages and allowances etc	16,603,787.00		0.00		0.00		911,231.00	
-Rent	0.00		0.00		0.00		0.00	
-Others	56,203,686.08		0.00		7,418,669.00		623,798,159.37	
-Depreciation	0.00		48,440,074.00		0.00		0.00	
Total		**72,807,473.08**		**48,440,074.00**		**7,418,669.00**		**624,709,390.37**
Total (C)		**97,361,820.26**		**48,440,074.00**		**7,418,669.00**		**624,818,532.37**
NET BALANCE AS AT THE YEAR-END (a+b-c)		**149,840,752.98**		**276,006,559.32**		**8,768,736.00**		**399,576,243.99**

Notes

1) Disclosures shall be made under relevant heads based on conditions attaching to the grants

2) Plan funds received from the Central/State Governments are to be shown as separate Funds and not to be mixed up with any other Funds.

3) Net additions during the year represents additions net of deductions during the year.

SCHEDULE 4 - SECURED LOANS AND BORROWINGS:	**NIL**
SCHEDULE 5 - UNSECURED LOANS AND BORROWINGS:	**NIL**
SCHEDULE 6 - DEFERRED CREDIT LIABILITIES:	**NIL**

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Amount in (Rs.)

SCHEDULE 3 - EARMARKED/ENDOWMENT FUNDS	FUND-WISE BREAK UP				TOTALS			
	SCHEDULE 3 - EARMARKED/ENDOWMENT FUNDS							
	Endowment Fund for Building		Donation		Current Year		Previous Year	
a) **Opening Balance of Project Fund**		0.00		2,631,788.00		911,744,376.60		1,187,969,732.29
b) **Additions to the Funds:**								
i. Donations/grants/Additions to Fund	0.00		0.00		692,608,959.38		517,126,675.94	
ii. Income from investments made on account of funds	0.00		0.00		0.00		0.00	
iii. Other additions (Interest Earned)	0.00	0.00	0.00	0.00	10,509,839.94	703,118,799.32	12,719,646.00	529,846,321.94
Total (a+b)		**0.00**		**2,631,788.00**		**1,614,863,175.92**		**1,717,816,054.23**
c) **Utilisation/Expenditure towards objectives of funds**								
i. Capital Expenditure								
Fixed Assets (net)	0.00		0.00		24,663,489.18		10,529,027.54	
Others	0.00		0.00		0.00		0.00	
Total		**0.00**		**0.00**		**24,663,489.18**		**10,529,027.54**
ii. Revenue Expenditure								
-Salaries, Wages and allowances etc	0.00		0.00		17,515,018.00		21,745,852.00	
-Rent	0.00		0.00		0.00		0.00	
-Others	0.00		0.00		687,420,514.45		721,734,781.09	
-Depreciation	0.00		0.00		48,440,074.00		52,062,017.00	
Total		**0.00**		**0.00**		**753,375,606.45**		**795,542,650.09**
Total (C)		**0.00**		**0.00**		**778,039,095.63**		**806,071,677.63**
NET BALANCE AS AT THE YEAR-END (a+b-c)		**0.00**		**2,631,788.00**		**836,824,080.29**		**911,744,376.60**

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Amount in (Rs.)

SCHEDULE-7 CURRENT LIABILITIES AND PROVISIONS	Current Year		Previous Year	
A. Current Liabilities				
1. Acceptances		0.00		0.00
2. Sundry Creditors				
-For Goods	0.00		0.00	
- Others	1,183,854.00	1,183,854.00	802,155.00	802,155.00
3. Advances Received		4,405,236.42		3,627,996.42
4.Interest accured but not due on:				
-Secured Loans/borrowings	0.00		0.00	
-Unsecured loans/borrowings	0.00		0.00	
		0.00		0.00
5. Satutory Liabilities:				
-Overdue	0.00		0.00	
-Others (TDS payable)	392,532.50		168,081.50	
		392,532.50		168,081.50
6. Others current Liabilities		34,511,601.92		29,311,362.52
Total (a)		**40,493,224.84**		**33,909,595.44**
B. Provisions				
1. For Taxation		0.00		0.00
2. Gratuity		6,137,980.00		6,137,980.00
3. Superannuation/Pension		0.00		0.00
4. Accumulated Leave Encashment		1,919,570.80		2,970,321.80
5. Trade Warranties/Claims		0.00		0.00
6. Others (Specify)		0.00		0.00
Total (b)		**8,057,550.80**		**9,108,301.80**
Balance as at the year end (a+b)		**48,550,775.64**		**43,017,897.24**

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NH-8, NAINWAL MORE, MANESAR, GURGAON
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SCHEDULE 8 - FIXED ASSETS/ DEPRECIATON

DESCRIPTION	Rate of Dep.	GROSS BLOCK: Cost / valuation As at beginning of the Year	Additions during the Year: More than 6 Months	Additions during the Year: Less than 6 Months	Deductions during the Year	Cost /valuation As at end of the Year	DEPRECIATION: As at the beginning of the Year	Depreciation for current year	On Deductions during the year	Total Depn. Upto 31.03.20	NET BLOCK: As at Current year-end	As at Previous year-end
A. **FIXED ASSETS:**												
1 LAND												
a) Freehold		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
b) Leasehold		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2 BUILDINGS:												
a) On Freehold Land		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
b) On Leasehold Land	10%	71,887,574.00	669,730,848.73	12,347,319.00	0.00	753,965,741.73	36,645,842.67	71,114,623.96	0.00	107,760,466.63	646,205,275.10	35,241,731.33
c) Ownership Flats/Premises		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
d) superstructures on land		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
not belonging to the entity		0.00				0.00	0.00	0.00		0.00	0.00	0.00
3 PLANT MACHINERY & EQUIPMENT	15%	331,692,590.85	4,065,686.69	22,965,025.04	0.00	358,723,302.58	208,580,680.02	20,799,016.51	0.00	229,379,696.53	129,343,606.05	123,111,910.83
4 VEHICLES	15%	4,145,034.00	0.00	0.00	0.00	4,145,034.00	1,979,233.80	324,870.03	0.00	2,304,103.83	1,840,930.17	2,165,800.20
5 FURNITURE, FIXTURES	10%	40,470,722.00	190,399.00	327,148.00	0.00	40,988,269.00	23,854,566.84	1,697,012.82	0.00	25,551,579.66	15,436,689.34	16,616,155.16
6 OFFICE EQUIPMENT	15%	47,101,085.95	264,820.00	502,848.00	0.00	47,868,753.95	25,644,514.65	3,295,922.30	0.00	28,940,436.95	18,928,317.01	21,456,571.30
7 COMPUTER/PERIPHERALS	40%	10,455,650.81	232,323.00	1,689,241.00	0.00	12,377,214.81	7,634,921.59	1,559,069.09	0.00	9,193,990.68	3,183,224.13	2,820,729.22
8 ELECTRIC INSTALATIONS		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
9 LIBRARY BOOKS	40%	268,721.00	144,512.00	141,311.00	0.00	554,544.00	53,744.00	172,057.80	0.00	225,801.80	328,742.20	214,977.00
10 TUBEWELLS & W. SUPPLY		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
11 OTHER FIXED ASSETS (Patents & Copyrights)	25%	5,355,643.00	0.00	0.00	0.00	5,355,643.00	4,176,054.75	294,897.06	0.00	4,470,951.81	884,691.19	1,179,588.25
TOTAL OF THE CURRENT YEAR		**511,377,021.61**	**674,628,589.42**	**37,972,892.04**	**0.00**	**1,223,978,503.07**	**308,569,558.32**	**99,257,469.55**	**0.00**	**407,827,027.87**	**816,151,475.20**	**202,807,463.29**
B CAPITAL WORK IN PROGRESS (Building)		669,730,848.73	0.00	0.00	669,730,848.73	0.00	0.00	0.00	0.00	0.00	0.00	669,730,848.73
C PROJECT EQUIPMENTS	15%	782,796,269.98	21,637,869.50	3,025,619.68	0.00	807,459,759.16	483,013,125.85	48,440,074.00	0.00	531,453,199.85	276,006,559.31	299,783,144.13
TOTAL (A+B+C)		**1,963,904,140.32**	**696,266,458.92**	**40,998,511.72**	**669,730,848.73**	**2,031,438,262.23**	**791,582,684.17**	**147,697,543.55**	**0.00**	**939,280,227.72**	**1,092,158,034.51**	**1,172,321,456.15**

(Note to be given as to cost of assets on hire purchase basis included above)

SCHEDULE 9 - INVESTMENT FROM EARMARKED/ENDOWMENT FUNDS: NIL

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Amount in (Rs.)

SCHEDULE 10 - INVESTMENTS-OTHERS			
		Current Year	**Previous Year**
1	In Government Securities	0.00	0.00
2	Other approved Securities	0.00	0.00
3	Shares	0.00	0.00
4	Debentures and Bonds	0.00	0.00
5	Subsidiaries and Joint Ventures	0.00	0.00
6	Others (CPF Fund)	25,108,109.99	29,112,172.79
	Total	**25,108,109.99**	**29,112,172.79**

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Amount in (Rs.)

SCHEDULE 11 - CURRENT ASSETS, LOANS, ADVANCES ETC.	Current Year		Previous Year	
A. Current Assets				
1 Inventories:				
a) Stores and Spares	0.00		0.00	
b) Loose Tools	0.00		0.00	
c) Stock-In-Trade				
Finished Goods	0.00		0.00	
Wrok-in-progress	0.00		0.00	
Raw Materials	0.00	0.00	0.00	0.00
2 Sundry Debotrs:				
a)Debts Outstanding for a period exceeding six months	0.00		0.00	
b) Others	0.00	0.00	0.00	0.00
3 Cash balances in hand (including cheque/drafts and imprest)		262,526.00		148,195.00
4 Bank Balances:				
a) With Scheduled Banks:				
-On Current Accounts	0.00		0.00	
-On Deposit Accounts (includes margin money)	800,636,949.00		469,020,130.00	
-On Savings Accounts	198,080,018.04		557,226,483.43	
		998,716,967.04		**1,026,246,613.43**
b) With non-Scheduled Banks:				
-On Current Accounts	0.00		0.00	
-On Deposit Accounts	0.00		0.00	
-On Savings Accounts	0.00	0.00	0.00	0.00
5 Post Office-Savings Accounts		0.00		
Total (A)		**998,979,493.04**		**1,026,394,808.43**

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Amount in (Rs.)

SCHEDULE 11 - CURRENT ASSETS, LOANS, ADVANCES ETC. (Contd.)	Current Year		Previous Year	
B. LOANS, ADVANCES AND OTHER ASSESTS				
1 Loans:				
a) Staff	6,014,946.87		6,830,166.87	
b) Other Entities engaded in activities/objectives similar to that of the entity	0.00		0.00	
c) Other (Imprest)	112,922.00		55,922.00	
		6,127,868.87		6,886,088.87
2 Advances and other amounts recoverable in cash or in kind or for value to be received				
a) On Capital Account	0.00		0.00	
b) Prepayments (Insurance)	1,208,124.00		1,169,770.00	
C) Other - Advance to Parties	6,556,871.86		1,892,638.75	
- Other Advances	5,762,502.45		5,762,502.45	
		13,527,498.31		**8,824,911.20**
3 Income Accured:				
a) On Investments from Earmarked/ Endowment Funds	0.00		0.00	
b) On Investments-Others	489,840.00		920,860.00	
c) On Loans and Advances	0.00		0.00	
d) Others (SB A/C)	17,740.00	507,580.00	6,628.00	927,488.00
b) (includes income due unrealised-Rs……)				
4 Claims Receivable (TDS Receivable) & Income Tax		10,627,700.80		4,625,231.80
Total (B)		**30,790,647.98**		**21,263,719.87**
Total (A+B)		**1,029,770,141.02**		**1,047,658,528.30**

O.P NAGAR
INCHARGE FINANCE OFFICER
NBRC

PROF. NEERAJ JAIN
DIRECTOR
NBRC

As per our separate report of even date attached
For Maheshwari PA & Associates
Chartered Accountants
(FRN-012023C)

ABHISHEK GOEL
PARTNER
Membership No. 412467
Date: 11.09.2020
Meerut

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGRAM
SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2020

Amount in (Rs.)

SCHEDULE 12 - INCOME FROM SALES/SERVICES	Current Year	Previous Year
1 Income from Sales	0.00	0.00
2) Income from Services	0.00	0.00
SCHEDULE 13 - GRANTS/SUBSIDIES		
(Irrevocable Grants & Subsidies Receivecd)	**Current Year**	**Previous Year**
1 Central Government	0.00	0.00
2 State Government(s)	0.00	0.00
3 Government Agencies	0.00	0.00
4 Institutions/Welfare Bodies	291,300,000.00	320,000,000.00
5 International Organisations	0.00	0.00
6 Others (Specify)	0.00	0.00
Total	**291,300,000.00**	**320,000,000.00**

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NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGRAM
SCHEDULE FORMING PART OF INCOME AND EXPENDITURE FOR THE YEAR ENDED March 31, 2020

Amount in (Rs.)

SCHEDULE 14 - FEES/ SUBSCRIPTIONS			
		Current Year	**Previous Year**
1	Entrance Fees	412,404.00	478,205.00
2	Annual Fees/Subscriptions	748,000.00	717,500.00
3	Seminar/Program Fees	0.00	0.00
4	Consultancy Fees	0.00	0.00
5	Others (Fellowship Grants)	0.00	2,120,598.00
	Total	**1,160,404.00**	**3,316,303.00**

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NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGRAM
SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2020

Amount in (Rs.)

SCHEDULE 15 - INCOME FROM INVESTMENTS	Investment from Earmarked Fund		Investment-Others	
(Income on invest. From Earmarked/Endowment Funds transferd to Funds)	**Current Year**	**Previous Year**	**Current Year**	**Previous Year**
1 Interest				
a) On Govt. Securities	0.00	0.00	0.00	0.00
b) Other Bonds/Debentures	0.00	0.00	0.00	0.00
2 Dividents:				
a) On Shares	0.00	0.00	0.00	0.00
b) On Mutual Fund Securities	0.00	0.00	0.00	0.00
3 Rents	0.00	0.00	283,250.00	358,250.00
4 Others (Project Receipts)	0.00	0.00	5,746,088.92	580,990.00
Total (B)	**0.00**	**0.00**	**6,029,338.92**	**939,240.00**
TRANSFERRED TO EARMARKED/ ENDOWMENT FUNDS				

SCHEDULE 16 -INCOME FROM ROYALITY, PUBLICATION ETC. **NIL**

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NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGRAM
SCHEDULE FORMING PART OF INCOME AND EXPENDITURE FOR THE YEAR ENDED March 31, 2020

Amount in (Rs.)

SCHEDULE 17 -INTEREST EARNED			
		Current Year	**Previous Year**
1	On Term Deposits:		
	a) With Scheduled Banks	29,953,243.00	17,128,965.54
	b) With Non-Scheduled Banks	0.00	0.00
	c) With Institutions	0.00	0.00
	d) Others	0.00	0.00
2	On Savings Accounts:		
	a) With Scheduled Banks	8,768,825.22	3,712,914.10
	b) With Non-Scheduled Banks	0.00	0.00
	C) Post Office Savings Accounts	0.00	0.00
	d) others	0.00	0.00
3	On Loans:		
	a) Employees/Staff	0.00	0.00
	b) Others	262,185.00	140,382.00
4	Interest on Debtors and Others Receivables	0.00	0.00
	Total	**38,984,253.22**	**20,982,261.64**

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NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGRAM
SCHEDULE FORMING PART OF INCOME AND EXPENDITURE FOR THE YEAR ENDED March 31, 2020

Amount in (Rs.)

SCHEDULE 18 -OTHER INCOME			
		Current Year	**Previous Year**
1	Profit on Sale/disposal of Assets:		
	a) Owned assets	0.00	0.00
	b) Assets acquired out of grants, or received free of cost	0.00	0.00
2	Export Incentives realized		
3	Fees of Miscellaneous Services		
4	Miscellaneous Income	2,041,033.00	4,701,483.00
5	Prior Period Income	0.00	0.00
	Total	**2,041,033.00**	**4,701,483.00**

SCHEDULE 19 -INCREASE/(DECREASE) IN STOCK OF FINISHED GOODS & WORK IN PROGRESS **NIL**

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NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGRAM
SCHEDULE FORMING PART OF INCOME AND EXPENDITURE FOR THE YEAR ENDED March 31, 2020

Amount in (Rs.)

SCHEDULE 20 -ESTABLISHMENT EXPENSES		
	Current Year	**Previous Year**
a) Salaries and Wages	59,576,344.00	60,969,873.00
b) Allowances and Bonous	0.00	0.00
c) Contribution to Provident Fund	646,110.00	1,374,949.00
d) Contribution to Pension Scheme	0.00	0.00
e) Staff Welfare Expenses	0.00	9,428.00
f) Expenses on Employees Retirement and Terminal Benefits	0.00	0.00
g) Others - Children education reimbursement	1,485,000.00	1,478,970.00
- Leave encashment	368,391.00	358,134.00
- LTC expenses	852,917.00	1,010,082.00
- Medical reimbursement	1,274,250.00	1,325,658.00
- NPS(employer subscription)	5,076,188.00	3,679,120.00
- overtime allowance	0.00	0.00
- Skilled manpower	18,644,639.00	14,277,821.00
- Medical insurance (Staff)	1,375,902.00	1,084,544.00
- Office expenses	229,262.00	725,444.00
Total	**89,529,003.00**	**86,294,023.00**

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ABHISHEK GOEL
PARTNER
Membership No. 412467
Date: 11.09.2020
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NH-8, NAINWAL MORE, MANESAR, GURGRAM
SCHEDULE FORMING PART OF INCOME AND EXPENDITURE FOR THE YEAR ENDED March 31, 2020

Amount in (Rs.)

SCHEDULE 21 -OTHER ADMIISTRATIVE EXPENSES			
		Current Year	Previous Year
1	Purchases	0.00	0.00
2	Labour and processing expenses	0.00	0.00
3	Cartage and Carriage inwards	0.00	0.00
4	Electricity and Power	36,303,226.00	38,758,940.00
5	Water Charges	0.00	0.00
6	Insurance	377,530.00	443,596.00
7	Repairs and maintenance	46,895,323.03	49,738,583.39
8	Excise Duty	0.00	0.00
9	Rent (Lease Rent), Rates and Taxes	1,405,777.00	1,405,777.00
10	Vechicles Running and Maintenance	137,090.00	94,287.00
11	Postage, Telephone and Communication Charges	488,506.00	644,650.00
12	Printing and Stationary	1,379,395.00	1,732,733.00
13	Travelling and Conveyance Expenses	6,325,034.47	5,871,140.61
14	Expenses on Seminar/Workshops	1,099,275.00	1,177,531.00
15	Subscription Expenses	2,825,204.40	2,225,055.82
16	Expenses on Fees	0.00	0.00
17	Auditor Remuneraion	24,000.00	24,000.00
18	Hospitality Expenses	202,323.00	318,176.00
19	Professional Charges	1,163,000.00	1,354,118.00
20	Provision for bad and Doubtful Debts/Advances	0.00	0.00
21	Irrecoverable Balances Written-off	0.00	0.00
22	Packing Charges	0.00	0.00
23	Freight and Forwarding Expenses	0.00	0.00
24	Distribution Expenses	0.00	0.00
25	Advertisement and Publicity	923,791.00	2,082,547.32
26	Foreign Exchange Fluctuation Loss/Gain	0.00	-8,840.52
27	Prior Period Expenses	0.00	7,599,724.96
28	Others - Bank charges	7,612.00	5,834.80
	- Misc. expenses	426,790.00	229,161.00
	- Books and Periodicals	126,858.00	112,217.00
	- Honorarium (others)	406,500.00	315,112.00
	- Petrol, Diesel & CNG etc.	705,879.00	717,443.00
	- Manpower	8,177,283.00	12,767,226.00
	- Horticulture	3,491,410.00	3,627,188.00
	- Training and networking expense	37,243,448.00	30,659,449.00
	- Laboratory & Animal Consumables	19,240,755.50	27,159,765.84
	Total	**169,376,010.40**	**189,055,416.22**

SCHEDULE 22 -EXPENDITURE ON GRANTS, SUBSIDIES ETC. **NIL**

SCHEDULE 23 -INTEREST PAID **NIL**

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As per our separate report of even date attached
For Maheshwari PA & Associates
Chartered Accountants
(FRN-012023C)

ABHISHEK GOEL
PARTNER
Membership No. 412467
Date: 11.09.2020
Meerut

SIGNIFICANT ACCOUNTING POLICIES & NOTES ON ACCOUNTS FORMING PART OF THE BALANCE SHEET AS AT 31ST MARCH, 2020 AND INCOME & EXPENDITURE ACCOUNT FOR THE YEAR ENDED 31STMARCH, 2020

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. Fixed Assets:

3.1 Fixed Assets are stated at historical cost. 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 Fixed 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 Fixed Assets have been created mainly out of grants received from the Department of Biotechnology, Ministry of Science and Technology, Government of India.

3.5 Capital WIP(Building) has been transferred to Building A/c amounting to Rs. 66,97,30,848.73 after its completion.

4. Depreciation:

4.1 Depreciation provided for current year on the fixed assets of Project for Rs. 4,84,40,074.00 (previous year Rs. 5,20,62,017.00) 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. 9,92,57,469.55 for current financial year (Rs. 3,24,46,934.00 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

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 only a few employees are under CPF(as they had joined NBRC before 01st January, 2004). The employee joined New Pension Scheme(NPS).

9.2 The NBRC has not made any provision for gratuity and leave encashment during financial year 2019-2020 as against the requirement of AS-15 issued by ICAI. However, the amount of gratuity and leave encashment to the extent of Rs. 61,37,980.00 and Rs. 19,19,570.80 respectively already exists on 31st March, 2020, (Rs. 61,37,980.00 and Rs. 29,70,321.80 respectively as on 31st March, 2019) 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.

12. Bank Balance:

All Banks accounts have been reconciled till 31st March, 2020.

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, 2020, 28 Projects have already closed which amount of Rs. 83.72 Lakh (Debit Balance) is still pending and 24 Projects closed which amount of Rs. 1.76 Cr is 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. 54,12,350.00 (Previous year Rs. 51,62,410.00) which is under representation before the concerned authorities. Further, TDS deducted and to be received as refund amounts to Rs. 46,25,231.80 out of which Rs. 40,30,217.52 is pending since 2008-09. The appeal has already been made to Income tax Authority(ITAT).

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).

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. 12,00,619.40

20.2 Expenditure in foreign currency:

a) Travelling charges Rs. 24,86,318.47

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. 24,000.00 (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. 11,83,854.00 (previous year Rs. 8,01,636.00).

22.2 Schedules 1 to 24 along with Annexures 1 to 59 are annexed to and form an integral part of the Balance Sheet as at 31st March, 2019 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.

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. 2,44,64,444.46 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. 2,99,76,350.00 against which appeals to CIT- Chandigarh has already been filed.

As per our separate report
of even date attached

OM PRAKASH NAGAR	**PROF. NEERAJ JAIN**	**For Maheshwari P A &Associates**
(INCHARGE OFFICER OFFICER)	**(DIRECTOR)**	**(Chartered Accountants)**
		(FRN-012023C)

(CA Abhishek Goel)
PARTNER
M.NO. 412467

Place: New Delhi
Date: 11th September, 2020

NATIONAL BRAIN RESEARCH CENTRE, NH-8, NAINWAL MORE, MANESAR GURGAON
ANNEXURE OF PROJECT GRANTS AND EXPENDITURE FOR THE YEAR ENDED 31.03.2020

S. No./ Annx. No.	NAME OF PROJECT	Opening Balance as on 01.04.2019	Grants received during the year 2019-20	Interest earned during the year 2019-20	Capital Exp. during the year 2019-20	Revenue Expenditure during the year 2019-20			Refund of Unspent Balance	Closing Balance as on 31.03.2020
						Manpower	Others	Total Expenditure		
2	Wellcom Trust/DBT Indian Alliance -Dr. Anindya Ghosh Roy	-505,371.00	4,890,569.00	0.00	467,650.00	165,903.00	1,410,209.52	1,576,112.52	0.00	2,341,435.48
3	CSIR Japanese Enccephalities - Dr. Anirban Basu	2,118,124.00	0.00	8,561.00	1,565,016.00	0.00	647,779.00	647,779.00	0.00	-86,110.00
4	InRNAs-Dr Basu	1,420,000.00	0.00	24,422.00	0.00	0.00	646,416.00	646,416.00	0.00	798,006.00
5	MicroRNA mediated Reg. of Neural stem(Dr. Anirban Basu)	-344,428.21	3,433,300.00	18,813.00	0.00	0.00	1,524,868.17	1,524,868.17	0.00	1,582,816.62
6	Tata innovation fellowship award- Dr. Anirban Basu	-82,188.53	894,000.00	8,079.00	0.00	0.00	536,408.00	536,408.00	0.00	283,482.47
7	Therapeutic Role DBT(Dr. Anirban Basu)	-22,642.35	841,133.00	5,740.00	0.00	0.00	807,081.69	807,081.69	0.00	17,148.96
8	Multifaceted Kinase CDK5 - Dr. Aparna Dixit	-354,315.93	353,092.00	0.00	0.00	0.00	0.00	0.00	0.00	-1,223.93
9	Mapping of Common Mental Disorders Over Lifespan- Dr Arpan Banerjee	0.00	26,735,200.00	0.00	0.00	0.00	578,750.00	578,750.00	0.00	26,156,450.00
10	Early Dignostics of structural and functional- Dr Arpan Banerjee	4,000,000.00	0.00	76,663.00	0.00	367,548.00	592,576.00	960,124.00	0.00	3,116,539.00
11	Dementia Tissue MRI studies(Dr. Dipanjan Roy)	1,754,801.00	0.00	35,096.00	0.00	0.00	0.00	0.00	0.00	1,789,897.00
12	Oscillatory network dynamics DST(Dr. Dipanjan Roy)	303,332.00	1,000,000.00	6,124.00	0.00	436,309.00	181,937.00	618,246.00	0.00	691,210.00
13	Ramalinga Swamy - Dr. Dipanjan Roy	166,043.26	757,084.00	6,675.00	0.00	0.00	38,550.00	38,550.00	0.00	891,252.26
14	Chromatin Remodelers in regulating associated - Dr. Ellora sen	-2,562.16	0.00	2,562.16	0.00	0.00	0.00	0.00	0.00	0.00
15	Implications in tumor progression- Dr. Ellora Sen	1,509,663.49	1,641,000.00	28,979.00	0.00	409,047.00	1,316,371.00	1,725,418.00	0.00	1,454,224.49
16	National Bioscience Award- Dr. Ellora Sen	60,153.29	0.00	0.00	0.00	0.00	33,750.00	33,750.00	0.00	26,403.29
17	Neurobiology of Dyslexia Brain & Behavior-Dr. Nandini C.Singh	1,892,135.00	0.00	0.00	0.00	0.00	1,277,167.00	1,277,167.00	0.00	614,968.00
18	Fetal neural stem cells to oligodendrocytes (Dr. Pankaj seth)	-378,532.00	791,000.00	2,638.00	0.00	0.00	220,730.00	220,730.00	0.00	194,376.00
19	Dyslexia Linked RNA(Dr. Pankaj Seth)	1,852,154.38	1,200,000.00	11,577.00	0.00	84,000.00	1,833,681.33	1,917,681.33	23,525.00	1,122,525.05
20	Effect of Hypoxia on different Neural-Dr Pankaj Seth	1,097,101.30	0.00	53,501.00	0.00	413,750.00	61,670.00	475,420.00	0.00	675,182.30
21	Hypoxia Ind. Change in Blood Brain- Dr Pankaj Seth	419,050.00	700,616.00	19,256.00	0.00	0.00	59,912.00	59,912.00	0.00	1,079,010.00

NATIONAL BRAIN RESEARCH CENTRE, NH-8, NAINWAL MORE, MANESAR GURGAON
ANNEXURE OF PROJECT GRANTS AND EXPENDITURE FOR THE YEAR ENDED 31.03.2020

S. No./ Annx. No.	NAME OF PROJECT	Opening Balance as on 01.04.2019	Grants received during the year 2019-20	Interest earned during the year 2019-20	Capital Exp. during the year 2019-20	Revenue Expenditure during the year 2019-20			Refund of Unspent Balance	Closing Balance as on 31.03.2020
22	A CROSS-CULTURE PERSPECTIVE(DBT-NETHERLANDS) -Dr. PRAVAT MANDAL	276,126.00	795,000.00	10,884.00	0.00	424,158.00	172,221.00	596,379.00	0.00	485,631.00
23	Characterizing biomarkers of Alzheimer's disease Dr. Pravat Mandal	95,042.50	0.00	0.00	0.00	93,214.00	0.00	93,214.00	0.00	1,828.50
24	National Programme on Preception Engineering - Phase II- Dr. Pravat Kumar Mandal	21,884.00	0.00	0.00	0.00	0.00	0.00	0.00	21,884.00	0.00
25	Dementia Imaging studies(Dr. Pravat Kumar Mandal)	1,754,801.00	0.00	35,096.00	0.00			0.00	0.00	1,789,897.00
26	Novel Imaging Dignostics Indo-Aus grant(Dr. Pravat Kumar Mandal)	5,199,360.00	2,237,252.00	94,195.00	0.00	2,505,698.00	1,021,049.00	3,526,747.00	0.00	4,004,060.00
27	SPECIFIC BRAIN TEMPLATE DST Dr. PRAVAT K MANDAL	22,864.50	500,000.00	0.00	0.00	482,080.00	227,895.00	709,975.00	0.00	-187,110.50
28	Tata innovation fellowship Award - Dr. Pravat Mandal	74,770.00	880,000.00	3,250.00	0.00	0.00	934,982.00	934,982.00	0.00	23,038.00
29	S&S LEARNING IN ZEBRA FINCHES Dr.SOUMYA IYENGAR	438,262.00	0.00	0.00	0.00	189,081.00	189,895.00	378,976.00	59,286.00	0.00
30	Crspri System - Dr. Sourav Banarjee	61,948.68	0.00	27,648.00	0.00	61,296.00	754,084.00	815,380.00	0.00	-725,783.32
31	DBT Mirna Meditate Control - Dr. Sourav Banarjee	515,566.97	0.00	16,517.00	0.00	0.00	343,074.00	343,074.00	0.00	189,009.97
32	Mechanism of Combinational Control- Dr Sourav	2,404,000.00	0.00	46,367.00	0.00	117,935.00	349,329.00	467,264.00	0.00	1,983,103.00
33	Innovation In Science Pursuit For Inspired Research(INSPIRE)- Dr. Yogita	-814,005.82	1,425,490.00	0.00	0.00	0.00	254,992.00	254,992.00	0.00	356,492.18
34	Influence of social cues omapatial cognition - Dr. Chetan Yadav	-4,873.00	78,423.00	0.00	0.00	0.00	73,550.00	73,550.00	0.00	0.00
35	DST-CSRI (Dr. Prem Chand)	-284,034.57	800,000.00	0.00	0.00	0.00	487,049.27	487,049.27	0.00	28,916.16
36	Centre for Excellence for Epilepsy(Phase-II)	74,588,380.00	3,296,876.00	2,088,331.00	3,719,004.00	6,523,172.00	20,079,990.00	26,603,162.00	0.00	49,651,421.00
37	Dementia Meeting	1,977,619.00	0.00	589,458.00	0.00	0.00	0.00	0.00	0.00	2,567,077.00
38	Dementia Science Programme	32,759,500.00	0.00	345,338.00	18,018,040.68	1,034,678.00	1,903,098.00	2,937,776.00	0.00	12,149,021.32
39	Dementia Basic Biology(Dr. Shiv Kumar Sharma)	5,244,894.00	0.00	85,885.00	448,638.50	0.00	464,000.00	464,000.00	0.00	4,418,140.50
40	Distributed Information Centre	2,609,376.33	1,548,700.00	21,727.00	335,998.00	2,736,747.00	264,445.00	3,001,192.00	0.00	842,613.33
41	Epilepsy Project of NBRC	5,394,883.30	0.00	0.00	0.00	12,816.00	0.00	12,816.00	0.00	5,382,067.30
42	PDF-SERB-Dr Sandeep Kumar	208,114.00	910,000.00	0.00	0.00	0.00	914,099.00	914,099.00	0.00	204,015.00
43	PDF-SERB(Soibam Shyamchand)	352,399.00	0.00	0.00	0.00	0.00	410,871.00	410,871.00	0.00	-58,472.00

NATIONAL BRAIN RESEARCH CENTRE, NH-8, NAINWAL MORE, MANESAR GURGAON
ANNEXURE OF PROJECT GRANTS AND EXPENDITURE FOR THE YEAR ENDED 31.03.2020

S. No./ Annx. No.	NAME OF PROJECT	Opening Balance as on 01.04.2019	Grants received during the year 2019-20	Interest earned during the year 2019-20	Capital Exp. during the year 2019-20	Revenue Expenditure during the year 2019-20			Refund of Unspent Balance	Closing Balance as on 31.03.2020
44	Mechanisms Of Adult Brain Reorganisation- Dr. Neeraj Jain	1,257,677.22	0.00	22,433.78	0.00	133,548.00	247,769.00	381,317.00	898,794.00	0.00
45	DST- Inspired Fellow (Sriparna Mukherjee)	60,288.00	37,140.00	0.00	0.00	93,140.00	0.00	93,140.00	0.00	4,288.00
46	TWAS-DBT (Saliu Ibrahim)	20,722.00	0.00	0.00	0.00	9,677.00	0.00	9,677.00	0.00	11,045.00
47	Workshop & Conference(NBRC)	-462,285.78	9,828,411.20	2,500.00	0.00	0.00	10,665,449.00	10,665,449.00	0.00	-1,296,823.58
48	IBRO RETURNED HOME START-UP GRANT-DR BHAVANI SHANKAR SAHU	0.00	773,173.00	0.00	0.00	0.00	0.00	0.00	0.00	773,173.00
49	UNDERSTANDING THE REGULATED SECRETORY PATHWAY AND ITS ROLE REGUATING PHYSIO-METABOLIC FUNCTION- Dr BHAVANI SHANKAR SAHU	0.00	2,156,297.00	0.00	0.00	0.00	526,404.00	526,404.00	0.00	1,629,893.00
50	ROLE OF EPHRINS/EPH RECEPTORS IN HIV MEDIATED NEUROPATHOGENSIS- DR PANKAJ SETH	0.00	3,572,000.00	43,424.00	0.00	0.00	1,479,480.10	1,479,480.10	0.00	2,135,943.90
51	ARTIFICIAL INTELLIGENCE - DR PRAVAT K. MANDAL	0.00	3,106,800.00	0.00	0.00	309,990.00	237,630.00	547,620.00	0.00	2,559,180.00
52	THE SENSITIVE PERIOD OF THE HUMAN AUDITORY CORTEX A NEUROANATOMICAL STUDY- DR SOUMYA IYENGAR	0.00	1,247,760.00	11,977.00	0.00	0.00	112,342.00	112,342.00	0.00	1,147,395.00
53	CRISPR-CAS13- DR SOURAV BANERJEE	0.00	3,581,520.00	0.00	0.00	0.00	0.00	0.00	0.00	3,581,520.00
54	EEG CORRELATES OF INSIGHT AND ITS FACILITATING THROUGH EMOTIONAL PRIMING- DR SHUBHAM KUMAR	0.00	946,000.00	0.00	0.00	0.00	287,253.00	287,253.00	0.00	658,747.00
55	INSPIRE FACULTY FELLOWSHIP (DST)- DR SWAGATA DEY	0.00	2,200,000.00	0.00	0.00	0.00	1,579,412.00	1,579,412.00	620,588.00	0.00
56	WELLCOME TRUST/DBT INDIA ALLIANCE FELLOW- DR SWAGATA DEY	0.00	1,333,514.00	9,096.00	0.00	0.00	294,029.00	294,029.00	0.00	1,048,581.00
57	WELLCOME TRUST/DBT INDIA ALLIANCE FELLOW- DR NIVETHIDA T.	0.00	2,158,769.00	0.00	0.00	0.00	0.00	0.00	0.00	2,158,769.00
58	DBT-TWAS FELLOWSHIP- DR ASHRAFUL HASSAN	0.00	549,680.00	0.00	0.00	0.00	161,438.00	161,438.00	0.00	388,242.00
59	BBNSC - Dr. Rema	1,809,628.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1,809,628.00
60	BBNSC - Dr. Shyamala	-392,947.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-392,947.00
61	COGNITIVE NEUROSCIENCE DBT-PROJECT- (Dr. Aditya)	-437,464.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-437,464.00

NATIONAL BRAIN RESEARCH CENTRE, NH-8, NAINWAL MORE, MANESAR GURGAON
ANNEXURE OF PROJECT GRANTS AND EXPENDITURE FOR THE YEAR ENDED 31.03.2020

S. No./ Annx. No.	NAME OF PROJECT	Opening Balance as on 01.04.2019	Grants received during the year 2019-20	Interest earned during the year 2019-20	Capital Exp. during the year 2019-20	Revenue Expenditure during the year 2019-20			Refund of Unspent Balance	Closing Balance as on 31.03.2020
62	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
63	Chandipura Virus Infection - Dr. Anirban Basu	-22,580.53	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-22,580.53
64	CSIR -II Study the Role of Neural Immune Respnce - Dr. Anirban Basu	-168,365.93	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-168,365.93
65	DBT National Bioscience Award 2010 - Dr. Anirban Basu	585.65	0.00	0.00	0.00	0.00	0.00	0.00	0.00	585.65
66	Study of Mole. Mechanism - Dr. Anirban Basu	-68,830.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-68,830.00
67	Neuro -Cognitive Networks Underlying Dr. Arpan Banerjee	18,438.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	18,438.00
68	Vision Guide Speech Percention- Dr. Arpan Banerjee	585,272.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	585,272.00
69	DST Inspired Faculty Award- Dr. Deepashri	1,900,000.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1,900,000.00
70	BBNSC - Dr. Ellora	-403,419.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-403,419.00
71	Understanding the Signaling Circuities - Dr. Ellora Sen	-575,915.39	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-575,915.39
72	DST Austism Spectrum Disorder - Dr. Nandini C. Singh	82,849.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	82,849.00
73	Autism Behavior and Diffusion Tensor Imaging - Dr. Nandini C. Singh	60,474.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	60,474.00
74	Comp. Analysis of Speech Imp. - Dr. Nandini C. Singh	-547,567.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-547,567.00
75	CSI Development and Validation of Screening Tools -Dr. Nandini C Singh	-303,509.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-303,509.00
76	DBT ITPAR Grant-Dr.Nandini C. Singh	556,234.89	0.00	0.00	0.00	0.00	0.00	0.00	0.00	556,234.89
77	Multi Displinary System of Parkinson Disease - Dr. Nandini C. Singh	1,189,000.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1,189,000.00
78	CSIR -Project Dr. Nihar Ranjan Jana	73,089.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	73,089.50
79	animal models of Huntington's disease Dr. Nihar Ranjan Jana	-2,999.59	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-2,999.59
80	Tata Innovation Fellowship- Dr. Nihar Ranjan Jana	309,758.91	0.00	0.00	0.00	0.00	0.00	0.00	0.00	309,758.91
81	Cellular & Mole. Basis - Dr. Pankaj Seth	-34,974.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-34,974.00
82	INDO-US & NIH RO1 - Dr. Pankaj Seth	-631,828.42	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-631,828.42
83	National Initiative On Glia Cell Research Project - Dr. Pankaj Seth	92,588.71	0.00	0.00	0.00	0.00	0.00	0.00	0.00	92,588.71

NATIONAL BRAIN RESEARCH CENTRE, NH-8, NAINWAL MORE, MANESAR GURGAON
ANNEXURE OF PROJECT GRANTS AND EXPENDITURE FOR THE YEAR ENDED 31.03.2020

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84	DBT BIRAC Under CRS Scheme Project Grant - Dr. Ranjit Kr. Giri	56,991.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	56,991.50
85	Ramalinga Swamy - Dr. Ranjit Kr. Giri	-68,440.70	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-68,440.70
86	Women Scientist Scheme DST -Dr. Sayali Ranade	-131,556.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-131,556.00
87	National Institute Glial Cell Research - Shiv Kumar Sharma	-84,803.61	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-84,803.61
88	Motivated Behaviour in Male Zebra Finches - Dr. Soumya Iyengar	73,194.65	0.00	0.00	0.00	0.00	0.00	0.00	0.00	73,194.65
89	DST Inspire Faculty Award -Dr. Supriya Bhavani	-12,189.65	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-12,189.65
90	IYBA DBT 2013- Dr. Supriya Bhavanani	49,737.51	0.00	0.00	0.00	0.00	0.00	0.00	0.00	49,737.51
91	Neural Network Mechanism - Dr. Yoganarashimha	-1,070,838.61	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-1,070,838.61
92	A critical assessment of the dual stream models of visual information processing- DST - Dr. Dipanjan Ray	220.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	220.00
93	EBM Including Alzheimer Disease - Dr. Vijaylaxmi Ravindranath	-230,717.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-230,717.00
94	DST Cognitive Science Research Initiative (CSI) - Dr. Chaitra Rao	-324,000.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-324,000.00
95	Spinal Cord Plasticity ILTP - Dr. Neeraj Jain	-31,869.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-31,869.00
96	Multifactorial Risk Factor - Prof. V. Ravindranath	-29,346.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-29,346.00
97	Est. of Translational Res. Unit - Prof. P.K. Roy	4,307,442.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	4,307,442.00
98	Func. Magnetic Resonance Imaging - Prof. V. Ravindranath	-355,435.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-355,435.00
99	DBT INCRE Grant (NBRC)	1,799,153.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1,799,153.00
100	Programme of Co-Operation Between India and Syria Project	3,558,649.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3,558,649.00
101	Material Malnutrition - Dr. Shyamala	-579,048.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-579,048.00
102	Mole. Role of Transc. Factors - Dr. Prabodha Kumar Swain	-644,021.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-644,021.00
103	PDF-SERB(AMIT NASKAR)	-128,935.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-128,935.00
104	PDF-SERB(Ashok Datusalia)	45,920.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	45,920.00
105	PDF-SERB(POONAM MEENA)	-149,358.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-149,358.00

NATIONAL BRAIN RESEARCH CENTRE, NH-8, NAINWAL MORE, MANESAR GURGAON
ANNEXURE OF PROJECT GRANTS AND EXPENDITURE FOR THE YEAR ENDED 31.03.2020

S. No./ Annx. No.	NAME OF PROJECT	Opening Balance as on 01.04.2019	Grants received during the year 2019-20	Interest earned during the year 2019-20	Capital Exp. during the year 2019-20	Revenue Expenditure during the year 2019-20			Refund of Unspent Balance	Closing Balance as on 31.03.2020
106	BBNSC - Dr. Neeraj	296,937.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	296,937.00
107	Collaboration for Trans. & Clin. Res. (GLUE) - Prof. P.K. Roy	-344,006.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-344,006.00
108	DBT Tata Innovation Fellowship -Dr P.K.Roy	667,424.60	0.00	0.00	0.00	0.00	0.00	0.00	0.00	667,424.60
109	DIT McGILL Linkage (NKN) - Prof. Prasum Kumar Roy	-596,926.84	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-596,926.84
110	J.C.Bose Fellowship(PROF. SUBRTA SINHA	0.58	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.58
	Total (A)	157,864,038.10	87,199,799.20	3,762,812.94	24,554,347.18	16,603,787.00	56,203,686.08	72,807,473.08	1,624,077.00	149,840,752.98
1	DELCON E-LIBRARY CONSORTIUM (B)*	437,201,571.36	580,959,268.00	6,233,937.00	109,142.00	911,231.00	623,798,159.37	624,709,390.37	0.00	399,576,243.99
	Grand Total (A+B)	**595,065,609.46**	**668,159,067.20**	**9,996,749.94**	**24,663,489.18**	**17,515,018.00**	**680,001,845.45**	**697,516,863.45**	**1,624,077.00**	**549,416,996.97**

Note:- Projects from Sl. No 59 to 110 are closed and non operational.

O.P Nagar
INCHARGE FINANCE OFFICER
NBRC

PROF. Neeraj Jain
DIRECTOR
NBRC

As per our separate report
of even date attached

For MAHESHWARI PA & ASSOCIATES
Chartered Accountants
(FRN-012023C)

ABHISEK GOYAL
PARTNER
Membership No. 412467

Date:
New Delhi

Compiled and Edited by

Anindya Ghosh Roy and Kedar Singh Bajetha

1. **Front Cover:** A part of the correlation matrix showing ROI-ROI resting-state functional connectivity between different regions of interest (ROI's) in the brains of macaque monkeys and humans. Each colour coded value denotes averaged Fisher-z transformed correlations (CCz) for different ROI pairs. This functional magnetic resonance imaging (fMRI) study was done to determine resting-state connectivity of the somatosensory cortex at higher resolution, and to compare brain organisation and information flow in the brains of monkeys and humans. For the complete figure and full description visit https://www.biorxiv.org/content/10.1101/775569v2

   Graph: John Thomas and Neeraj Jain;

   Design: Shiladitya Laskar

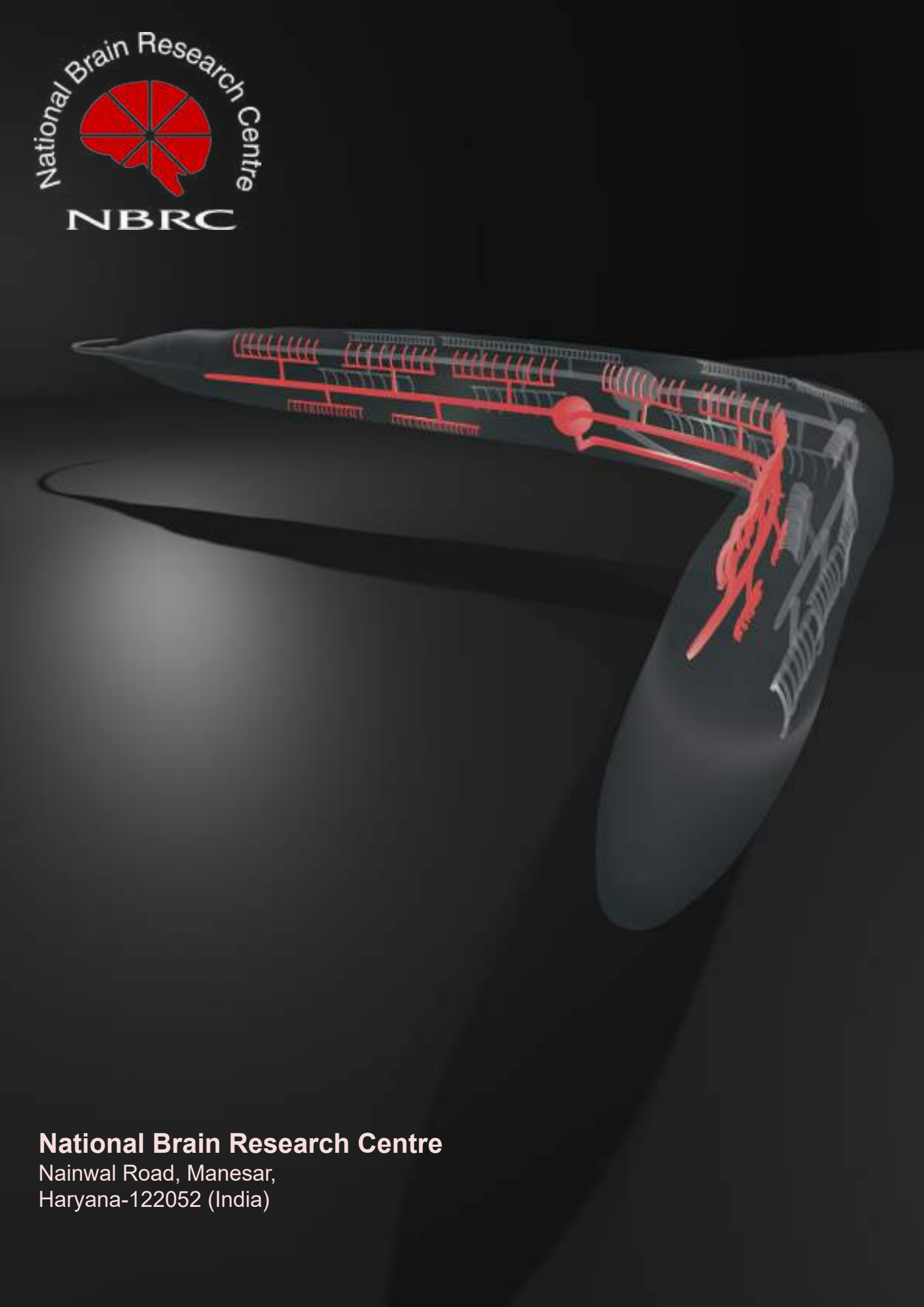
2. **Back Cover:** The spatial spread of a pair of mechanosensory neurons (PVD) across the nematode *C. elegans* body is rendered using an open-source 3D creation suite 'Blender'.

   Shiladitya Laskar and Anindya Ghosh Roy

3. **Images in the separator pages:** Sourav Banerjee and Sibaram Behera

National Brain Research Centre

NBRC



National Brain Research Centre
Nainwal Road, Manesar,
Haryana-122052 (India)