National BRAIN RESEARCH Centre

Manesar, Haryana (India)

Annual Report 2017-18

National Brain Research Centre

Annual Report
2017-18

Contents

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.

Director's Desk

Prof. Neeraj Jain

NBRC was established with a mandate to understand brain function in health and disease, and to train manpower for advanced neuroscience research. It is with great pleasure I present this annual report for the years 2017-18, which reiterates that NBRC scientists and staff have been steadfastly working to fulfil this mandate while continuously setting higher goals for themselves. NBRC scientists have made several discoveries during last year using multidisciplinary approaches and various model systems, buttressed by intra-institutional and inter-institutional collaborations.

Research that directly benefits society is a major component of work at NBRC. Japanese Encephalitis Viral (JEV) infection, which is endemic in parts of India has high mortality. Basic research at NBRC on mice, which was followed by a clinical trial has shown that Minocycline, a drug of tetracycline family approved for other diseases, provides benefit in management of JEV. Following deaths of infants in a hospital at Gorakhpur, ICMR and Department of Health Research announced last year that minocycline may be used for an observational study in infants with acute encephalitis. Further research on JEV has shown that knockdown of HSP60 leads to decreased IL-1ß production during JEV infection, which eventually leads to decreased inflammation and increased survival of JEV-infected mice. This study helps understand complex signaling mechanisms involved in neuro-inflammation, and also suggests HSP60 as a potential therapeutic target for the amelioration of various neuro-inflammatory and neurodegenerative diseases.

Glutathione (GSH) is a major antioxidant in the brain. Research at NBRC has discovered that GSH can exist in extended and closed conformations using MR spectroscopy. Results show that closed form of GSH is reduced significantly in the hippocampal regions when a healthy person develops mild cognitive impairment (MCI). Thus, GSH can be used as an early diagnostic biomarker for Alzheimer's disease. Work also continues on building an Indian Brain Template for MRI studies, for which a new MATLAB based software package called 'BRAMHA' has been developed.

A fundamental problem of cognitive neuroscience is understanding processes that sculpt functional correlations in the brain despite a relatively fixed anatomical connectivity matrix. This has been addressed using machine learning approach. This new method has been used for making prediction of subject-specific functional connectivity with high accuracy. Further, understanding of latent variables and parameters using these methods helped characterize age-specific developmental reorganization in the brain structure and function.

Brain connectivity analysis has provided crucial insights into developmental differences between autistic and typically developing children. Work at NBRC using Autism Brain Imaging Data Exchange (ABIDE) data set, which is divided into two cohorts - children (9–12 years) and adolescents (13–16 years), has demonstrated how age, disease, and their interactions affect intrinsic connectivity of brains of children and adolescents in autism spectrum disorder (ASD). The results showed that ASD exhibits increased functional integration at the expense of decreased functional segregation. This study lends support to a model of global atypical connections and further identifies functional networks and areas that are independently affected by age, disease, and their interactions.

Resting-state functional magnetic resonance imaging (rs-fMRI) analysis of the brain network involved in sensorimotor processing shows that these are complex networks that are organized on the basis of functional and connectional framework of individual body parts. Interestingly, the network organization of non-human primates and humans shows great similarities permitting extension of observations, such those after spinal cord injuries, to the human conditions.

Basic studies remain an important component of the overall research program at NBRC. We believe that effective applied and translational research requires a solid foundation of basic research, including in animal and cell culture model systems. Work on learning and memory shows that activation of a signaling pathway leads to long-lasting activation of a kinase that critically regulates synaptic plasticity and memory. Further studies show that new RNA synthesis and new protein synthesis is required for long-lasting activation of the kinase, which may play important role in synaptic plasticity and memory. A novel non-proteolytic function of protein ubiquitination has been identified in hippocampal synapse maturation. Further, work has also shown that functional

Director's Desk

impairment of E3 ligase - Rnf2, a critical component of the three-enzyme cascade responsible for protein degradation, is linked to Angelman Syndrome.

Song birds are a valuable model to understand brain circuits involved in vocalization. Mechanisms involved in modulation of vocalization through the endogenous opioid system have been identified using the song bird - Zebra finch. Blocking opioid receptors in the avian basal ganglia region, Area X, led to changes in spectral and temporal features of individual syllables in songs that male birds use to court females. In addition, opioid receptor activation was seen to be necessary for motivation to vocalize.

Neurons align themselves in a specific polarity in the normal brain during development. Using in vivo imaging of microtubule dynamics in neurons of C. elegans, it was found that kinesin13 family microtubule depolymerizing enzyme KLP-7 helps establish proper orientations of microtubule cytoskeleton in axon and dendrites. Regulation of this protein is critical for establishment of neuronal polarity.

Work on glioblastoma, a particularly aggressive kind of brain tumor shows a previously unknown non-metabolic role of glycolytic enzyme Hexokinase 2 (HK2) as a transcriptional co-activator of redox regulatory gene, and a novel role of metabolic gene Isocitrate dehydrogenase (IDH1) in the regulation of genes associated with immune-surveillance.

During the year Prof Subrata Sinha superannuated on 28th December, 2017, after seven and a half years at the helm of NBRC. His leadership of NBRC is recognized. I also would like to acknowledge DBT generously supporting NBRC programmes, and members of all the statutory committees of NBRC, and other members of the wider Indian scientific community who have supported us throughout the year in various invaluable ways.

Prof Neeraj Jain
Director (Additional Charge)

Molecular & Cellular Neuroscience

Sourav Banerjee

Research Fellows
Balakumar Srinivasan
Sarbani Samaddar
Gourav Sharma
Tapasya Pal
Pushapa Kumari

Project Assistants
Utsav Mukherjee
Nandu Raj
Budhaditya Basu
Namrata Roy
Ananya Ghosh

Technical Assistant
D Narendar
Musadiq Hussain

Modulation of Homeostatic Synaptic Plasticity by Co-ordinated Control of Protein Synthesis and Degradation Linked to Microrna Silencing Complex

Synaptic scaling, a form of homeostatic plasticity, make compensatory changes in synaptic strength to reset the baseline level of firing rate following destabilization of network activity. The network activity is destabilized when neural circuits are engaged in hebbian form of plasticity mechanisms, such as long-term potentiation (LTP) and depression (LTD) that are thought to contribute in learning and information storage. Central neuron in culture has been shown to restore homeostatic set point of network activity from an offset induced by chronic pharmacological perturbation of excitability. The ability to make compensatory synaptic modifications to achieve homeostatic set point can occur globally in all synapses or a locally through a subset of synapses of a neuron. The global mechanism of homeostatic scaling occurs slowly over a period of 24 - 72 hours. Several studies have indicated that the activity-dependent change in intracellular calcium act as a "sensor" for detecting the offset from a threshold point of network activity. Prolonged activity manipulation adjusts the set point from offset by tuning synaptic expression of AMPA type glutametergic receptor that is emerging as a consensus endpoint "effector" in vitro and in vivo. Detailed proteomeic analysis revealed that homeostatic scaling did not alter the absolute number of distinct newly synthesized proteins, rather elicited targeted adjustment in protein synthesis from similar sets of transcripts involved in translational regulation depending on the sign of scaling. Reversible and modular changes in the proteome composition in post-synaptic density also occur through protein degradation mechanism upon global activity manipulation of hippocampal neuronal culture for a prolong period of ~48 hours. Prompted by these observations, we hypothesized that combinatorial control of protein synthesis and degradation could make adaptable changes at the synapse for maintenance of homeostatic synaptic balance.

Maintenance of homeostatic set point of synaptic activity by coordinated control of protein synthesis and degradation

We set out to study how co-ordinated control of protein synthesis and degradation can maintain homeostatic set point of synaptic activity using cultured hippocampal neuron as a model system. We have measured amplitude and frequency of miniature Excitatory Post Synaptic Current (mEPSC) using whole-cell patch clamp recording from cultured hippocampal neuron following inhibition of protein synthesis and proteasome activity either alone or in combination. We observed that inhibition of proteasome by lactacystion treatment (10 um for 24 hr) leads to significant increase in mEPSC amplitude (Figure 1). The observation is similar to inhibition of network activity by application of Tetrodotoxin (TTX) and block of NMDA receptor activity by AP5. In contrary, inhibition of protein synthesis by anisomycin treatment (40 um for 24 hr) leads to significant decrease in mEPSC amplitude (Figure 1). This observation mirror change in synaptic acitivity when network activity is elivated by bicucullin. However, co-application of both protein synthesis and proteasome inhibitors could able to restore the set point of network activity by adjusting mEPSC amplitude that is comparable to the untreated neurons (Figure 1).

Importantly, inhibition of protein synthesis or degradation either alone or in combination did not cause any change in mEPSC frequency. Our data indicates that impairment of either protein synthesis or degradation can push the basal network activity to

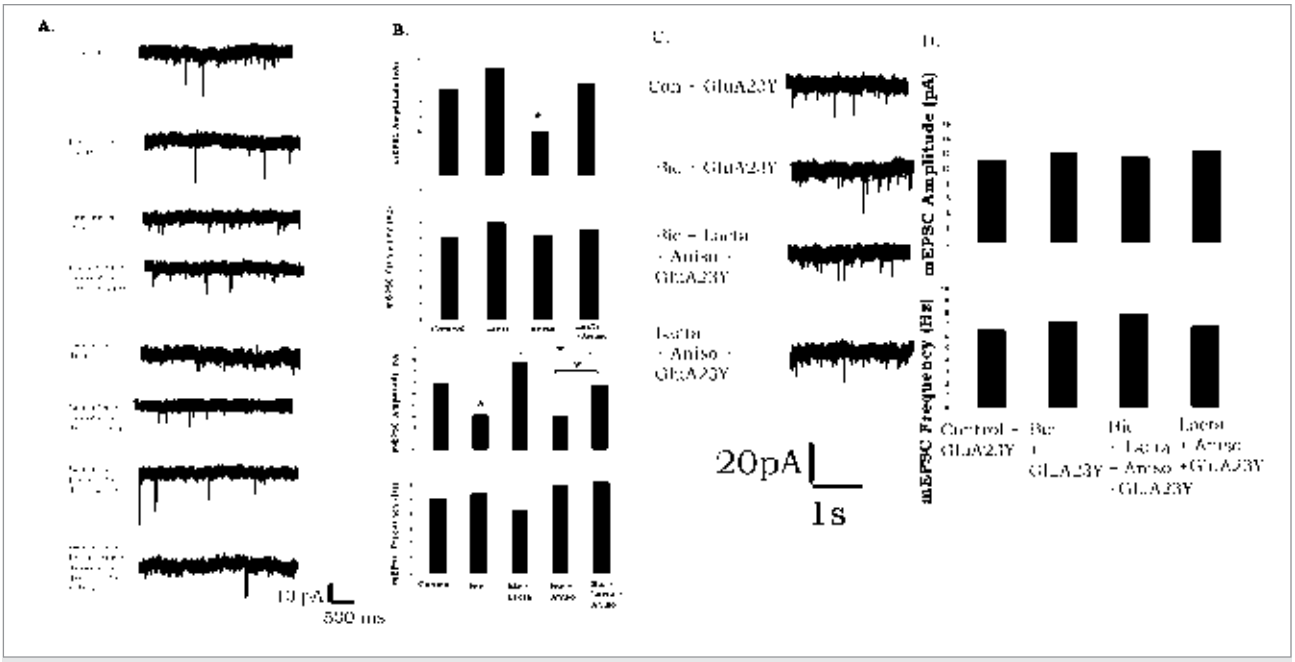


Figure 1: Combinatorial control of protein synthesis and degrdation maintains homeostatic synaptic balance. A) Traces from whole cell-patch clamp recording after manipulation of network activity. B) Ananlysis of mEPSC amplitude and frequency from whole-cell patch clamp recording after manipulation of network activity.

an offset from a set-point. The restoration of threshold level of network activity could be achieved by maintaining ensemble of essential plasticity-related protein complex through combinatorial control of protein synthesis and degradation. Our data indicates proteomic remodeling occurs at the post- synaptic compartment as we did not observe any change in frequency of mEPSC.

We then tested the combinatorial effect of protein synthesis and degradation in modulation of synaptic scaling when network activity is elevated following bicucullin treatment for 24 hours. Similar to previous observations, our whole-cell patch clamp recording from bicucullin treated hippocampal neuron showed significant decrease in mEPSC amplitude (Figure 1) without any alteration of its frequency, indicating down-scaling of network activity following synaptic activation. Consistent with our previous observation, we observed that the bicucullin-induced alteration of network activity was restored to set-point when neurons were co-incubated with proteasome inhinitor - lactacystin and protein synthesis inhibitor- anisomycin for 24 hours. However, block of protein synthesis or inhibition of proteasomal degradation alone could not adjust the set-point from an offset induced by bicucullin. These observations further confirm that neuronal network maintain homeostatic balance of synaptic strength through coordinated control of protein synthesis and degradation at the post-synaptic compartment.

Among two key glutametergic receptors, AMPA receptor expression at the synaptic surface emerging as a consensus end point effector for maintenance of homeostatic synaptic scaling. AMPA receptor function is reversibly regulated by dynamic insertion or removal of two critical subunits, namely GluA1 and GluA2. Trafficking of GluA2 but not GluA1 subunit of AMPA receptor has been shown to regulate synaptic scaling after TTX treatment of primary cortical neuronal culture as well as visual deprivation by TTX injection. we have delineated influence of GluA2 containing AMPA receptor in homeostatic synaptic scaling of cultured hippocampal neuron following bicucullin-induced activation of network activity. We have measured amplitude and frequency of mEPSC from bicucullin treated cultured hippocampal neuron after blocking endocytosis of GluA2 containing AMPA receptor using GluA23Y, a synthetic peptide derived from the GluA2 carboxy tail of AMPA receptor. We observed that bicucullin-induced downscaling of mEPSC amplitude is completely blocked after inhibition of GluA2 containing AMPA receptor endocytosis. However, GluA23Y peptide has no influence on mEPSC frequency confirming the scaling of network activity is a post-synaptic function involving selective insertion of GluA2 subunit of AMPA receptor. Furthermore, we did not observe any further increase or decrease of mEPSC amplitude when GluA23Y treated hippocampal neurons co-incubated with both lactacystin and anisomycin in presence or absence of bicucullin (Figure 1). These observations indicates that GluA23Y locks sufficient amount of GluA2 containing AMPA receptor at the synaptic surface to maintain the set-point of network activity that is modulated by combinatorial control of protein synthesis and degradation.

Cross-talk between protein synthesis and degradation machinery

Our whole-cell patch recording of basal neuronal activity point towards combinatorial control of protein synthesis and degradation

to maintain a threshold level of hippocampal network activity. These data prompted us to evaluate association between protein synthesis and degradation machineries. We have fractionated actively translating polysome from hippocampus on linear sucrose density gradients and assessed distribution of proteasome as well as components of ubiquitin-dependent protein degradation factors and translation regulators in polysome fractions. Our western blot analysis of polysome fractions obtained from hippocampus showed that overlapping distribution of 20S proteasome core and subunits of 19S proteasome cap - Rpt6, Rpt3 and Rpt1 with components of protein synthesis machineries, such as ribosomal protein S6, translation initiation factor eIF4E, translation initiation regulators; such as p70S6 kinase and phosphorylated p70S6 kinase (Figure 2). Apart from core proteasome machinery, we have also detected E3 ubiquitin ligases, such as Ube3A in actively translating polysome fractions (Figure 2).

depencent protein synthesis and proteasomal degradation for compositional changes of synaptic proteome and make adaptable changes at the synapses to maintain the set point of network activity.

Remodeling of microRNA containing silencing complex by coordinated control of protein synthesis and degradation

Co-ordination between protein synthesis and degradation has been implicated in fear memory formation in amygdala and thought to regulate synaptic activity through mechanisms associated with hebbian form of synaptic plasticity. Fear conditioning of mice increased polyubiquitination of MOV10 - a component of miRNA containing RNA inducing silencing complex (miRISC) involved in protein synthesis from subset of synapse-enriched mRNAs in amygdala. Importantly, this learning induced polyubiquitionation

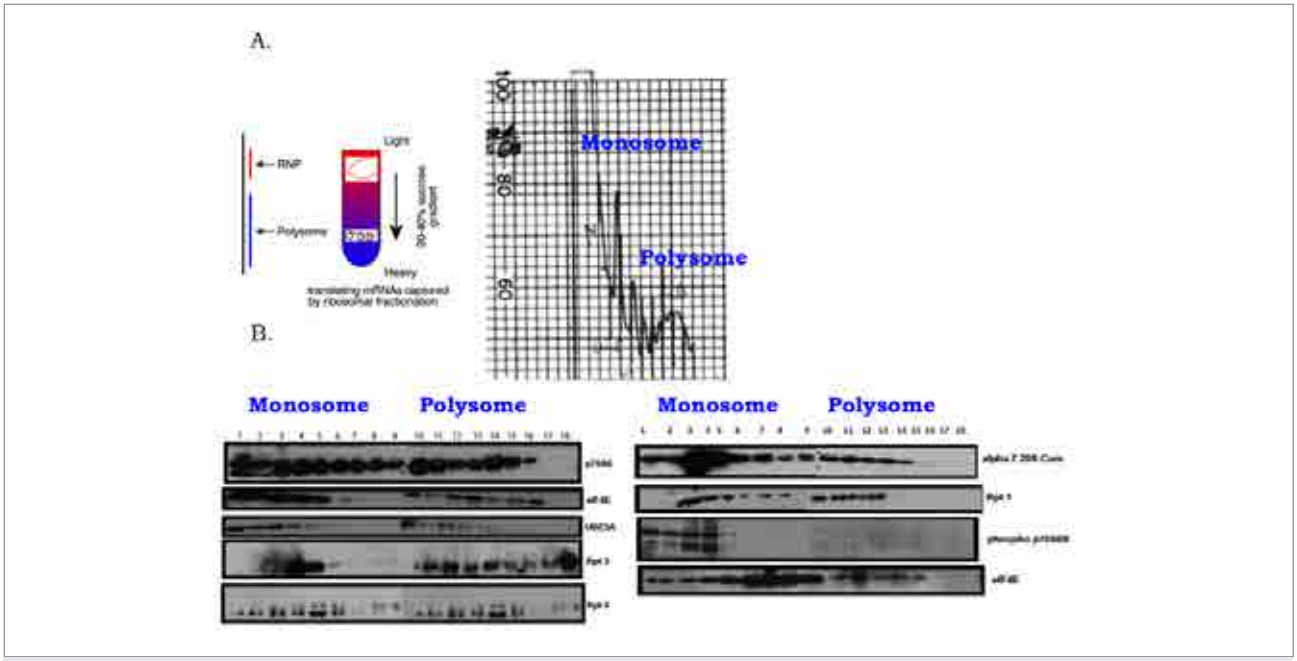


Figure 2: Association of protein synthesis and degradation machinaries. A) Absorbance (O.D. 254) spectra from sucrose density gradient fractionation. B) Western blot analysis of monosomal and polysomal fracrtions. Western blot shows overlapping distribution of factors influencing protein synthesis and subunits of proteasome as well as E3 ligase, Such as Ube3A.

These data indicate that core protein degradation machineries are associated with factors essential for translation regulation through direct interaction. To evaluate this possibility, we have immunoprecipitated proteasome using antibody specific for Rpt6 and analyzed association of protein synthesis regulators with proteasome. Western blot analysis of immunoprecipitated protein complex revealed that translation regulator, such as p70S6 kinase as well as its phosphorylated form directly interacts with proteasome (Figure 2). It is important to note that phosphorylation of p70S6 kinase has been shown to be a key factor influencing translation initiation via mammalian Target Of Rapamycin (mTOR) - dependent protein synthesis control. Taking together, these observations point toward a direct interaction between mTOR-

of MOV10 mirrors protein synthesis that is regulated by activation of mTOR as detected by increase in phosphorylation of immediate downstream target, p70S6 Kinase. mTOR-dependent localized translational control has also been linked to acute form of homeostatic signaling. Loss of excitatory synaptic input after blocking AMPA receptor function for 30 minutes triggers mTOR signaling in the post-synaptic neuron leading to dendritic synthesis of BDNF that retrogradely influence pre-synaptic release to adjust the synaptic strength. More recently, miR-92a has been shown to regulate dendritic synthesis of GluA1 in response to activity blockade by TTX and AP5 and regulate upscaling of synaptic strength. These observations prompted us to test miRISC remodeling via combinatorial control of protein synthesis

and degradation in response to bicucullin-induced synaptic downscaling.

To evaluate this hypothesis, we have analyzed components of miRISC following bicucullin treatment of hippocampal neuron for 24 hours. Of particular interest, we have focused on miRISC associated E3 ligase, Trim32 and MOV10. To confirm Trim32 is an integral component of miRISC in hippocampal neurons, we have immunoprecipitated MOV10 and observed that both Trim32 as well as Argonaute co-precipitated with MOV10. After confirming Trim32 is a core component of miRISC, we then analyzed remodeling of miRISC by assessing protein level of MOV10 and Trim32 following bicucullin treatment of hippocampal neurons for 24 hours. Our data showed that bicucullin-induced synaptic activation leads to synthesis of Trim32 with concomitant proteasomal degradation of MOV10 (Figure 3). To further confirm MOV10 degradation requires Trim32, we have transduced hippocampal neuron with shRNA against Trim32 to significantly reduce its protein level and tested amount of MOV10 by western blot analysis. Our western blot data showed that the loss of Trim32 could able to protect degradation of MOV10 (Figure 3). This observation clearly point toward remodeling of miRISC upon bicuculling-induced synaptic down scaling through combinatorial control of protein synthesis and degradation.

Taken together, our data demonstrates that synaptic down scaling is modulated by coordinated control of protein synthesis and degradation that regulates miRNA function to make compositional change of the synaptic proteome (Figure 4).

Future experiments are needed to test physiological implication of coordinated protein synthesis and degradation for synaptic homeostasis in vivo, such as during sleep and wake cycles. Emerging studies have shown that sleep is crucial for memory consolidation. Therfore, establishment of physiological relevance for homeostatic synaptic scaling through combinatorial control of protein synthesis and degradation is essential to understand cognitive function of brain, such as memory consolidation.

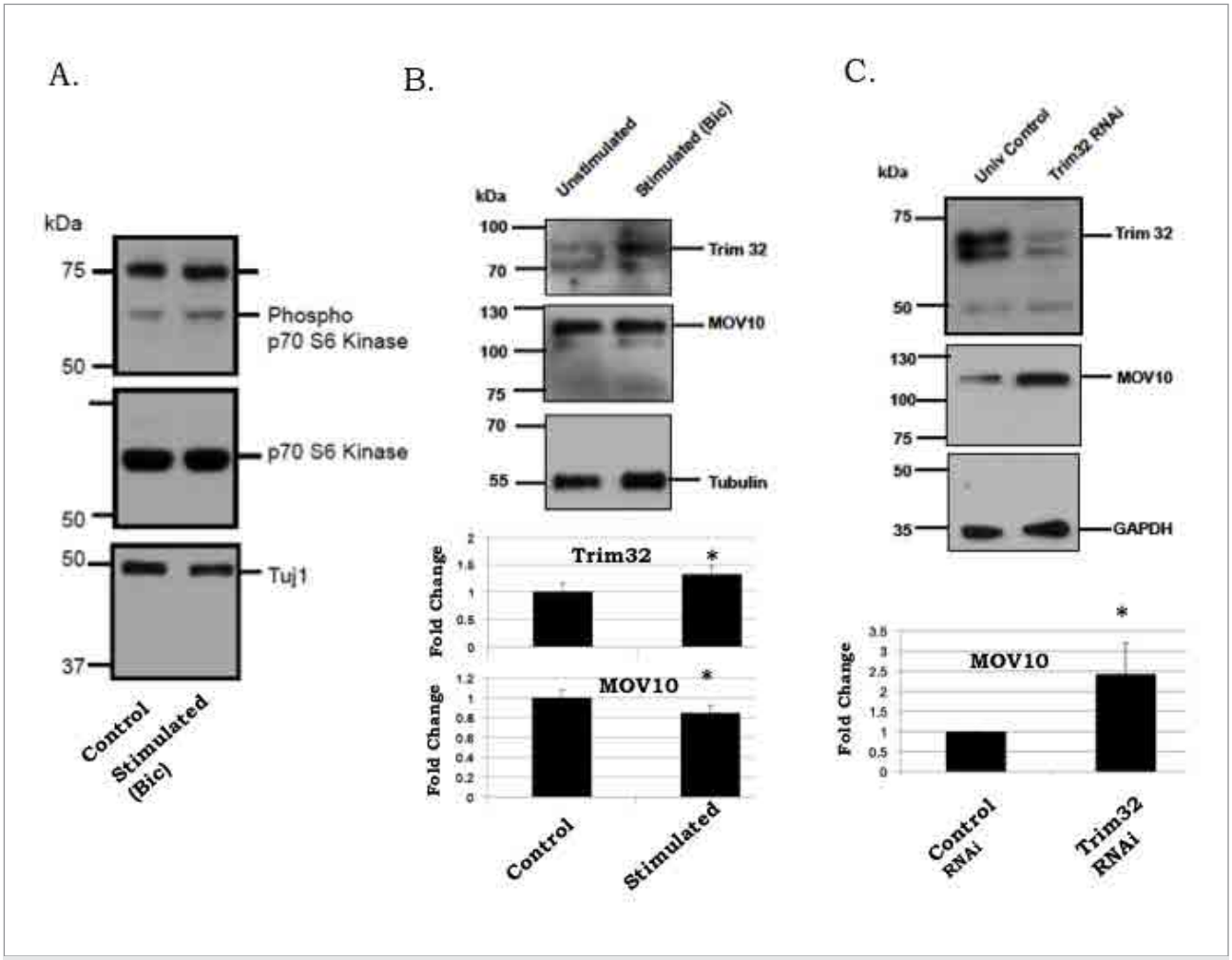


Figure 3: Remodeling of miRISC during synaptic down scaling. A) Bicucullin-induced synaptic down scaling trigger phosphorylation of p70S6 Kinase – a down stream target of mTOR. B) Bicucullin treatement of hippocampal neurons for 24 hours induce synthesis and degrdation of miRISC components Trim32 and MOV10 respectively. C) Loss of Trim32 function leads to enhancement of its target MOV10.p<0.05, t-test.

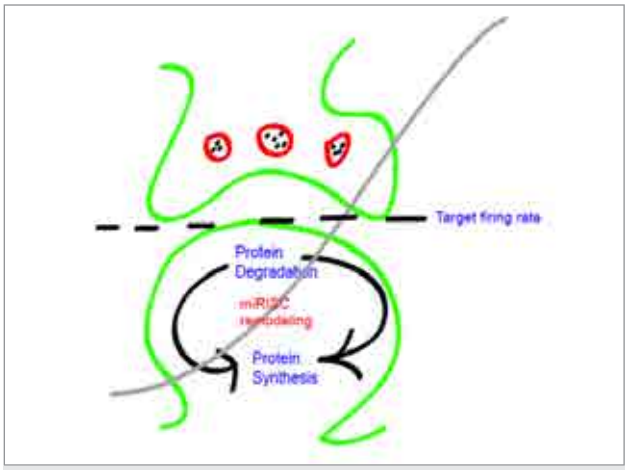


Figure 4: Proposed model for maintenance of homeostatic synaptic balance by combinatorial control of protein synthesis and degradation to modulate miRNA function through remodeling of miRISC.

Apart from influencing brain function under physiological condition, impairment of homeostatic scaling leads to epilepsy that is characterized by elevated network activity. Since, our study has shown dynamic remodeling of miRISC during bicucullin-induced down scaling of synaptic strength, it will be a step-forward to obtain an insight into how alteration of miRISC function at specific cell type within a specific brain area via virus-mediated loss or gain of function could possibly prevent epileptic seizure by restoring the threshold point of network activity.

Publications

1. Kumari, P., Balakumar, S., and **Banerjee, S.** (2017) Modulation of hippocampal synapse maturation by activity-regulated E3 ligase via non-canonical pathway. Neuroscience, 19;364:226-241. doi: 10.1016/j.neuroscience.2017.08.057.
2. Kim, J.W., Seung, H, Kim, K.C., Gonzales, E.L. Oh, H.A., Yang, S.M., Ko, M.J., Han, S.H., **Banerjee, S.**, Shin, C.Y. (2017) Agmatine rescues autistic behaviors in the valproic acid-induced animal model of autism. Neuropharmacology 113(Pt A):71-81. doi: 10.1016/j.neuropharm.2016.09.014. Epub 2016 Sep 14.

Presentations

1. **Banerjee, S.**, Samaddar, S., and Balakumar, S. Creative Destruction: Localized control of dendritic protein synthesis by selective degradation of miRNAs. EMBO meeting on "RNA localisation and local translation" Barga, Italy. July 2017.
2. **Banerjee, S.**, Balakumar, S., Samaddar, S., and Basu, B. Harmony or conflict: Interplay between constructive and destructive mechanisms modulating synaptic plasticity. Molecular & Cellular Cognition Society (Asia) Annual Meeting. Singapore. August 2017.
3. **Banerjee, S.**, Kumari, P., and Balakumar, S. Regulatory of mechanism of synapse formation by non-canonical function of polyubiquitination. Indian Society for Neurochemistry Annual Meeting. Varanasi. September 2017.
4. **Banerjee, S.**, Kumari, P., and Balakumar, S. Regulatory of mechanism of synapse formation by non-canonical function of ubiquitination. Minisymposium on "Regulatory mechanisms of functional synapse development, remodeling and repair" at Indian Academy of Neuroscience Annual Meeting. Cuttack. October 2017.

Presentation by Student

5. **Samaddar, S.**, Balakumar, S., and Banerjee, S. Think global act local: The role of miRNA turnover in modulating local translation at the synapse. Janelia Farm – HHMI Junior Scientists Workshop on Neuronal Cell Biology. Ashburn, USA. May 2017.

Funding

- Ramalingaswami Fellowhip, DBT
- RNAi grant, DBT
- Genome Engineering grant, DBT
- NBRC core fund

Collaborators

- Dasradhi Palakodeti, inStem, Bangalore
- Sharba Bandyopadhyay, IIT Kharagpur
- Ted Abel, University of Iowa, USA

Award

Student Award

Sarbani Samaddar, a Ph.D. student received fellowship from Janelia Farm-HHMI to present her research in Junior Scientists Workshop on Neuronal Cell Biology, May 2017.

Degrees Awarded

Pushpa Kumari, Ph.D.
Utsav Mukherjee, M.Sc.

Molecular Approaches to Understand the Pathophysiology and Pharmacology of Infection and Inflammatory Disorders of Central Nervous System

Anirban Basu

Research Fellow
Shalini Swaroop
Abhishek Kumar Verma
Surojit Chakrabarty
Meenakshi Bhaskar

DST Inspire Fellow
Sriparna Mukherjee

Research Associate
Dr Bibhabasu Hazra

SERB-National Post-Doctoral Fellowship
Dr Suvodip Mallick

Project Assistant
Irshad Akbar
Sujata Dev

Technical Assistant
Kanhaiya Lal Kumawat

Lab attendant
Manish Dogra

Our group at NBRC has long been interested in curing diseases of the nervous system. Our current research is focused on identifying the role of microglia and neural stem/progenitor cells in the healthy and diseased central nervous system. The group of people who currently work with us is testing strategies to develop disease modifying therapy by abrogating inflammation in CNS disorders. Besides studying fundamental aspects of virus induced neuropathology we are keen to do translational research to develop newer generation therapy for Neurotropic Viruses. We are also studying the role of IL-1 in understanding the fundamental aspects of molecular mechanisms happening during the process of neuro-inflammation in brain disorders.

A recent work from our lab has delineate the role of PLVAP (Plasmalemma vesicle associated protein) and GKN3 (Gastrokine3), two critical host cell receptor in Japanese Encephalitis Virus Entry into Neurons. The E glycoprotein of the virus mediates its attachment to the host cell receptors. In this study, we cloned and purified JEV- E glycoprotein in pET28a vector using E. coli BL21 (DE3) cells. A pull down assay was performed using plasma membrane fraction of BALB/c mouse brain and E glycoprotein as a bait protein. 2DE based separation of the interacting proteins was further analyzed by mass spectrometry. Among all the identified partners of E glycoprotein, PLVAP and GKN3 showed significant up-regulation in both JEV infected mouse brain and neuro2a cells. In-silico studies also predicted significant interaction of these receptors with E glycoprotein. Additionally, overexpression and silencing of these proteins resulted in increase and reduction in viral load respectively, suggesting them as two critical cellular factors governing JEV infection and propagation in neurons. In support, we observed a significant expression of PLVAP receptor but not GKN3 in post-mortem autopsied human brain tissue. Our results establish two novel viral receptors in neurons in case of JEV infection, thus providing potential targets for antiviral research.

We have earlier showed that the JEV-induced expression of miR-301a led to inhibition of the production of type I IFN pathway by targeting the transcription factor IFN regulatory factor 1 (IRF1) and the signaling protein SOCS5 (suppressor of cytokine signaling 5). Neutralization of miR-301a restored the host innate immune response by enabling IFN-β production, thereby restricting viral propagation in mouse neurons. Furthermore, activation of the transcription factor nuclear factor κB (NF-κB) was required for the induction of miR-301a expression during JEV infection. In addition, inhibition of miR-301a in mouse brain rescued the production of IRF1 and SOCS5, increased the generation of IFN-β, and reduced the extent of JEV replication, thus improving mouse survival. As a continuation to our previous work recently we have found that in JEV-infected microglia, miR-301a induced NF-κβ activation by targeting NF-κβ repressing factor (NKRF) and augmented inducible nitric oxide synthase, cyclooxygenase-2, and pro-inflammatory cytokine expression. Hence, in vitro knockdown of miR-301a resulted in significant over-expression of NKRF and subsequent decrease in microglial activation. Furthermore, in vivo deactivation of miR-301a reduced inflammatory cytokines and neuronal

death. In conclusion, miR-301a inhibition not only induces type I interferon to strengthen neuronal innate immunity but also inhibits bystander damage of neurons by reducing microglial activation. Thus targeting miR-301a could provide a new insight to develop effective antiviral strategy.

We are also working with Chandipura Virus (CHPV) a negative-stranded RNA virus belonging to the Rhabdovirdae family. It has been previously reported CHPV causes neuronal apoptosis by inducing oxidative stress. Our in silico data suggested the involvement of Angiotensin II in intracellular Ca2+ secretion within CHPV infected cells that further lead to enhancement of ROS level and mitochondrial dysfunction. ROS is also known to phosphorylate p38 that leads to neuronal apoptosis through FasL-FADD pathway during CHPV infection. Minocycline a broad-spectrum antibiotic well-known for its anti-oxidative and anti-inflammatory role was used in the present study to investigate its efficacy against CHPV. The results obtained from this on going study showed minocycline to be effective in mitigating the levels of cytoplasmic Ca2+, ROS, phosphorylation of p38 molecules and hence cellular apoptosis. Thus minocycline apart from being an anti-inflammatory and anti-oxidative agent, our study showed that minocycline has an additional Ca2+ chelation activity (Figure 1).

The process of neuro-inflammation being the first line of defense in the CNS, behaves as a double-edged sword as exaggerated inflammatory response may exacerbate CNS injury. IL-1β, which is a potent pro-inflammatory cytokine secreted by activated microglia, initiates a vicious cycle of inflammation and orchestrates various molecular mechanisms involved in neuroinflammation. However, the role of IL-1β has been extensively studied in neurodegenerative disorders but the underlying molecular pathways are still poorly understood. Therefore, we have studied different molecular pathways involved in IL-1β induced inflammation in microglia

Microglial activation resulted from various stress signals (including pathogenic invasion and neurodegeneration) is responsible for forming the first line of defense in the CNS and results in the secretion of various cyto-chemokines. IL-1β is the most important cytokine that initiates a vicious cycle of inflammation by inducing the expression of other pro-inflammatory cytokines along with its own production. Microglia mediated IL-1β production is a tightly regulated mechanism which involves the activation of nucleotide binding oligomerization domain leucine rich repeat and pyrin domain containing 3 (NLRP3) inflammasome pathway. In our previous study we found that heat shock protein 60 (HSP60), plays a critical role in IL-1β induced inflammation through

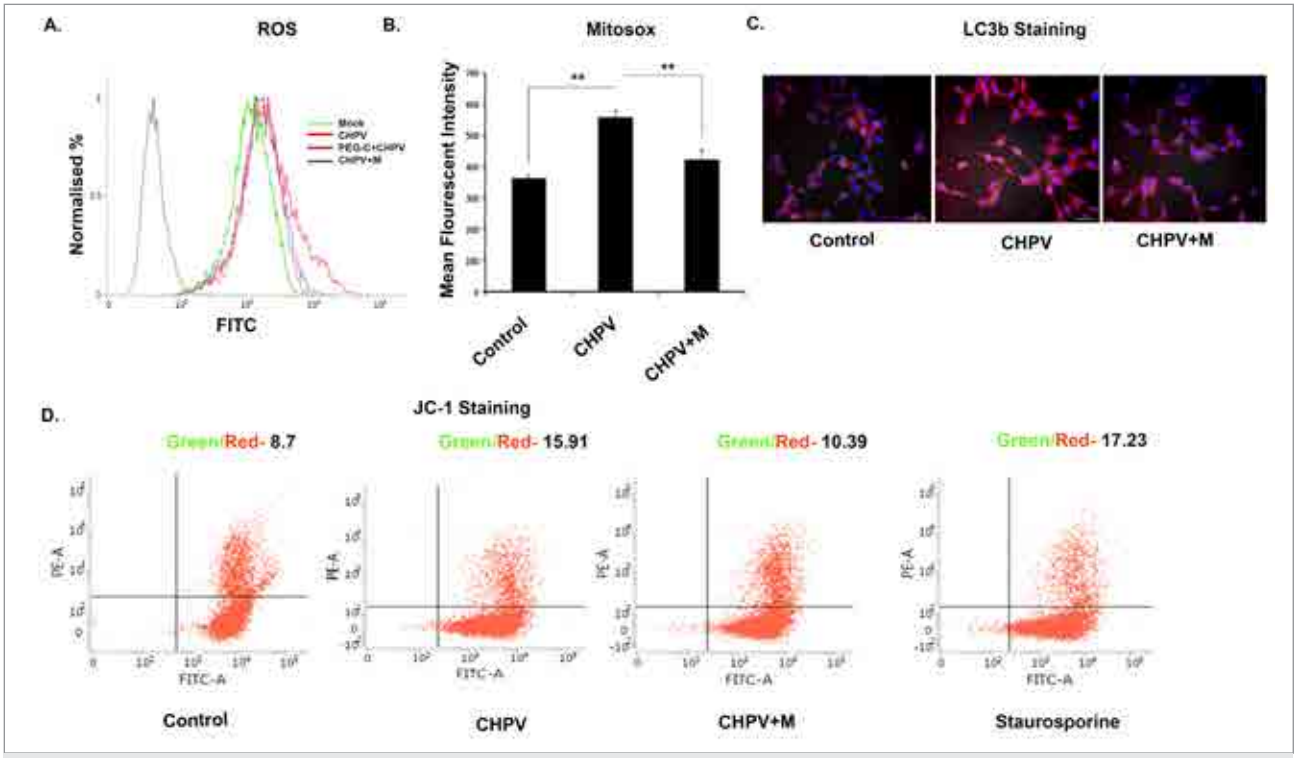


Figure 1: CHPV infection induced mitochondrial dysfunction in the neuronal cell line. A)

ROS was measured at 4 hpi and was found to be increased against the mock infected group. Minocycline (CHPV+M) treated group showed decreased level of ROS generation against CHPV infected group. B) Superoxide production level was measured using Mitosox. MFI was maximum in CHPV infected sample and was decreased in minocycline treated group. C) LC3B staining, a marker for autophagy showed more expression in CHPV infected group as compared to minocycline treated samples, suggesting minocycline treatment inhibited induction of autophagy. D) JC-1 staining showed more green:red signal in CHPV infected group indicating altered mitochondria. Compared to the CHPV infected group, minocycline treated group showed a reduced ratio of green: red signal signifying its treatment rescued mitochondrial alteration. Three independent experiments were performed to reach a conclusion .*p < 0.05, **p < 0.01

activating TLR4-p38 MAPK axis. However, whether HSP60 regulates endogenous IL-1β production, is not known. Therefore, to probe the underlying mechanism, we have elucidated the role of HSP60 in endogenous IL-1β production using in vitro (N9 murine microglial cells) and in vivo (BALB/c mouse) models. The results of our overexpression and knockdown studies of HSP60 gene suggest that it induces the phosphorylation of NF-κB and increases its nuclear localization both in N9 murine microglial cells and mice brains. HSP60 also induces perturbation in mitochondrial membrane potential and enhances reactive oxygen species (ROS) generation in N9 cells. HSP60 further leads to activation of NLRP3 inflammasome pathway by elevating NLRP3 expression both at RNA and protein level. Furthermore, HSP60 enhances caspase-1 activity and increases IL-1β secretion by microglia. Knockdown of HSP60 reduces the IL-1β induced production of IL-1β both in vitro and in vivo. Thus, these results suggest that HSP60 plays a very important role in IL-1β production by regulating NLRP3 inflammasome pathway (Figure 2). Our results thus identify an important signaling mechanism underlying microglial inflammation and suggest HSP60 as a novel molecule which can be targeted to regulate IL-1β production to ameliorate inflammatory conditions in CNS.

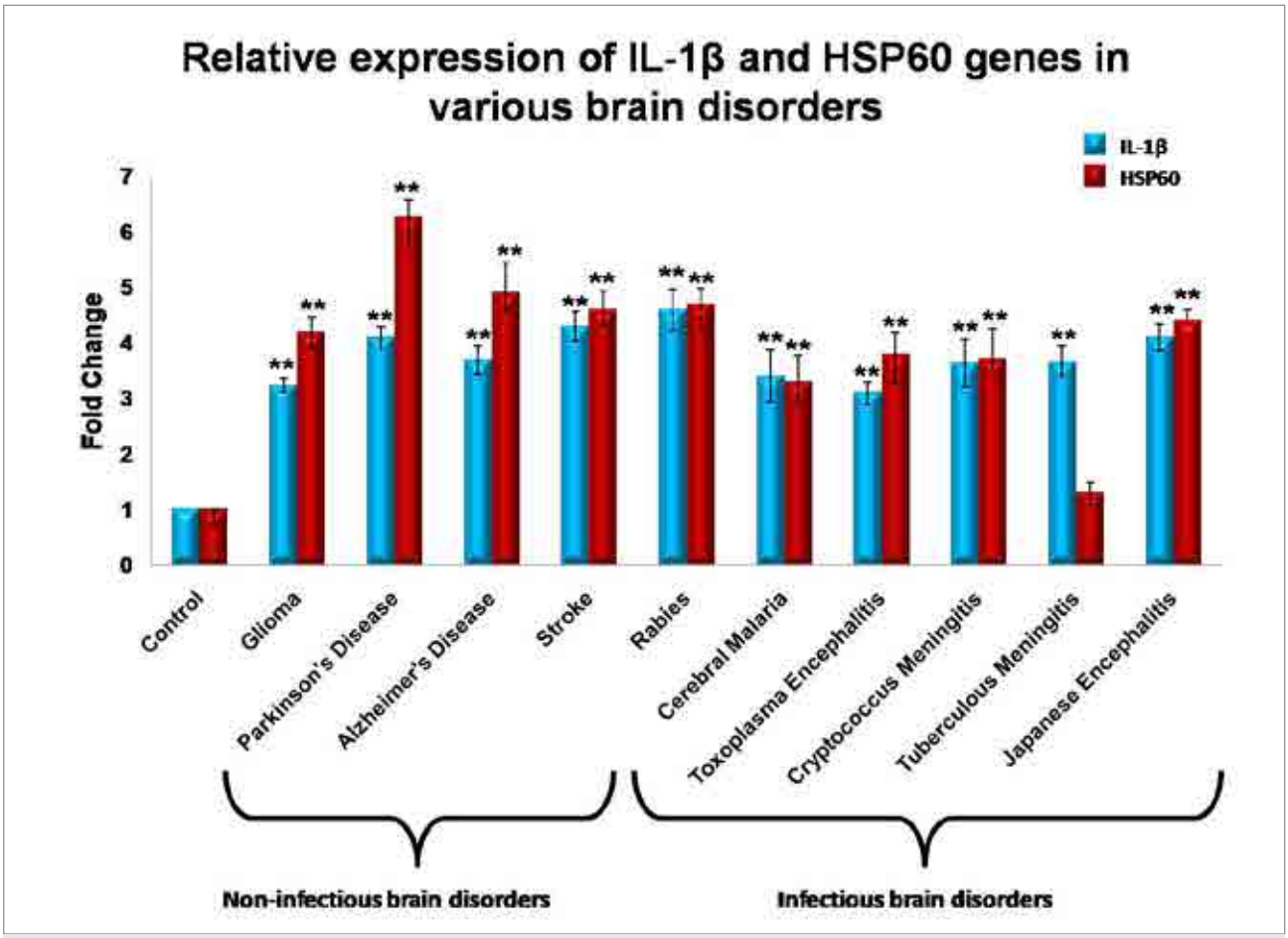


Figure 2: Expression of HSP60 and IL-1 increases in various brain disorders.

qRT-PCR analysis of IL-1β and HSP60 gene in human brain sections of the frontal cortex of control and diseased brains. The levels of IL-1β and HSP60 gene expression were checked in both non-infectious and infectious brain diseases. For Glioma, qRT-PCR was done with tissue sample and the expression of IL-1β and HSP60 were compared with that of control tissue. The transcript levels of the genes were normalized with the levels of GAPDH. Data represent mean ± SD from three different sets of experiments. **p<0.01 in comparison to control condition.

Publications

1. S Mahanti, A Majhi, R Adhikary, S Ghosh, A Basu, and B Bishayi (2017) Exogenous Interleukin-10 and ciprofloxacin treatment reduces inflammation and helps to improve cognitive behavior in acute and chronic restrain stressed mice infected with Eschericia coli. Indian Journal of Bichemistry & Biophysics 54: pp 241-257.
2. A Verma, P Tripathi, N Rai, A Basu, A Jain, V Atam, M Agarwal, and R Kumar (2017) Long-Term Outcomes and Socioeconomic Impact of Japanese Encephalitis and Acute Encephalitis Syndrome in Uttar Pradesh, India. Int J Infect. 4(4):e15607.
3. S C Philkhana, A Verma, G R. Jachak, B Hazra, A Basu* and D S Reddy (2017) Identification of new anti-inflammatory agents based on nitrosporeusine natural products of marine origin. Eur Journ of Med Chemistry Jul 28;135:89-109 [* joint corresponding author].

Editorial

B Hazra, S Chakraborty, and A Basu (2017) miR-301a mediated immune evasion by Japanese encephalitis virus. Oncotarget Vol. 8, (No. 53), pp: 90620-90621.

Book Chapter

K Dutta, and A Basu (2018) Overview on Japanese Encephalitis in South and Southeast Asia. In Neglected Tropical Diseases –South Asia. ed. Sunit K Singh. Springer -Science.

Presentation

1. A Basu (2018) Host pathogen interaction in Japanese Encephalitis Virus infection: from pathogenesis to therapy. Prof S S Katiyar Endowment Lecture of the Indian Science Congress Association, Manipur University, 16-20th March, 2018.
2. A Basu (2018) Host pathogen interaction in Japanese Encephalitis Virus infection: from bench to bedside. Bioscience and Bioengineering, IIT-Jodhpur, 16th February 2018.
3. A Basu (2018) Japanese Encephalitis Virus infection: Pathobiology and therapy. Dept. of Microbiology, Institute of Home Economics, 10-11th January, 2018.
4. A Basu (2017) Host pathogen interaction in Japanese Encephalitis Virus infection: from bench to bedside Sreenivasaya Memorial Award -SBC (I), JNU, 16-19th November, 2017.
5. A Basu (2017) Neural Stem/Progenitor cells shows versatility in their Response following Japanese encephalitis virus infection. Bioscience and Biomedical Engineering, IIT-Indore, 27th July, 2017.

Projects funded by external agency

1) MicroRNAs as a potential therapeutic target in Neuro-tropic Viral infection [Tata Innovation Fellowship from the Department of Biotechnology (BT/HRD/35/01/02/2014)] (2015-2018) * Request has been sent to DBT for the extension of the fellowship for 2 more 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.

Award

Prof S S Katiyar Endowment Lecture of The Indian Science Congress Association (ISCA)-2018.

Elected as a Fellow of the Indian Academy of Sciences (IASc)-2018.

Sreenivasaya Memorial Award of Society of Biological Chemist (India)-2017.

Student's Award

Shalini Swarup: International Society of Neurochemistry (ISN) travel award to attend ISN-ESN Biennial Meeting, Paris, 20-24th August, 2017.

Sriparna Mukherjee: SFN-IBRO Travel award to attend Annual meeting of Society for Neuroscience, 11-15th November, 2017, Washington DC.

Collaborators

Arpan Banerjee, Pankaj Seth, and Dipanjan Roy, NBRC

Sunit Singh, Institute of Medical Sciences, BHU, Varanasi

Sudhanshu Vrati, and Prasenjit Guchait, RCB, NCR Biotech Cluster Faridabad

Manjula Kalia, and Arup Banerjee, VIDRC, THSTI, NCR Biotech Cluster, Faridabad

SK Shankar, and Anita Mahadevan, NIMHANS, Bangalore

Vivek Sharma, Department of Biological Sciences, Birla Institute of Technology and Science Pilani, Hyderabad Campus, Hyderabad

Ranjit Kumar Giri

Lab. Attendant
Lalit Bidla

Understanding Cellular Pathologies in Differentiated Brain Cells Derived from Neurosphere Cultures Expressing APPswe and PSEN1ΔE9 Mutations of Alzheimer's Disease

Alzheimer's disease (AD) is a progressive and irreversible neurodegenerative disease of elderly people. It is the most common cause of dementia worldwide. Genetic linkage studies of early onset familial Alzheimer's disease (FAD) had identified amyloid precursor protein (APP), Presenilin 1 (PSEN1) and Presenilin 2 (PSEN2) as three causative genes. Mutations in these genes result in increased production and aggregation of beta amyloid peptides, the hallmark pathology of Alzheimer's disease. However, very little is known about the exact role of beta amyloid peptides on each cell type of diseased brain.

In order to study the mechanisms of neuropathology in AD brain, transgenic animals expressing human FAD genes were developed. Though these transgenic mice show beta amyloid deposits and mild cognitive impairments, the effect of beta amyloid peptides on various mature brain cells is also not known. To simplify these complexities and to understand disease associated pertubation of cellular processes, we have developed an alternative cellular model (neurospere) of AD from emryonic mouse either negative or positive for human APPswe and PSEN1ΔE9 mutations. Neurosphere culture positive for both these transgenes exhibited robust beta amyloidopathy meaning increased production of beta amyloid peptide, oligomerization and aggregation of beta amyloid peptide within cells and secreted to extracellular media more than any known cellular model of AD (Figure 1).

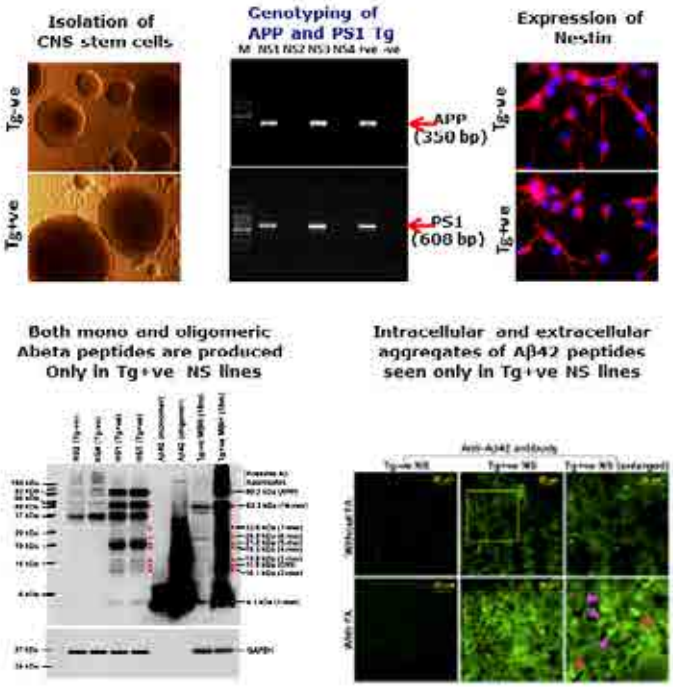


Figure 1: Development of beta amyloidopathy in neurosphere cultures expressing APPswe and PSEN1ΔE9 mutations of familial AD.

Since neurosphere cultures from both transgene negative (Tg-ve) and positive (Tg+ve) were enriched with CNS stem/progenitor cells, such cell culture system provides opportunity to study the dynamic alteration of mature brain cells to increased beta amyloid environment (similar to AD brain) as these cells retain the property to differentiate towards, neuron, astrocyte and oligodendrocyte in defined media. Therefore, we differentiated both Tg-ve and Tg+ve neurosphere cultures using same culture condition in vitro. Upon differentiation, these cells lost their stemness as observed by significant decrease in nestin expression (an established marker for CNS stem cell/neuroepithelial cell) (Figure 2a). In addition, Tg+ve neurosphere cultures upon differentiation show numerous but shorter processes from cell bodies. Unlike these cultures, Tg-ve neurosphere cultures show fewer but longer processes (Figure 2b), suggesting a phynotypic difference between Tg-ve and Tg+ve cells. Collectively, our results show, neurosphere cultures from both Tg-ve and Tg+ve genotype can differentiate and provide robust morphological variations to study cytopathologies in mature brain cell types such as neuron and astrocytes in these cultures.

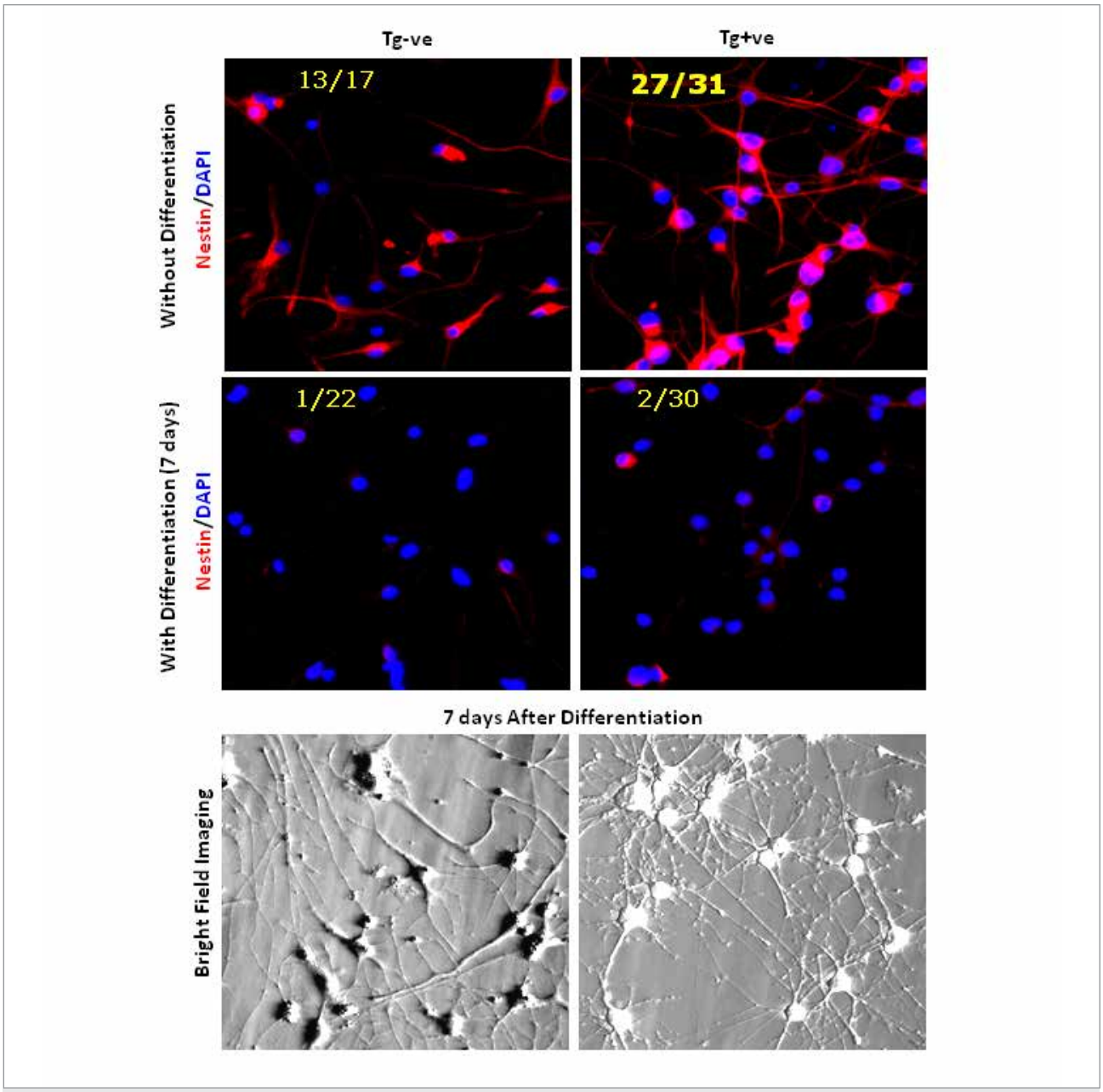


Figure 2: A) Differentiation of cells from Tg-ve and Tg+ve neurosphere cultures show robust repression of nestin than undifferentiated cells. B) Bright field images show multiple short processes and unpolarized cells in differentiated Tg+ve but longer and polarized in differentiated Tg-ve cells.

Understanding the Pathogenesis of Neurodegenerative Disorders Involving Protein Aggregation

Nihar Ranjan Jana

Research Fellow
Brijesh Kumar Singh
Naman Vatsa
Shashi Sekhar
Vipendra Kumar
Tripti Joshi

Research Associate
Romita Thounaojam

Technical Assistant
Ankit Sharma
Mahendra Singh

One of the common pathological hallmark of most age-related neurodegenerative disorders including Huntington's disease (HD) and Alzheimer's disease (AD) is the accumulation of mutant disease proteins as inclusion bodies. Protein inclusions could be observed extracellularly (like amyloid plaques in AD) or intracellularly (like neurofibrillary tangles in AD or cytoplasmic and nuclear inclusions in HD). Appearance of aggregates of the misfolded mutant disease proteins suggest that cells are unable to efficiently degrade them, and failure of clearance leads to the severe disturbances of the cellular protein quality control system. Furthermore, the cellular ability to maintain protein homeostasis declines with age. In HD, AD and other neurodegenerative diseases, distinct proteostasis nodes such as molecular chaperones, ubiquitin proteasome system (UPS) and autophagy are found to be severely affected. Therefore the mechanism that restores protein homeostasis either by upregulating the function of chaperones or enhancing the clearance of mutant disease proteins are capable to delay the progression of the disease in various animal models.

In my laboratory, we are using HD and AD as a model system to understand the mechanistic basis of impaired protein homeostasis and how that can be restored. Earlier we have demonstrated that Ube3a function as a cellular protein quality control ubiquitin ligase and involved in the clearance of misfolded nutant huntingtin (causes HD) and mutant superoxide dismutase (causes ALS) (J. Biol. Chem., 2008, 2009 and Neurobiol. Aging, 2013). Deficiency of Ube3a in HD mice brain also increased global aggregate load and aggravated HD pathogenesis (Hum. Mol. Genet., 2014). We have also reported significant down-regulation of the expression of HSF1 in HD mice brain, which could also lead to impairment of proteostasis at very early stage of the disease progression (Hum. Mol. Genet. 2014).

Since Ube3a is implicated in the pathogenesis of HD and ubiquitination of amyloid precursor protein (APP) regulates its trafficking and the generation of amyloid beta (Aβ), we further aimed to investigate the role of Ube3a in the metabolism of Aβ and progression of AD using APPswe/PSEN1δE9 transgenic mouse model. We first noted that the level of Ube3a was age-dependently decreased in AD mice compared to age-matched controls. Next, we generated brain Ube3a-deficient AD mice (taking the advantage of imprinted expression of Ube3a in the brain) that exhibited accelerated cognitive and motor deficits compared to AD mice. Interestingly, these Ube3a-deficient AD mice were excessively obese from their age of 12 months and having shorter lifespan. Biochemical analysis revealed that the Ube3a-deficient AD mice had significantly reduced level of Aβ generation and amyloid plaque formation in their brain compared to age-matched AD mice and this effect could be due to the increased activity of α-secretase, ADAM10 (a disintegrin and metalloproteinase-10) that shift the proteolysis of APP towards non-amyloidogenic pathway. These findings suggest that aberrant function of Ube3a could influence the progression of AD and restoring normal level of Ube3a might be beneficial for AD. Currently, we are investigating the cause of obesity in these mice.

In another project (in collaboration with scientist at IACS, Kolkata), we are testing nanoparticle based strategy to prevent fibrillation and aggregation of mutant huntingtin as well as other amyloid proteins. We have observed that nanoparticle form of some of the sugar molecules can dramatically enhance their chaperone performance in inhibiting protein aggregation and in lowering of amyloidogenic cytotoxicity. Interestingly, these nanoparticles have excitation dependent green/yellow/orange emission and surface property identical to respective sugar molecule. We have also

shown that poly(trehalose) nanoparticle (composed of 6 nm iron oxide core and zwitterionic polymer shell covalently linked with trehalose) are highly efficient in preventing amyloid aggregation including mutant huntingtin in cellular and mouse model of HD.

Understanding the physiological function of Ube3a and pathogenesis of Angelman syndrome

Ube3a (also known as E6 associated protein, E6-AP) is a HECT domain family E3 ubiquitin ligase, an enzyme involved in targeting specific protein for ubiquitination and degradation through proteasome. Apart from its ubiquitin ligase function, Ube3a also acts as a transcriptional co-activator of steroid hormone receptors. Interestingly, paternally-inherited UBE3A is imprinted in neuronal tissues and loss of function of maternally-inherited UBE3A causes Angelman syndrome (AS), a neurodevelopmental disorder characterized by severe mental retardation, speech impairment, susceptibility to seizures, ataxia and unique behavioural features such as improper laughter and autistic features. Duplication of the UBE3A gene is also reported in autism. Ube3a-maternal deficient mice not only exhibit classical cognitive and motor deficits, but also display audiogenic seizure, anxiety-like behaviour, and disturbance in circadian clock and sleep homeostasis. In depth study in this mouse model further demonstrates defect in hippocampal calcium/calmodulin dependent protein kinase-II and long-term potentiation, experience-dependent synaptic plasticity and imbalance of excitatory/inhibitory circuitry. These results strongly indicate that Ube3a plays a crucial role in regulating synaptic function, although, the molecular mechanism is poorly understood. Since my lab is working on the role of Ube3a in HD and AD pathogenesis, we were also interested to know how Ube3a deficiency could lead to AS. Some common mechanism might be involved in the pathogenesis of these diseases.

Past several years my laboratory is involved in exploring the physiological function of Ube3a and how its defect in AS is linked with cognitive and other behavioural deficits using a specific mouse model of AS. In addition to identify the novel interacting partner of Ube3a, we are also trying to identify novel miRNA that regulates Ube3a as well as miRNA that are directly linked with AS pathogenesis. We are also exploring the defects in signalling pathways that contributes behavioural deficits in AS mouse model and how those behavioural abnormalities can be reversed.

Last year we have shown that the aberrant increase in HDAC1/2 activity in the brain of adult AS mice might be linked with synaptic dysfunction and associated behavioural anomalies in these mice (Neurobiol. Dis., 2017). Our finding also suggests that HDAC inhibitors could be promising candidate to treat AS. We further continued our study about mechanistic basis of the increased activity of HDAC1/2 in the brain of AS mice. We have found that HDAC1/2 activity was unaffected in E16 embryonic cortex in AS mice compared to wild type control. Increased HDAC1/2 activity in the AS cortical area were observed from the postnatal day 5 onwards, when complete silencing of paternally inherited Ube3a was observed. Significant decrease in the acetylation of histones H3(K9) and H4 (K12) was also observed from the postnatal day 5. These results indicate that increased HDAC1/2 activity in AS mice brain can be seen from early developmental days and probably directly linked with Ube3a deficiency. In co-immunoprecipitation assay, Ube3a failed to pull-down HDAC1 or HDAC2 indicating HDAC1/2 is not a target of Ube3a. We are now checking the transcriptional regulation of HDAC1/2 by Ube3a.

In another project, we are studying the role of miRNA in the pathogenesis of AS. We performed genome wide analysis of altered miRNA in AS mice with respect to wild type controls. Several up-regulated and down-regulated miRNA were identified. Currently, we are characterizing one down-regulated miRNA (miR-708). The down-regulation of miR-708 in the AS mice brain was further confirmed using real-time RT-PCR. We have now identified neuronatin as one of the novel target of miR-708 and charactered extensively. Neuronatin is a developmentally regulated protein and implicated in the regulation of ion channels particularly sarcoplasmic reticulum Ca2+-ATPase (SERCA) in the ER. Notably, Ca2+ is a critical regulator of synaptic function and plasticity. We therefore hypothesized that miR-708-mediated targeting of neuronatin might lead to impaired regulation of intracellular Ca2+ and altered synaptic function and plasticity. We have confirmed that the level of neuronatin is significantly increased in the early developmental days in AS mice brain with respect to wild type mice. We are now analysing possible impact of increased level of neuronatin in Ca2+ homeostasis and altered activity of Ca2+-dependent protein kinases using primary neuronal culture obtained from both wild type and AS mice brain.

Publications

1. B.K. Singh, N. Vatsa, V. Kumar, S. Shekhar, A. Sharma and **N.R. Jana.** Ube3a deficiency inhibits amyloid plaque formation in APPswe/PS1δE9 mouse model of Alzheimer's disease. Human Molecular Genetics (doi:10.1093/hmg/ddx295), 2017.
2. I. Jamal, V. Kumar, N. Vatsa, S. Shekhar, B.K. Singh, A. Sharma and **N.R. Jana.** Rescue of altered HDAC activity recovers behavioural abnormalities in a mouse model of Angelman syndrome. Neurobiology of Diseases, 105, 99-108, 2017.
3. K. Debnath, N Pradhan, B.K. Singh, **Nihar R. Jana*** and Nikhil R. Jana* Poly(trehalose) Nanoparticles Prevent Amyloid Aggregation and Suppress Polyglutamine Aggregation in a Huntington's Disease Model Mouse. ACS Applied Materials & Interfaces, 9(28), 24126-24139, 2017. *Both are corresponding author.

4. P. Majumder, K. Roy, B.K. Singh, **N.R. Jana** and D. Mukhopadhyay. Cellular levels of Grb2 and cytoskeleton stability are correlated in a neurodegenerative scenario. Disease models & mechanisms, 10 (5), 655-669, 2017.
5. R. Kumar, D. K. Jangir, G. Verma, S. Shekhar, P. Hanpude, S. Kumar, R. Kumari, N. Singh, N. S. Bhavesh, **N. R. Jana**, T. K. Maiti. S-nitrosylation of UCHL1 induces its structural instability and promotes α-synuclein aggregation. Scientific Reports, 7, 44558, 2017.

Presentations

1. N. Vatsa and N.R. Jana. Understanding the role of microRNA in Angelman Syndrome pathogenesis using mouse model. IAN 2017, Bhubaneswar, October, 2017.
2. S. Shekhar and N.R. Jana. Topotecan, a topoisomerase-1 inhibitor retards the disease pathogenesis in a mouse model of Huntington's disease. IAN 2017, Bhubaneswar, October, 2017.
3. V. Kumar and N.R. Jana. Simvastatin ameliorates behavioral deficits in Angelman syndrome model mouse. IAN 2017, Bhubaneswar, October, 2017.
4. N. R. Jana. Rescue of altered protein homeostasis in a mouse model of Huntington's disease. IAN 2017, Bhubaneswar, October, 2017.
5. N. R. Jana. UBE3A and its link with autism and autism spectrum disorder. IBRO meeting, BHU, Varanasi, April, 2017.
6. N. R. Jana. Altered protein homeostasis and neuronal dysfunction in Huntington's disease. International Symposium on Neurodegenerative Disorders (ISND2017), NIMHANS, Bengaluru, March, 2017.
7. **Popular lectures** given in many undergraduate colleges, (Midnapore College, Goaltore College, RNLK Women's College in West Bengal) and Universities (Amity University, Jamia Hamdrad University, Dibrugarh University and Tezpur University) and IBRO-2017 and IAN-2016 meeting.

Funding

- Ube3a as a therapeutic target of Huntington's disease. TATA Innovation project, Department of Biotechnology, Govt. of India. Grant No: BT/HRD/35/01/03/2013.

Collaborators

Dr. Nikhil Jana, Indian Association for the Cultivation of Science, Kolkata.

Dr. Subramanian Ganesh, IIT Kanpur.

Anindya Ghosh Roy

Development and Repair of Neural Circuit in C. elegans

Research Fellows
Dharmendra Puri
Atrayee Basu
Harjot Kaur
Sibaram Behera

Post-doctoral Fellows
Sandeep Kumar
Swagata Dey

Project Assistants
Keerthana P
Revathi Muthuvel
Titash Mukherjee

Technical Assistant
Sumit Mahapatra
Yunis Khan

Background and overall summary

Our lab is interested in understanding how nervous system develops and after injury how it repairs. Towards this goal we use a combination of genetics, molecular biology and imaging in Caenorhabditis elegans.

1) Regulation of neuronal polarity:

Microtubule (MT) cytoskeleton is the basis of the polarized structure of neuron. We found that loss of the kinesin-13 family depolymerizing factor KLP-7 stabilizes microtubules and causes multi-polar neuron formation (1). 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 (Figure 1). 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 2).

We have been able to set up the live imaging system to image microtubule dynamics in vivo. We are using plus end binding protein EBP-2 tagged with GFP to image plus ends of microtubules in touch neurons. We found that microtubules are arranged in a plus-end-out manner in the long anterior process of ALM or PLM, whereas MTs are of mixed polarity in the short posterior process. Loss of klp-7 stabilizes the MTs and their polarity becomes plus-end-out in the posterior process. We further found that WNT signalling might negatively regulate KLP-7 to establish microtubule polarity in touch neuron (Fugure 3).

2) Nerve regeneration study:

To study how nervous system is repaired after neuronal injury, we have established the neurosurgery protocol using femto-socond lasers of 2-photon microscope. We showed that axotomy of posterior touch neurons on both sides of a worm leads to a dramatic loss of posterior touch sensation. During the regenerative phase only the axons those get fused to their distal counterparts contribute to regain of gentle touch sensation. Further we have found that loss of let-7 miRNA overcomes the age-related decline in functional restoration (Figure 4). Axon fusion has is observed in many systems after neuronal injury and it was proposed that axon fusion would perfectly repair the damage to restore the lost function. Our study addresses this question with quantitative behavioural assay (Basu et al 2017 in PNAS).

We have initiated a project to understand how dendrite responds to mechanical injury. We have found that the DLK-1 MAP kinase pathway that is important for axon regeneration is not required for dendrite regeneration of PVD neuron (Figure 5).

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

Objective 1a. Finding novel regulators neuronal polarity

Kinesin-13/KLP-7 can depolymerize microtubules from both the plus and minus ends. We hypothesized that protection of nucleating

filaments against this kinesin could stabilize microtubules during neuronal polarization. First, we propose to test known microtubule stabilizing factors and further uncover novel molecular mechanisms by mapping the mutations that suppress the multi-polar phenotype seen in klp-7 mutants.

Progress: To test the known microtubule regulators those could interact with KLP-7 in neuron we tested the loss of function mutants that affect the centrosomal, non-centrosomal, plus end binding proteins and microtubule associated proteins/MAPs. As of now most of the candidate mutants did not show any interaction with klp-7 mutant. However, microtubule destabilizing drug Cochicine reversed the overgrowth phenotype seen klp-7(0) mutant (shown in the past report).

We have performed a forward genetic screening in klp-7(0) mutant using Ethyl Methane Sulfonate (EMS). We have isolated 26 suppressors from 8830 F1s in a clonal screening (Figure1). To identify the exact causal mutant, the suppressors were crossed with Hawaiian polymorphic strain to isolate multiple F2s recombinants. We sequenced the pooled lysates of these recombinants and the Whole Genome Sequence (WGS) data were analyzed in local MIModD integrated Galaxy server. Using this strategy, we have mapped ju1128 to mbl-1(Figure 2A-B).

mbl-1 encodes for a RNA binding protein whose function in muscle development has been reported earlier. MBL-1 belongs to polypyrimidine tract binding protein family, which is known to regulate splicing in variety of cell types. C. elegans codes for only one muscleblind gene mbl-1, which is similar to neuronal muscleblind-2 (mbl-2). We found that Loss of mbl-1 causes short axon phenotype of PLM and ALM neurons (Figure 2C). By expressing wild type copy of isoform-3 of mbl-1 under neuronal and muscle specific promoter, we showed that mbl-1 is required in neuron for proper axon growth (Figure 2D). A functional construct of MBL-1, tagged with GFP, is present in both nucleus and axoplasm. To identify the possible targets of MBL-1, that regulate axon growth, we have performed genetic epistasis test. We selected those genes, which either play roles in axon development, or code for RNA that binds to MBL-2. We found that mbl-1 is epistatic to genes coding for beta- tubulin MEC-7, kinesin26A (KIF26A) family motor protein VAB-8, adaptor for vesicular transport in axon UNC-76, etc (Figure 2E-F). We hypothesize that MBL-1 regulates the RNAs of unc-76, vab-8 and mec-7 during developmental axon growth (Manuscript under preparation).

Objective 1b. In vivo imaging of neuronal microtubules to determine microtubule polarity

To understand how microtubule cytoskeleton is organized in neuron and how loss of microtubule depolymerising enzyme KLP-7 affect the normal organization, we have established the state of the art in vivo imaging of MT dynamics using spinning disc confocal microscope. We have asked how polarity of microtubules are established and maintained in neuron. We have visualized the growing ends of MTs using the plus end binding protein EBP-2 tagged with GFP.

Progress: Both anterior and posterior touch receptor neurons are unipolar with a long anterior process, which, connects to its post-synaptic cell, and a short posterior process (Figure 3A). Loss of klp-7 leads to excess stabilization of microtubules leading to an overgrowth of the short posterior process. In vivo imaging of microtubules with EBP-2::GFP reporter reveals that the short process of PLM has mixed polarity of MTs, whereas the long anterior process has all plus-end-out unipolar MTs (Figure 3A). The MTs in the ectopically extended posterior process in klp-7(0) becomes plus-end-out. Therefore, activity of KLP-7 is important to maintain the MTs with mixed polarity in the short posterior neurites (Figure 3B).

Previous study indicated that loss of Wnt signaling reverses the polarity of touch neurons in that short posterior process becomes axon and makes synapse. We found that in the mutant lin-17(0) that lacks Wnt receptor, the microtubule polarity in the posterior process is plus-end-out and that in anterior process is mixed (Figure 3C). We found that loss of klp-7 resets the MT polarity in lin-17(0) (Figure 3D). This indicates that the activation of Wnt signalling, during neuronal polarization might regulate KLP-7 to establish microtubule polarity (Manuscript in preparation). We will be further investigating how KLP-7 is regulated during the establishment of neuronal polarity.

2) Neuronal Regeneration

Objective 2a. Study of axon regeneration

Although using laser-based protocols few groups have identified cellular and molecular components those govern axon regeneration using C. elegans, very little has been understood how behavior is perturbed by axotomy and subsequently recovered after regrowth has taken place. To perform axonal injury experiment, we have set up the axotomy system using the two-photon microscope in our institute. We have discussed about this set up in past in previous reports. We have also shown that after cutting PLM neurons on both the sides, response to gentle touch becomes significantly and severely affected. In past, we and others showed that about 40% of the regrowing processes get fused to their distal counterpart, thereby preventing degeneration of the distal processes those get disconnected from the soma as a result of laser axotomy. This phenomenon was also noticed in other system such as Crayfish, leech, Aplysia etc. We found that the worms, in which axotomized processes could fuse to their distal counterparts show complete recovery in touch response. The mutants such as eff-1(0) or psr-1(0) that fail to fuse does not show any recovery. These observations undoubtedly proved that axonal fusion leads to functional repair after axonal injury (discussed in earlier report).

Progress: We have further shown that functional restoration after injury decline with age in worm (Basu et al 2017, PNAS). Using

this assay for axon regeneration, we have done a screening for mutants that earlier showed enhanced total regrowth (10-12). We found that loss of let-7 miRNA enhanced functional restoration by enhancing the frequency of axon fusion events in a cell autonomous manner in larval and adult stages. We further showed that in let-7 mutant the mRNA level of the cell recognition molecule ced-7 is upregulated and the 3'UTR of ced-7 has a let-7 binding site (Figure 4B). We further showed that loss of let-7 helps overcome regeneration barrier due to aging (Figure 4). In collaboration with Sandhya Koushika's lab at TIFR Mumbai we have imaged axonal transport in vivo in touch neuron and found as worm ages the transport is declined (Figure 4A) and the a key fusogen molecule EFF-1 becomes limiting at the growing tip of the axon. Loss of let-7 overcomes this barrier by maintaining a healthy axonal transport in older worm (Figure 4A). This study reveals a very fundamental property of regenerating neurons in which axons can self-repair themselves by fusion like mechanism (see the model in Figure 4B). This manuscript is published in PNAS during early November 2017 (Basu et al 2017).

Aim2b. 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.

Progress: 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 dendrites and axon initial segment (AIS) of this neuron. After the primary dendrite was severed near the cell body, we noticed sprouting of new branches from the cut site at 3-hour (Figure 5B). By 24-hours the primary dendrite regrew, following similar trajectory and formed more complex branching patterns unlike the original menorah observed in uninjured PVD (Figure 5A). These branches often lacked self-avoidance phenomenon. We quantified the regeneration pattern in two aspects - length of primary dendrite and number of branches. The primary dendrite regrew in length by 83.5±64.7 µm and 201.1±56.1 µm at 24-hour and 48-hour respectively (Figure 5D). Severing the AIS led to complete retraction of the proximal axon after 3 hours. This was followed by the formation of a new process either from cell body or from sites of primary dendrites adjacent to the cell body. Eventually, these processes were guided to the ventral nerve cord (Figure 5C). This response is reminiscent to the repolarization phenomenon observed in fly and vertebrates after cutting AIS.

The extent of regrowth of the primary dendrite and the number of branches were not affected by the loss of dlk-1. This indicated that dendrite regeneration is independent of dlk-1 as seen in fly. Our future goal is to identify signalling mechanism that is important for the dendrite regrowth. We are prioritizing the kinases specific to dendrite for this direction.

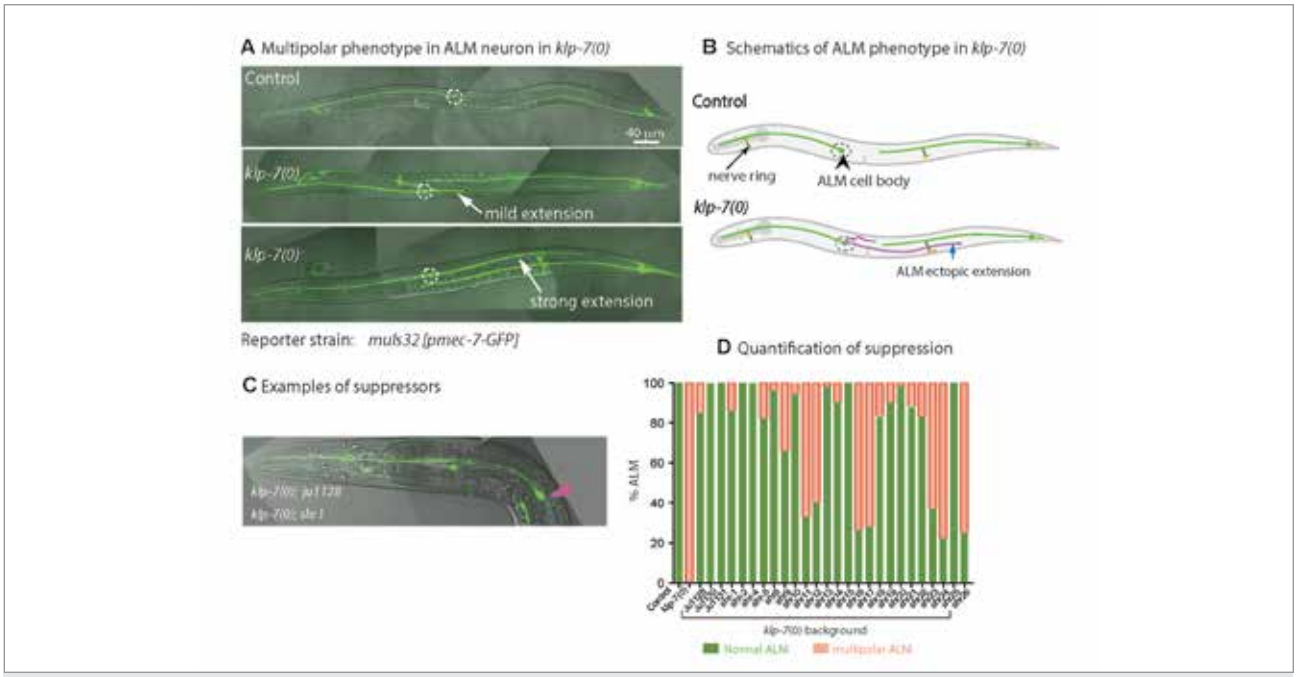


Figure 1: ***Legend:*** (A) Shows GFP labeled PLM and ALM touch neuron. These neurons are polarized during early embryonic development. In klp-7(0) mutant very frequently more than one process is extended. (B) Illustration of the developmental defect in klp-7(0). (C) The bar chart showing the quantification of the neuronal polarity defect of ALM neuron in klp-7(0) mutant and different suppressior strains.

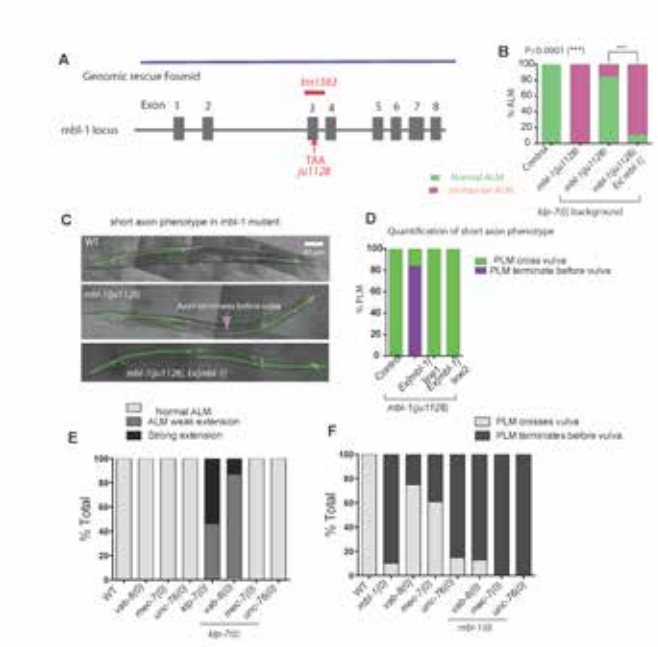


Figure 2: ***Legend:*** (A-B) ju1128 mutation map to mbl-1 gene. (C-D) Short axon phenotype in mbl-1 mutant. (E-F) Genetic interaction between mbl-1 and other other genes affecting axon growth.

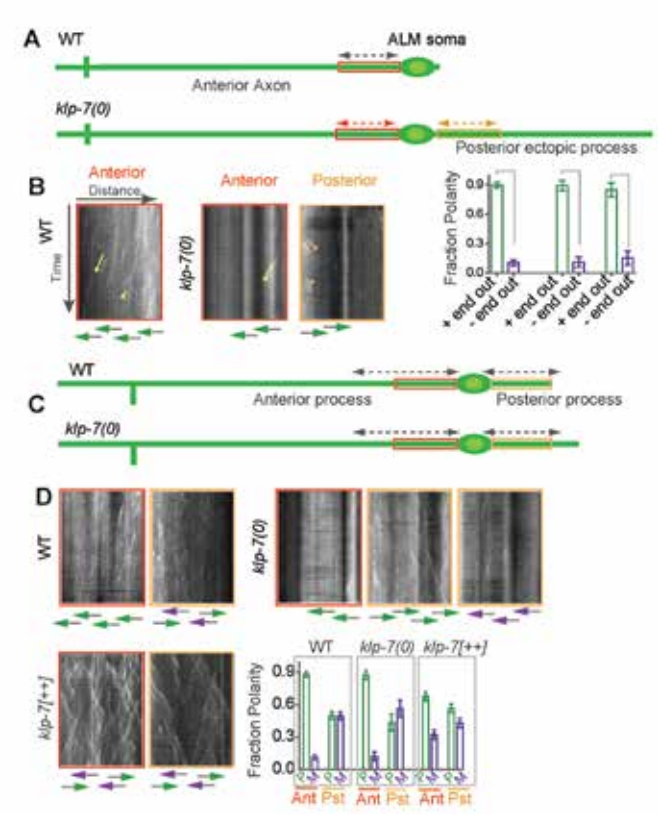


Figure 3: ***Legend:*** (A-B) In vivo imaging of growing microtubules and determination of their polaroity using EBP-2::GFP as reporter in ALM neuron. In klp-7(0), the ectopic processes have unipolar plus end out micritubels. (C-D) Similar analysis in PLM neuron. The short posterior process of PLM neuron has microtubules with mixed polarity, which is dependent on klp-7. KLP-7 is sufficient to induce mixed polarity in the microtubules in the anterior process of PLM.

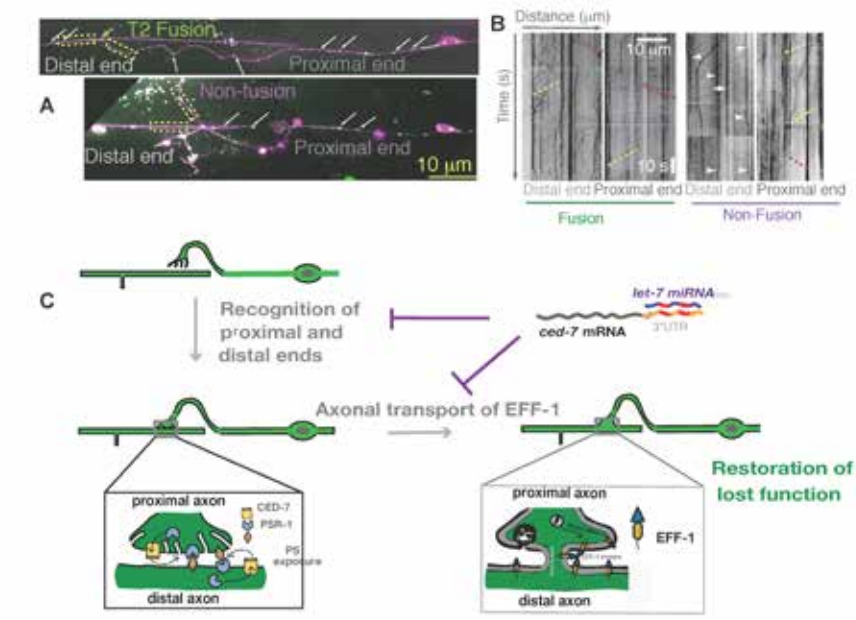


Figure 4: (A) Still images from time-lapse movies of PLM with GFP::RAB-3 using spinning disc confocal at 24-h post-axotomy. (B) Kymographs from the movies from the "ROIs" (yellow dotted box in a-a') placed on distal and proximal ends of fused neuron. Diagonal tracks represent events of anterograde (dotted yellow arrow trace) or retrograde (dotted red arrow trace) movements. (C) Represents the working model depicting how let-7 miRNA pathway negatively regulates axon fusion.

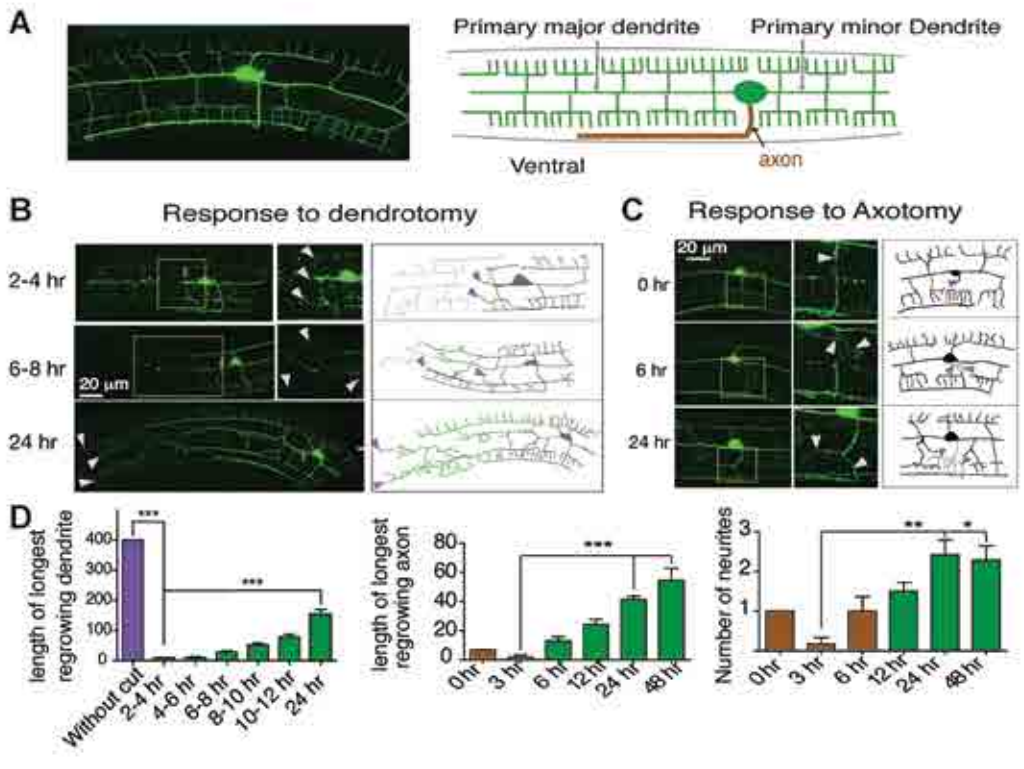


Figure 5: ***Legend:*** (A-B) Confocal image and schematics of PVD neuron with branched dendrites. (B) Primary dendrite regrows new processes from the cut dendrite tip. (C) After axotomy, new nerites grow towards ventral nerve cord. (D) Quantification and dendrite and axon regeneration.

Publications

1. Atrayee Basu, Shirshendu Dey, Dharmendra Puri, Nilanjana Das Saha, Vidur Sabharwal, Pankajam Thyagarajan, Prerna Srivastava, Sandhya Koushika, **Anindya Ghosh-Roy** (2017). Axonal fusion restores the gentle touch sensation lost due to neuronal injury. **Proc Natl Acad Sci U S A** 2017 November, 114 (47) E10206-E10215. https://doi.org/10.1073/pnas.1704372114 .

Presentations

1. **Anindya Ghosh Roy** "Microtubule organization in C. elegans neurons" in 'Current Trends in Intracellular Transport and Molecular Motors' (CTITMM) between Dec 21-23, 2017 at IIT-Bombay.
2. **Anindya Ghosh Roy** "Microtubule organization in touch neuron" 2nd India C elegans meeting held in NII-Delhi during 23rd to 26th Feb 2018
3. **Anindya Ghosh Roy** "Restoration of Functional Connectivity After Neuronal Injury" in Wellcome Researcher Meetings: Cell and Developmental Biology at Warwick Conference Centre, London during 15-16 March 2018.

Funding

- Wellcome Trust-DBT
  NBRC Core

Collaborators

Sandhya Koushika, TIFR, Mumbai, India
Sourav Banerjee, NBRC, India
Smarajit Polley, Bose Institute, Kolkata

Award

Wellcome Trust-DBT Intermediate fellowship-2013-2018
Ramalingaswami Fellowship-2013 (declined)

Degrees Awarded

i) Kasturi Biswas was awarded MSc degree.

ii) Sreyashi Chandra was awarded MSc degree

Interplay Between Metabolism and Inflammation: Implications in Glioblastoma Progression

Ellora Sen

Research Fellows
Sk. Touseef Ahmad
Pruthvi Gowda
Shruti Patrick
Kirti Lathoriya

Technical Assistant
Shanker Datt Joshi

Lab attendant
Rajesh Kumar Kumawat

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. In addition to aberrant metabolism, global epigenetic abnormalities in conjunction with numerous genetic alterations promote glioma progression. Also, accumulating evidences are linking metabolism and activation of inflammatory pathways in the progression of metabolic disorders. As metabolic reprogramming deregulates a number of cellular functions and since targeting metabolic remodelers is regarded as a potential anti-cancer strategy; the focus of our study is to dissect molecular circuitries that regulate expression of metabolic modelers to subsequently affect genes associated with cellular bioenergetics and immune evasive responses in GBM.

(i) The rapid glycolytic rate in glioblastoma is concomitant with elevated levels of hexokinase-2 (HK2) that catalyzes the first step of the glycolytic pathway. We observed that NAD+ dependent class III Histone deacetylase (HDAC) SIRT6 regulate expression of glycolytic gene HK2 under inflammatory conditions. HIF-1 dependent SIRT6 serves as the node in integrating metabolic signals under inflammatory conditions. SIRT6 availability establishes a condition whereby reconfiguration of the HK2 promoter chromatin structure makes it receptive to interaction with MZF1/SIRT6 complex, to favor a regulatory state conducive to diminished HK2 transcription, under inflammatory conditions. Since HK2 inhibition would restrict glucose utilisation at the very initial step, endeavors to target HK2 expression and functional activation by enhancing SIRT6 would serve as effective therapeutic strategy.

(ii) In addition to its ability to extensively metabolise glucose for aiding increased energy demands, cancer cells are also under oxidative stress associated with increased production of ROS. As considerable overlap between metabolism, inflammatory responses and redox homeostasis exists; we investigated the role of the pro-inflammatory cytokine IL-1β in connecting these processes. Our results highlight a non-metabolic role of HK2 as transcriptional coactivator of Nrf2 to regulate expression of xanthine oxido-reductase (XOR) under conditions of pro-inflammatory and metabolic stresses. This study underscore the importance of non-cannonical nuclear function of HK2 in the regulation of genes involved in redox homeostasis (Sheikh T et al, Journal of Biological Chemistry 2018, 293(13) 4767-4777).

(iii) 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) predicts longer survival. The ability of IDH1-MT to affect the immune component of gliomas has been associated with improved clinical outcomes. CD47 - a transmembrane glycoprotein that mediates a "self/don't-eat-me" signal on normal cells communicates with macrophages to prevent their phagocytosis. Upregulation of anti-phagocytic CD47 in malignancies facilitates immunological evasion of tumor cells, by rendering tumor cells resistant to immune surveillance. As IDH1-MT alters transcriptional program in gliomas; and since elevated CD47 levels have a direct bearing on the immune escape mechanism; the regulation CD47 in IDH1-

MT was investigated. Our findings suggested the involvement of pyruvate kinase isoform M2 (PKM2) in regulation of CD47 transcription, as diminished nuclear PKM2--catenin-TCF4 complex in IDH1-MT gliomas translated into diminished CD47 expression. Importantly, the increased ability of microglia to engulf IDH1-MT glioma cells may contribute in part to the differences in prognoses of IDH1-MT and IDH1 wild type.

(iv) Mutation in telomerase reverse transcriptase (TERT) promoter correlates with poor clinical outcome in GBM. Elevated expression of histone H3K27 methyltransferase - enhancer of zeste homolog 2 (EZH2) was observed in gliomas harboring TERT promoter mutations. Inhibition of TERT either pharmacologically or through genetic manipulation not only decreased EZH2 expression and fatty acid accumulation, but increased ataxia-telangiectasia-mutated (ATM) phosphorylation levels. A positive correlation was observed between TERT and EZH2. Importantly, TERT promoter mutant tumors exhibited greater microsatellite instability and heightened lipid accumulation. Coherent with in vitro findings, pharmacological inhibition of TERT by costunolide decreased lipid accumulation and elevated ATM expression in heterotypic xenograft glioma mouse model. Also, by bringing TERT-EZH2 network at the forefront as driver of dysregulated lipid metabolism, we have highlighted a non-canonical role of TERT in metabolic reprogramming and DNA damage responses in GBM.

(v) Not only does the differentiation of macrophages from monocytes involve adoption of glycolytic metabolism, but the impact of autophagy in the differentiation process is well documented. The importance of modulating autophagy in tumor-associated macrophages (TAMs) as a promising strategy for limiting tumor progression is being increasingly appreciated. On investigating the molecular links between metabolic restructuring and autophagy during monocyte differentiation, we observed a previously unknown reciprocal influence of SIRT6 and HK2 in regulating autophagy driven monocyte differentiation. By providing mechanistic insights into metabolism driven macrophage differentiation, our findings raise the possibility of pharmacologically manipulating the SIRT6-HK2 cross-talk to affect the differentiation potential of monocytes.

(vi) Gangliogliomas (GGs) are the most commonly diagnosed long-term epilepsy-associated tumors (LEATs). Global microarray based miRNA expression profile on a set of GGs indicated several microRNA to be differentially expressed in GG as compared to normal brain. As microRNA-217 was found to be the most down-regulated, the functional impact of miR217 in regulating GG related epilepsy was investigated. Our study indicated the involvement of miR-217–Caesin Kinase (CK)-2α cross talk in the regulation of known epileptogenic factors in GG. By showcasing the potentially valuable role of microRNAs in regulating GG related epilepsy, our study has underscored the role of miRNAs in linking metabolic and epileptogenic pathways in ganglioglioma.

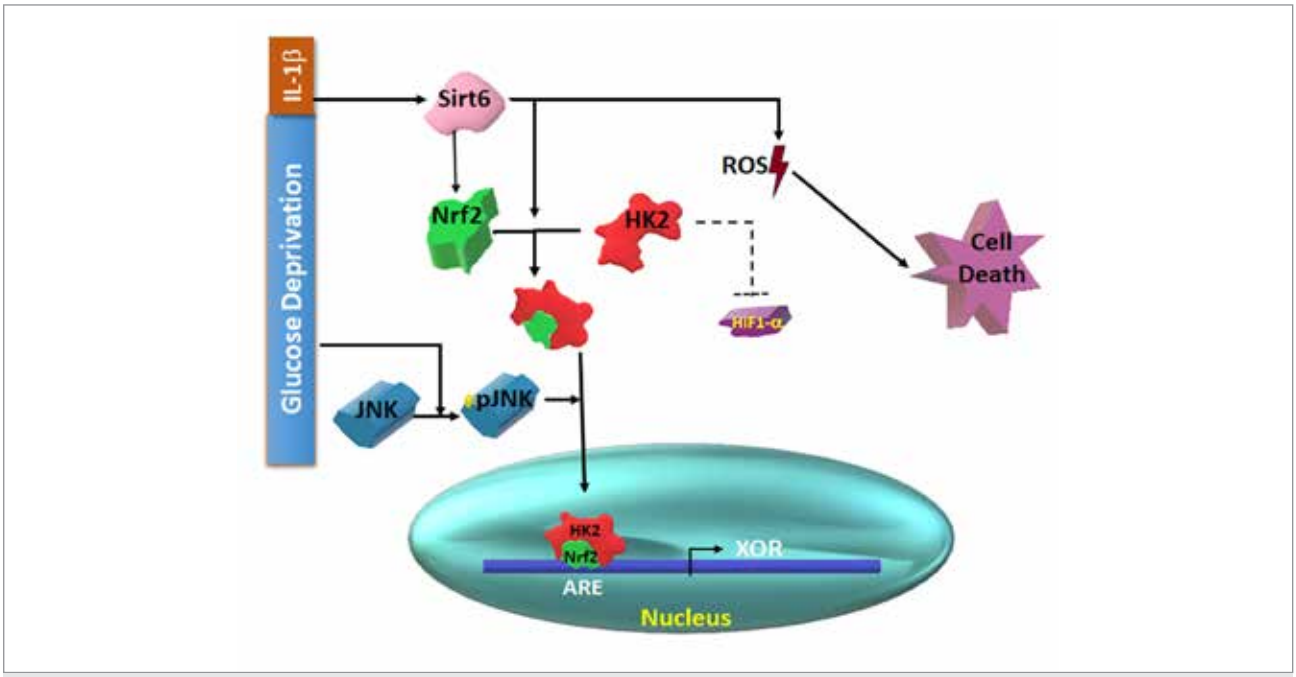


Figure 1: Non-metabolic role of hexokinase 2 (HK2) as regulator of gene expression. Schematic depiction of HK2 as a coactivator of Nrf2 in the regulation of XOR under inflammatory and metabolic stress. Journal of Biological Chemistry 2018

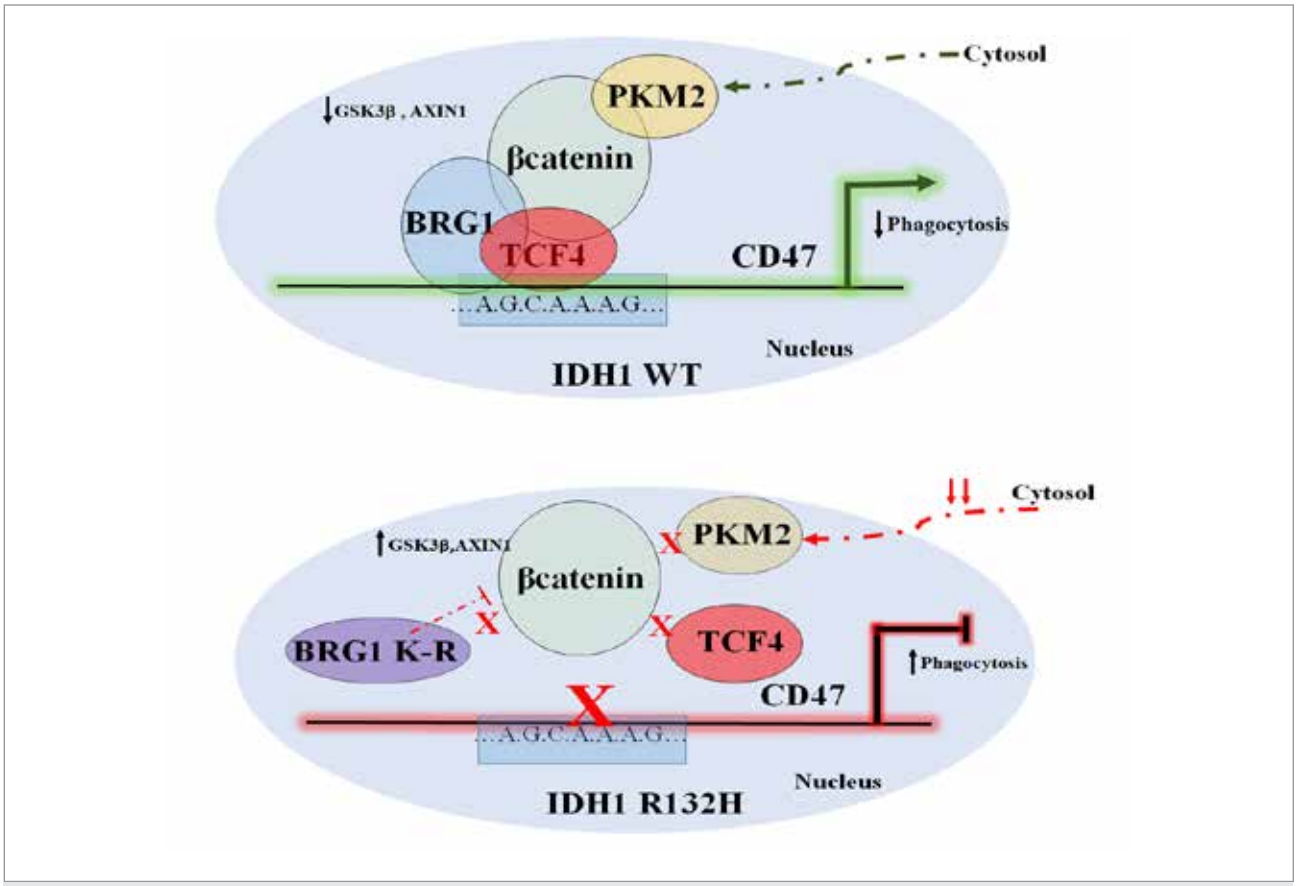


Figure 2: Regulation of CD47 in IDH1-MT gliomas plays a crucial role in innate immune surveillance. Model depicting the role of PKM2 and BRG1 in β-catenin/TCF4 dependent CD47 expression in IDH-WT and IDH1-MT glioma. Molecular and Cellular Biology, 2018, 38: 9

Publications

1. Sheikh T, Gupta P, Gowda P, Patrick S and Sen E. Hexokinase 2 and nuclear factor erythroid 2-related factor 2 transcriptionally coactivate xanthine oxidoreductase expression in stressed glioma cells. Journal of Biological Chemistry 2018, 293(13) 4767-4777.
2. Gowda P, Patrick S, Singh A, Sheikh T and Sen E. Mutant IDH1 disrupts PKM2--catenin-BRG1 transcriptional network driven CD47 expression. Molecular and Cellular Biology, 2018, 38: 9.
3. Gupta P, Sheikh T, Sen E. SIRT6 regulated nucleosomal occupancy affects Hexokinase 2 expression. Exp Cell Res. 2017; 357(1):98-106.
4. Ahmad F, Patrick S, Sheikh T, Sharma V, Pathak P, Malgulwar PB, Kumar A, Joshi SD, Sarkar C, Sen E. TERT-EZH2 network regulates lipid metabolism and DNA damage responses in glioblastoma. J Neurochem. 2017, 143(6):671-683.
5. Ankita Singh, Ellora Sen. Reciprocal role of SIRT6 and Hexokinase 2 in the regulation of autophagy driven monocyte differentiation. Exp Cell Res. 2017, 360(2):365-374.
6. Majumdar A, Ahmad F, Sheikh T, Bhagat R, Pathak P, Joshi SD, Seth P, Tandon V, Tripathi M, Saratchandra P, Sarkar C, Sen E. miR-217-casein kinase-2 cross talk regulates ERK activation in ganglioglioma. J Mol Med (Berl). 2017, 95(11):1215-1226.

Presentations

1. Ellora Sen. IL-1 induced cell death under glucose deprivation is dependent on SIRT6-Hexokinase 2 cross talk (Invited Talk). 5th Annual Meeting of the International Cytokine & Interferon Society (ICIS) Kanazawa, Japan, 2017.
2. Ankita Singh and Ellora Sen. Hexokinase 2 crosstalk in monocyte differentiation. (Poster). 5th Annual Meeting of the International Cytokine & Interferon Society (ICIS) Kanazawa, Japan, 2017.
3. Fahim Ahmad, Shruti Patrick, Vikas Sharma, Pathak P, Anupam Kumar, Shanker Datt Joshi, Chitra Sarkar and Ellora Sen. (Poster). Regulation of lipid metabolism in gliomas bearing TERT promoter mutation. Keystone Symposia Conference E4: Integrating Metabolism and Immunity, Dublin, Ireland, June 2017.

4. Ellora Sen. Interplay of inflammatory and metabolic networks in glioma progression. Indian Association of Cancer Research, Kolkata, February 2018.
5. Pruthvi Gowda, Shruti Patrick, Ankita Singh, Touseef Sheikh and Ellora Sen. Involvement of β-catenin transcriptional network in CD47 expression and phagocytosis of IDH1R132H glioma cells. Indian Association of Cancer Research, Kolkata, February 2018.
6. Ellora Sen. Therapeutic challenges in brain tumors. Extension Lecture Govt. College for Girls, Gurugram, February 2018
7. Ellora Sen. Tumor heterogeneity: Influence on therapeutic response Lady Brabourne College, Kolkata, February 2018
8. Ellora Sen. Inflammation-metabolism crosstalk in glioma: Deconstructing the network. Advanced Centre for Treatment, Research & Education in Cancer ACTREC, Navi Mumbai November, 2017.
9. Ellora Sen. Triathlon in glioma: Metabolism - inflammation - epigenetics interplay. University of Hyderabad November, 2017 .
10. Ellora Sen. Interplay between Metabolism and inflammation: Perspective on cancer dynamics. Institute of Life Sciences, Bhubaneswar October, 2017.
11. Ellora Sen. Metabolic reprogramming in Glioma: Influence of epigenetic landscape. 31st Annual Conference of Society for Neurochemistry, India (SNCI), Benaras Hindu University, Dept. of Zoology, September, 2017.
12. Ellora Sen. Metabolism, inflammation and epigenetics in glioma: Connecting the dots. Institute of Medical Sciences, Molecular Biology Unit, Benaras Hindu University, September, 2017.

Funding

- Inflammation regulated metabolic reprogramming: Implications in tumor progression. Unit of excellence in cancer biology DBT. (#BT/MED/30/SP11016/2015).
- Understanding inflammation driven regulation of macrophage function: Implications in glioblastoma progression. DBT. National Bioscience Award for Career Development, 2013.

Collaborators

Dr. Chitra Sarkar, AIIMS New Delhi

Awards

Ellora Sen, Milstein Travel Award International Cytokine & Interferon Society (ICIS), 2017.

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

Pankaj Seth

Research Fellows
Chitra MS Singal
Hriday S. Pandey
Reshma Bhagat
Priyanka Singh
Himali Arora
Bindu
Vini Tiwari

Project Assistants
Kanza Saleem
Anuradha Mehta
Sonia Narwal

Technical Assistants
Durgalal Meena
Naushad Alam

The advent of antiretroviral therapy has helped in prevention of large scale mortalities amongst AIDS patients and enhanced survival rates of HIV-1 infected individuals. Due to success and availability of anti-HIV therapies globally, HIV/AIDS is no longer a death warrant for people diagnosed with HIV/AIDS, however patients experience several side effects, health and mental issues. AIDS patients exhibit compromised cognitive and motor functions that are collectively termed as HIV-1 Associated Neurocognitive Disorders (HAND). Neurocognitive deficits in HIV-1/AIDS survivors are the major cause of morbidity. HIV-1 infections impacts mental abilities of up to 40% of AIDS patients, affecting quality of life of a large population of AIDS survivors. This is mostly because the combinatorial anti-retroviral therapy (cART), fails to clear the virus from the niche areas in body, including brain. The cART drugs have poor penetration into the brain due to its inability to cross the blood brain barrier. To overcome the problem of HAND and in search for a cure, basic and clinical neuroscientists are striving to eradicate HIV-1 from brain.

The frontal cortex, hippocampus and basal ganglia are amongst the most affected regions. Brain is comprised of two major types of cells, the glial cells and neurons. Glia and neurons are engaged in dynamic crosstalk to support optimal functioning of the human brain. The two main glial cells that harbour the virus in brain - are the microglia and astrocytes. Neuronal damage and death are mediated through infected astrocytes leading to perturbed cellular functioning and release of neurotoxic HIV-1 viral protein transactivator of transcription (Tat), along with other viral toxins. Role of astrocytes in harbouring HIV-1 and mediating neuronal damage is quite well established by us and others in the field. In fact some of the major contributions in this area have been from our laboratory that were reported in annual reports of previous years. We continue to investigate the cellular and molecular mechanisms for astrocyte mediated neuronal damage, the major cause neuronal damage in post cART era.

Ephrins and Eph receptors are important for neuron-glia communication and are present on astrocytes and neurons respectively. Eph receptors comprise of receptor tyrosine kinases (RTK) family of proteins. Ephrins are ligands that binding to the Eph receptors and elicit signaling in these cells. Eph receptors and ephrins have been long known to have function in axon guidance and retinotopic mapping during embryonic development. Lately its role in regulating dendritic spine morphology and glutamate levels in the synapses has been reported. Interaction of EphrinA3 with its receptor EphA4 alters spine density in neurons and glutamate levels in the synapse during neuron-astrocyte crosstalk. We are investigating the mechanisms of Eph-Ephrin signaling and its potential role in HIV-1-associated-pathogenesis in primary neuron-glia co-cultures of human origin. Our preliminary experiments with human astrocyte-neuron co-culture system reveal extensive expression of ephrin A3 in astrocytes and Eph A4 in neurons, which makes our co-culture of primary cells an apt model. Interestingly, the preliminary data suggest a possible interaction of ephrinA3 and ephA4 that lead to glutamate excitotoxicity in presence of HIV-1 Tat. This observation is highly relevant in the current context as glutamate induced excitotoxicity of neuron is well documented in HIV-1 neuropathogenesis. Our results suggest a comprehensible indication that their role could be a potential therapeutic target in HIV-1-related neuropathogenesis. Further integrative studies for delineating the functions of eph-ephrin signaling and miRNA

targeting them and its potential role in HIV-1 pathogenesis are in progress.

In addition to our work on HIV-1 neuropathogenesis, we are also investigating molecular mechanisms of Zika virus (ZV) induced microcephaly that is common in infants. Zika Virus induces quiescence in human neural stem cells (hNSCs) that impacts the pool of brain precursor cells that may result in microcephaly. We are investigating the underlying molecular mechanisms of ZV induced quiescence on NSCs using primary cultures of human fetal neural stem cells (fNSCs). Our experimental data using FACS suggests that among other ZV proteins, over expression of ZV envelope (E) protein in fNSCs causes most effective quiescence in human fNSCs and accumulates cells in G0/G1 phase of cell cycle as compared to other non-structural ZV proteins. We also performed global microRNA sequencing (miRNA Seq) of fNSCs following transfection with ZV E-protein and control vectors. The analysis of the miRNA Seq data suggests that E protein modulates miRNA circuitry of fNSCs that may have direct impact on proliferating abilities of fNSCs. These are being validated by PCRs and some functional assays. Our efforts are focused on to in-depth study to gain novel insights into ZV induced microcephaly.

Publications

1. E. Sen, A Majumdar, F. Ahmad, T. Sheikh, R. Bhagat, P. Pathak, S.D Joshi, P. Seth, V. Tandon, M. Tripathi, P. Saratchandra and C. Sarkar (2017). miR-217 - Casein Kinase-2 crosstalk regulates ERK activation in Ganglioglioma. Journal of Molecular Medicine 95(11):1215-1226.
2. A. Ahmad Naik, N. Patro, P. Seth and I.K. Patro (2017). Intra-generational protein malnutrition impairs temporal astrogenesis in rat brain. Biology Open Jul 15;6(7):931-942.

Book Chapter

3. M. Tewari, H.S Pandey and P. Seth (2017). Using Human Neural Stem Cells as a Model to Understand the "Science of Ashwagandha". In: Science of Ashwagandha: Preventive and Therapeutic Potentials. Springer-Nature, Eds - Sunil C. Kaul and Renu Wadhwa; pp 319-344.

Presentations

1. P. Seth (Invited Speaker), "A novel model for understanding virus induced neurodegeneration" at the 10th NIPER Symposium on Nano-based Therapies for Neurodegenerative Diseases at National Institute of Pharmaceutical Education and Research (NIPER), Raebareli, March 27-28, 2018.
2. P. Seth (Invited Speaker), "What we know and what we need to know about virus induced neurodegeneration" at the Faculty Development Program of Delhi Technical University, New Delhi, India, March 14, 2018.
3. P. Seth (Plenary Speaker), "Human Neural Stem Cells as Models to Understand NeuroAIDS" at World NeuroCongress-2017, Aligarh Muslim University, Aligarh, India, Dec 9-10, 2017.
4. P. Seth (Invited Speaker), "Role of glia mediated neuronal damage in HIV neuropathogenesis", a meeting on Challenges in Clinical Neuroscience: from bench to bed side, at AIIMS-Bhubneshwar, Bhubneshwar, India, November 1, 2017.
5. P. Seth (Invited Speaker), "Cellular and Molecular Mechanisms of HIV-1 Neuropathogenesis", 35th Annual meeting of Indian Academy of Neurosciences (IAN-2017), at Ravenshaw University, Cuttack, India, October 29-31, 2017.
6. P. Seth (Director Nominee), "Human neural stem cells – Cell based assays for CNS disorders", Brain Storming meeting for - Alternatives to Animals – Cell Based Assays, organized by ICMR, at NIOP New Delhi, India, October 11, 2017.
7. P. Seth (Guest Lecturer), "Insights into mechanisms of neurodegeneration in HIV-1/AIDS", at Era University, Lucknow, India, October 3, 3017.
8. P. Seth (Invited Speaker), "Astrocyte mediated neuronal damage in HIV-1 neuropathogenesis - how friends turn foe", at Society of Neurochemistry Conference - 2017, Banaras Hindu University, Varanasi, India, September 20-22, 2017.
9. P. Seth (Invited Faculty) at the IBRO/APRC Neuroscience School, "Human Neural Stem Cells as Model Systems to Understand Neurodegeneration", organized at Banasthali University, Banasthali, Rajasthan, India, August 21-26, 2017.
10. P. Seth (Invited Faculty) at the IBRO/APRC Neuroscience School "Molecular insights into HIV-1 neuropathogenesis", organized at National University of Singapore, Singapore, July 3-7, 2017.
11. P. Seth (Invited Speaker), "Neural Stem cells as a model to understand virus induced neurodegeneration", Central Inter-Disciplinary Research Facility, Mahatma Gandhi Medical College and Research Institute, Pondicherry, India, June 20, 2017.
12. P. Seth (Invited Speaker), "Use of Human Neural Stem Cells as a Model to Understand Neurodegenerative Disorders", hands-on workshop on Molecular Biology Techniques & Stem Cells in Human Health and Diseases at Amity Institute of Molecular Medicine and Stem Cell Research (AIMMSCR), Amity University NOIDA, India, June 12-16, 2017.

Funding

- This work is supported by NBRC Core, DST and DBT funds.

Collaborators

E. Sen, A. Basu and S. Sinha, NBRC, Manesar, India.

B. Sindhu, S. Sharma, and A. Singh, Civil Hospital, Gurgaon, India.

J. Sen, IIT-Kanpur, Kanpur, India.

V. Vaidya, TIFR, Mumbai, 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.

I. Patro, Jiwaji University, Gwalior, India.

A. Nath, National Institute of Health, Bethesda, USA.

D. Wang, National Institute of Health, Bethesda, USA.

S. Buch, University of Nebraska Medical College, Nebraska, USA.

Awards

Nominated and Elected as Fellow, of The National Academy of Sciences (India) (2017).

Nominated and Elected as Member of the Guha Research Conference (2017).

Therapy of Glioma: Role of Hypoxia and Aberrant Gene Expression

Subrata Sinha

National Post Doctoral Fellow
Akansha Jalota

Technician
P Manish

Hypoxia is an intrinsic feature of all tumours, especially of high grade glioma. Indeed hypoxic changes in histopathological features are a specific feature of Grade IV Glioblastoma. The molecular and cellular adaptations due to hypoxia and their resultant events are a focus of my laboratory. We have been addressing the role of hypoxia and its consequences in terms of gene expression, drug resistance and tumour progression. We had earlier identified FAT1, an atypical cadherin as a major contributor to the pro tumorigenic inflammatory pathway in glioma. FAT1 has been earlier identified by us to be a major activator of HIF1α transcription as well as to increased translational efficiency of its mRNA. We have now been working on its role in increasing the stemness and EMT properties, as well as cell invasion under hypoxia in glioma cells. We have been able to show that some of the downstream activators act through HIF1α, while others like Nestin, are independent of HIF1α.

We are also studying the factors upregulating FAT1 expression in some sets of high grade glioma. Another aspects relates to the abrogation of hypoxia induced drug resistance. A combination of a prototype Cox 2 inhibitor, NS398 and the and BCNU, a drug approved for glioma has been found to be useful in abrogating this resistance, as well as providing synergism during normoxia.

Tumpur targeting is another aspect of therapy. The Placental Isozyme of Alkaline Phosphatase (PLAP) is an oncofetal antigen which our group is working on. It is overexpressed in germ cell tumours of the brain (amongst other tumours). We had earlier generated a recombinant antibody that targeted PLAP. We have been now awarded a US patent for its promoter (along with an NFκB enhancer, that is active only where PLAP transcription is active.

Publication

1. Srivastava C, Irshad K, Dikshit B, Chattopadhyay P, Sarkar C, Gupta DK, **Sinha S**, Chosdol K. FAT1 modulates EMT and stemness genes expression in hypoxic glioblastoma. Int J Cancer. 2018 Feb 15;142(4):805-812. doi: 10.1002/ijc.31092. Epub 2017 Oct 17. PMID: 28994107.

Patent awarded

Placental Like Alkaline Phosphatase (PLAP) Promoter Mediated Cell Targeting **S Sinha**, I Khan, K Ahmad, K Chosdol and P Chattopadhyay. (Provisional Indian Patent No 1400/DEL/2013. Filed on 10 May, 2013, PCT/IB2014/061350 dated May 10, 2014, **US Patent Granted** - Application No.: 14/722,361 filed on September 03, 2015 (jointly by DBT, AIIMS and NBRC). **US Patent granted**, 16 Jan 2018.

Presentation

1. Subrata Sinha Molecular diagnostics and cancer assessment in the clinic. Biotechnology in Health care: Challenges and Opportunities. Jamia Hamdard University, New Delhi. 19 March 2017.

Collaborators

Dr. Kunzang Chosdol, Department of Biochemistry, AIIMS

Dr. Parthaprasad Chattopadhyay, Department of Biochemistry, AIIMS

Dr. Chitra Sarkar, Department of Pathology, AIIMS

Dr. P S Chandra, Department of Neurosurgery, AIIMS

Dr. Deepak Gupta, Department of Neurosurgery, AIIMS

Genetic Analysis of Dyslexia

Subrata Sinha

Post Doctoral Fellow
Dr. D Subhashree

Research Fellows
Bharat Prajapati
Teesta Naskar

Project Assistants
Mena Fatima
Aditi Charak

We are studying the genetics of dyslexia with a hope to finding clues to its biology. The etiology of dyslexia is multifactorial. It has a strong familial component. It affects 5-10% of the population, and could exist by itself or with other comorbidities, like ADHD. Genetic studies on dyslexia, both population and family based, have identified several susceptibility genes, but have not been able to identify any single predisposing genetic marker. However, varying degrees of replicability have been shown for several loci. We are working with Dr Nandini Singh who has identified three large extended multi-generational families from different endogamous groups which we ae studying in detail. Endogamous groups with their comparative genetic homogeneity help in better identification of genetic aberrations associated with the disability. We are studying three multi-generational families for genetic studies from three distinct groups, using exome sequencing followed by validation. Each family has distinct patterns of inheritance.

One pathway, involving a member of the proto-cadherin family (PCDHG) has been identified by us, where a block of 17 SNPs segregate with the disability in an autosomal dominant manner. This also has implications for the evolution of speech. The dyslexia associated allele is preponderant in primates and in Neanderthals, while the typical readers have the modern human preponderant form. Finally, we hope to get a better understanding of cell-cell signaling in brain development and the role of cadherin signaling in the same. The clear distinction between the genomes of modern humans and Neanderthals, chimpanzees and gorillas, also points to the role of PCDHG in the development of cognitive processes that enable the ability to read and write, a function that is unique to humans.

Our family studies also make it clear that dyslexia comprises of a number of endophenotypes, and the molecular basis of different affected individuals may vary considerably. These phenotypes are indistinguishable on routine testing. The genetic studies are being followed up for validation and functional characterization. In one instance, a novel function of a long non coding RNA linked to inherited dyslexia has been found to be related to neural progenitor differentiation.

Publication

1. Naskar T, Faruq M, Banerjee P, Khan M, Midha R, Kumari R, Devasenapathy S, Prajapati B, Sengupta S, Jain D, Mukerji M, Singh NC, **Sinha S**.Ancestral Variations of the PCDHG Gene Cluster Predispose to Dyslexia in a Multiplex Family. EBioMedicine. 2018 Feb;28:168-179. doi: 10.1 016/j. ebiom.2017.12.031. Epub 2018 Jan 9.PMID: 29409727.

Presentations

1. Subrata Sinha Combining genetics and cell biology in the study of dyslexia Amity University, NOIDA Campus, New directions in Cell Signalling, 21 April 2017.
2. Subrata Sinha Improved specificity by recombinant antibody targeting and tumor specific transcription. Inaugural talk. Gene therapy for curing rare genetic disorders. JNU, New Delhi 16 September 2017.

3. Subrata Sinha Dyslexia genetics opens a window to brain development and stem cell differentiation. Invited Talk MS University, Baroda, September 2017.
4. Subrata Sinha Studies in familial dyslexia help in identifying novel neurodevelopmental pathways; Keynote lecture. 31st Annual Conference of the Society of Neurochemistry; Banaras Hindu University, Varanasi 20 September 2017.
5. Subrata Sinha A study of familial dyslexia identifies a novel long non coding RNA essential for human neural progenitor cell differentiation. RNA Meet 2017. Banaras Hindu University, Varanasi 28, October 2017.
6. Subrata Sinha Translational neuroscience and its applications. Opening Talk, as President, Indian Academy of Neurosciences. XXXV Annual Meeting of the Indian Academy of Neurosciences, Ravenshaw College, Cuttack, Odisha, 29 October 2017.
7. Subrata Sinha Family studies in dyslexia: windows to neurobiology World Neurocongress Aligarh Muslim University, 9 December 2017
8. Naskar T , Faruq M, Kumari R, Khan M, Midha R, Devasenapati S, Prajapati B, Mukerji M, Singh N C and Sinha S India| EMBO Symposia titled "Big Data in biomedicine" held from 25-27 February, 2018 at Delhi, India Whole exome sequencing and genome-wide genotyping in a multiplex family identified novel genetic loci on chromosome 5 for dyslexia. (Best Poster Awarded).

Collaborators

Dr Nandini Singh, NBRC

Dr Pankaj Seth, NBRC

Dr Mitali Mukherjee, Institute of Genomics and Integrative Biology

Dr M Faruq, Institute of Genomics and Integrative Biology

Targeting Of Infectious Diseases: Generation of Neutralizing Antibodies to HIV1 Clade C

Subrata Sinha

In HIV encephalopathy cross clade neutralizing antibodies have an important role for reducing infectivity and in immunogen design. .HIV encephalopathy is increasing with the improvement in the outcome of HIV infections leading to more long term survivors. Using our expertise on recombinant antibody technology, we are collaborating with Dr Kalpana Luthra at AIIMS. Antibody libraries have been generated from peripheral blood lymphocytes of infected donors, including children, and several neutralizing antibodies have been obtained.

Publications

1. Khan L, Kumar R, Thiruvengadam R, Parray HA, Makhdoomi MA, Kumar S, Aggarwal H, Mohata M, Hussain AW, Das R, Varadarajan R, Bhattacharya J, Vajpayee M, Murugavel KG, Solomon S, **Sinha S**, Luthra K. Cross-neutralizing anti-HIV-1 human single chain variable fragments(scFvs) against CD4 binding site and N332 glycan identified from a recombinant phage library. Sci Rep. 2017 Mar 23;7:45163. doi: 10.1038/srep45163.
2. Kumar S, Kumar R, Khan L, Makhdoomi MA, Thiruvengadam R, Mohata M, Agarwal M, Lodha R, Kabra SK, **Sinha S**, Luthra K.CD4-Binding Site Directed Cross-Neutralizing scFvMonoclonals from HIV-1 Subtype C Infected Indian Children. Front Immunol. 2017 Nov 15;8:1568. doi: 10.3389/fimmu.2017.01568. e Collection 2017. PMID; 2918785.

Collaborator

Dr Kalpana Luthra, AIIMS

Yogita K. Adlakha

Molecular Details of Neurodevelopment Using Induced Pluripotent Stem Cells as Model

Project Assistant
Asha S C

The utmost requirement for cognition and behavior is appropriate differentiation, maturation and function of neuronal networks as interruption of these processes can lead to neurodevelopmental disorders such as autism, schizophrenia, Huntington's disease or intellectual disability. Consequently, the processes underlying neural development, including neural stem cell self-renewal and differentiation, fate specification, neuronal migration, maturation, and integration, are regulated by the dynamic interplay of several molecular factors and transcriptional programs have been well established to play major roles in neural development. 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 and development, maturation and 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 one of the most important tasks in neuroscience.

Several studies have revealed the essential roles for 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 one of the 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. With regard to its significant function 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.

Several reports using mouse stem cells establish that expression of miR-137 gets upregulated significantly when ESCs and neural stem cells differentiate into neuronal lineage. However, underlying molecular role of miR-137 in neural development remains elusive.

Since September 2017, we have made some novel discoveries in understanding the molecular regulation underlying effects of miR-137 as to how it regulates the dynamics of proliferation and differentiation. To pursue this goal, we derived induced pluripotent stem cells (iPSCs) from peripheral blood of healthy subjects in-house and generated neural stem cells (NSCs) from iPSCs which stained positive for neural stem cell markers i.e. Nestin and Sox2. Further, these NSCs were differentiated into neurons using neuronal differentiation media until day 21 and expression of neuronal markers including Tuj1, Map2, NeuroD1 and Ascl1 increased in the neuronal population. We assessed the expression profile of different miRNAs in PBMCs, iPSCs, NSCs and neurons using Taqman miRNA assay. Enhanced expression of miR-137 was observed in iPSCs and mature neurons as compared to NSCs. To investigate the role of miR-137 on proliferation and differentiation of NSCs, we modulated miR-137 levels in NSCs using overexpression and knock down experiments and immuno-stained the cells with Ki67

antibody, a well-accepted proliferation marker. Overexpression of miR-137 demonstrated significant reduction in Ki67 positive NSCs whereas knock down of miR-137 caused increase in Ki67 positive NSCs after 24 hrs of transfection. Next, for assessing the effect of miR-137 on NSC differentiation, transcript levels of different pro-neural genes were determined. Quantitative RT-PCR analysis revealed significant increase in the mRNA levels of ROBO2, SPOCK1 and DCX (pro-neural genes) after overexpression of miR-137. Transcript levels of neuronal markers i.e. Tuj1, Map2, NeuroD1 and Ascl1 were further increased in response to miR-137. Thus, miR-137 induces neuronal differentiation and reduces proliferation of NSCs. Since mitochondria dynamics alter during neural development, hence, based on our results, we hypothesize that this miRNA might be modulating mitochondrial dynamics to achieve enhanced neuronal differentiation and to achieve the necessary oxidative capacity. Mitochondrial dynamics include the interplay between biogenesis, fusion and fission. TargetScan, a bioinformatic target prediction software illuminated Myocyte Enhancer Factor 2A (MEF2A) as target gene of miR-137. MEF2A is an upstream regulator of PGC-1α which is the central mediator and controller of mitochondrial biogenesis. The mRNA levels of different genes involved in mitochondrial biogenesis and fusion were assessed in presence of miR-137. Overexpression of miR-137 decreases the transcript levels of MEF2A (Being target), PGC-1α while simultaneously increases TFAM levels in a dose dependent manner. Ectopic expression of miR-137 also increases mRNA levels of mitochondrial fusion gene MFN1 in a dose dependent manner. Thus, these experiments suggest alteration of mitochondrial dynamics by miR-137 to achieve neuronal differentiation of NSCs. Further experiments are in process to prove this hypothesis.

These findings would help in better understanding of the molecular mechanisms underlying miR-137 mediated cellular effects and illuminate its therapeutic potential for treatment of neurodevelopmental disorders.

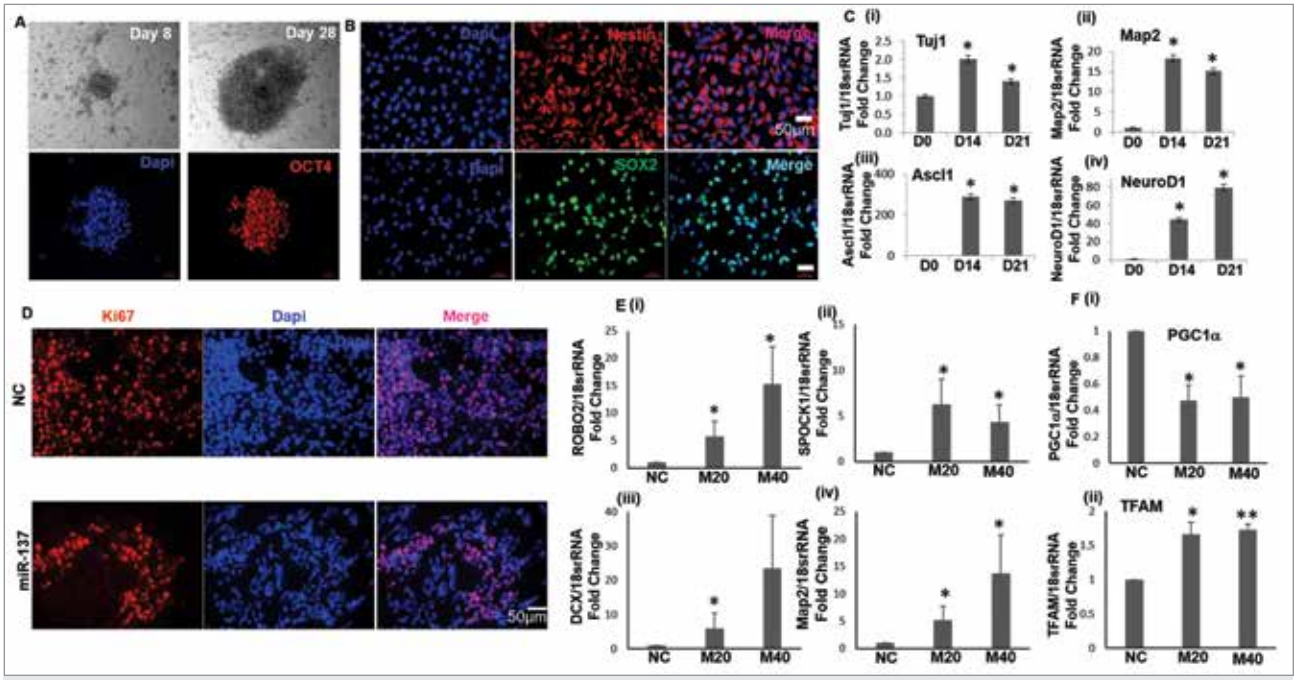


Figure 1: MiR-137 induces differentiation of NSCs by altering mitochondrial dynamics. A. Bright field images of PBMC derived iPSC colonies at day 8 and 28. These colonies stained positive for OCT4 (pluripotency marker). B. Neural stem cells stained positive for NSC markers including Nestin and Sox2. C. Neuronal markers increased upon differentiation of NSCs into neurons at subsequent days. D. MiR-137 reduces proliferation of NSCs as immunofluorescence shows less number of Ki67 (a proliferation marker)-positive cells in presence of miR-137. E. MiR-137 induces differentiation of NSCs as qRT PCR shows increased expression of proneuronal genes and neuronal marker at 20nM and 40nM concentration of miRNA. F. MiR-137 alters mitochondrial biogenesis upon differentiation of NSCs as qRT PCR shows increased expression of TFAM and reduced expression of PGC-1α.

Publications

1. **Adlakha Y.K.** and Seth P. (2017). The Expanding Horizon of MicroRNAs in Cellular Reprogramming. Progress in Neurobiology Jan 148:21-39.
2. **Adlakha Y.K.** and Swaroop A. (2018). Determination of Mitochondrial Oxygen Consumption in the Retina Ex Vivo: Applications for Retinal Disease. Methods in Molecular Biology 1753:167-177.

Presentations

1. Swaroop S, Sengupta N, **Adlakha YK,** and Basu A. HSP60 plays a regulatory role in IL-1b induced microglial inflammation via TLR4-p38 MAPK axis at International Society of Neuroscience meeting, Paris, France, August 20-24, 2017.
2. **Adlakha YK,** Shimada-Ishii H, Ratnapriya R, Brooks M, Gieser L, Meral Gunay-Aygun, Jacobson SG and Swaroop A. Transcriptome profiling of developing human retinal organoids at Keystone Symposia "Transcriptional and epigenetic regulation of stem cells" Olympic Valley, CA, USA, January 8-12, 2017.

Funding

- This work is supported by DST INSPIRE Faculty grant and NBRC Core funds.

Collaborators

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

A. Swaroop, National Institute of Health, Bethesda, USA.

Systems & Cognitive Neuroscience

Yoganarasimha Doreswamy

Neural Mechanisms of Spatial Navigation

Post Doctoral Fellow
Chetan Yadav

Research Fellows
Apoorv Sharma
Guncha Bhasin
Indrajit Nair
Shelly Paul
Shiladitya Laskar

Brain constructs an internal representation of the outside world and these stored representations are recalled as conscious memories, thus forming a spatial relation between an organism and its environment. The research focus of our laboratory is to understand how these representations are formed and the interaction amongst various brain regions during these processes. The components of spatial memory is encoded in hippocampus and related medial temporal lobe areas as a cognitive map of the external environment, resulting in efficient spatial navigation, orientation and successful interpretation of external sensory cues. Place cells, grid cells and head direction cells in specific brain areas such as hippocampus, subiculum, entorhinal cortex and subcortical areas play a very critical role in spatial memory and navigation, and acts as model system for deciphering the neural network mechanisms by which the brain constructs these cognitive representations from multimodal inputs. Spatially active place cells selectively fires at specific location in an environment, indicating that the hippocampus may form the locus of a cognitive map of the surrounding environment. Head direction cells present in various cortical and subcortical areas, fire selectively when the rat's head is pointed in a particular direction in allocentric space regardless of its location and serve as internal compass for the animal. Our lab is interested in understanding the dynamics of directional headings and the neural mechanisms of spatial navigation through behavioral and in vivo neurophysiological studies.

Network communication between hippocampus and neocortex is involved in transfer, storage, organization and retrieval of information associated with learning and memory. Encoding in hippocampal place cell network is governed by various extrinsic and intrinsic factors, including ongoing behavioral demand. Previous studies revealed that hippocampus plays an important role in reinforcement learning and hippocampal neurons can be modulated by reward parameters. Orbitofrontal cortex encode various aspects of motivational information and stimuli that predicts the reinforcement. Neurons in the orbitofrontal cortex code for chosen reward, reward value, reward magnitude, reward flavor and stimulus that predicts these rewards. Few studies have suggested the role of orbitofrontal cortex neurons even in encoding the spatial representation of reward. However, the interaction between hippocampus and orbitofrontal cortex (which encodes the current task space) during encoding of a change in spatial representation is unclear. Our ongoing studies are aimed to understand the information processing that occurs in or between hippocampus and orbitofrontal cortex during spatial association of different reward parameters (flavor and magnitude) and the processing dynamics when these associations are altered. In order to address the question, we have simultaneously recorded ongoing neural activity from CA1 region of the hippocampus and orbitofrontal cortex through in vivo multitetrode electrophysiolgical technique in awake behaving rodents. Preliminary results so far has suggested a strong coherence in reorienting the spatial representations in place cells recorded from hippocampal CA1 region. We have observed that the place cells coherently and dynamically bind to either the distal landmark or reward parameters, within a session. Further, there was rapid switching over in terms of their binding preference to either the environmental cues or reward parameters in orientation of spatial representation. These observations indicate that hippocampal representations are coherently modulated by the reward parameters. We have also observed orbitofrontal cortex neurons that are selectively encoding either a specific type of reward or reward expectations, and encoding generally the reward zone. Further analysis of orbitofrontal cortex neural activity and its interaction with hippocampal activity is under progress.

Previously, we found that the heading dynamics to be a scale invariant phenomenon (published last year). Self-organized criticality was quantified through power law distributions of event

measures. We showed that the distributions of Lateral Head Scanning (LHS) event magnitudes, durations and inter-event-intervals follow power law, suggesting that the heading dynamics is a self-organized critical system and plays an important role in information processing during spatial navigation. Further, we analyzed the LHS dynamics in two other behavioral states where the spatial exploration was altered, under partial anesthesia which induced a state of below normal spatial exploration, and under the influence of amphetamine which induce a hyperactive spatial exploratory state. The exploratory architecture under normal behavior state was found to be neither random (as in the case of partial anesthesia) nor too ordered (as in the case of amphetamine), supporting active decision making in normal rats reflected in their LHS dynamics. We observed that the power law exponents computed for probability distribution functions in case of partial anesthesia and amphetamine deviated from normal behavioral state by exhibiting below normal and above normal power law distributions. In order to achieve a critical state, the system has to be balanced somewhere between an inhibited and an excited states and our findings on power law exponents in altered behavioral states provided strong evidence for LHS behavior as an example of criticality during normal spatial exploration. During this period, we extended this study to understand the spatial exploratory pattern under various behavioral states by analyzing the movement trajectories of rodents. Our observations suggests that an imbalance between upstream and downstream movement speeds during these excursion events are responsible for driving the system towards criticality. Also, the imbalances in time, speed, distance covered and displacements in these excursion events during exploration were found to be scale free in nature, suggesting optimization of decision making efforts during the spatial navigation. Scale invariance for these events were observed only under normal behavioral state, diminished under partial anesthesia, and was out scaled under the influence of amphetamine.

We have also analyzed the influence of social vs physical cues on exploratory profiles during homing behavior in rodents, as the rodents are social animals and presence of a social partner might influencing the navigational strategies of the exploring rat. Recently, it has been reported that rats not only differentiate between "self" and "other" positions in social context, can also mimic corresponding neural correlates of "other" animal. Preliminary results from our experiments have indicated different exploratory profiles in presence of social cues as compared to physical cues, or when no cues were provided. The exploratory profiles were found to be sensitive to type and position of the cues, suggesting phase transitions in various environmental conditions.

Analysis of in vivo neural activity from different sub regions of the hippocampus in awake behaving rodents is under progress. The CA2 region of the hippocampal circuitry has unique connections and striking differences in its biophysical and synaptic properties as compared to CA3 and CA1 firing, thus influencing the spatial navigation mechanisms within the hippocampus. Accordingly, the synchrony between hippocampal sub regions and replay of firing sequence during sleep is being studied while the animals establish a spatial relation between self and the surrounding environment.

During this year, we have completed the analysis of in vivo neurophysiology studies to understand the network dynamics of neural representation in subicular complex region in various experimental conditions to identify the functional properties of subicular complex neurons during spatial navigation. We found an attractor-like network activity in subicular complex region, wherein different types of cells (place cells, grid cells, head direction cells and place x direction cells) coherently encode the environment as an ensemble. Further, the network representation showed switching of directional bearings to stable landmarks, indicating a distinct way of information processing at the subicular complex region.

Funding

- NBRC Core Funds

Soumya Iyengar

Research Fellow
Sandeep Kumar

Project Assistant
Alok Nath Mohapatra

Technicians
Arvind Singh Pundir
Ram Mehar
Krishan Sharma

Opioid Modulation of Song in Adult Male Zebra Finches

Songbirds such as zebra finches are excellent model systems to study the link between neuromodulatory systems in the brain and behavior. We have been studying the role of the endogenous opioid system in modulating the motivation of adult male zebra finches to produce female-directed songs. Different components of the song control system or neural circuitry dedicated to song learning, vocalization and auditory perception express μ-opioid receptors (μ-ORs), which are inhibitory G-protein coupled receptors known to bind the endogenous opioids (Fig. 1). The neural circuit connecting the song control nuclei HVC and RA (robust nucleus of the arcopallium) is important for vocalization. HVC also projects to Area X (a nucleus of the avian basal ganglia) which in turn projects to DLM (dorsolateral nucleus of the thalamus). Neurons in DLM project to LMAN (lateral magnocellular nucleus of the anterior nidopallium, avian pallium or cortex), which projects to both Area X and RA, forming loops within the SCS. Area X further projects to a region called the ventral pallidum (VP) which projects to the ventral tegmental area – substantia nigra complex (VTA-SNc). Earlier studies have shown that there is an increase in dopamine (DA) release by the VTA-SNc into Area X whenever male zebra finches sing to females. It has also been shown that LMAN and Area X are involved in context-dependent singing.

We had earlier demonstrated that systemic administration of the opioid antagonist naloxone led to decreases in female-directed (FD) as well as undirected (UD) song and changes in their acoustic features (Khurshid et al., 2010). These results suggested that naloxone administration led to a decrease in the motivation to sing, since μ-ORs were present in the VTA-SNc (ventral tegmental area - subtantia nigra complex) and other areas underlying motivation and reward.

To study the effects of opioid modulation on the AFP, different doses of naloxone were infused into Area X of adult males while they were singing to females. We found that there was an increase in their motivation to sing FD song during infusions of high doses of naloxone (200ng/ml) compared to the vehicle or lower doses of naloxone. While infusions of a low dose (100ng/ml) of naloxone were associated with a significant increase in the levels of DA in Area X, the levels of DA increased above baseline but were significantly lower during infusions of 200ng/ml naloxone. These results suggest that blocking μ-ORs in Area X can alter DA release downstream by the VTA and also affect the motivation to sing FD song (Fig. 2). We also found that there were significant changes in frequency as well as amplitude-related spectral features in the motifs sung by experimental birds, blocking μ-ORs in Area X led to changes in syllable length and spectral features such as frequency modulation, mean frequency, wiener entropy and pitch and pitch goodness. These findings suggest that besides affecting the motivation to sing, opioid neuromodulation in Area X can affect the vocal motor pathway, likely through the Area X→DLM→LMAN→RA circuit.

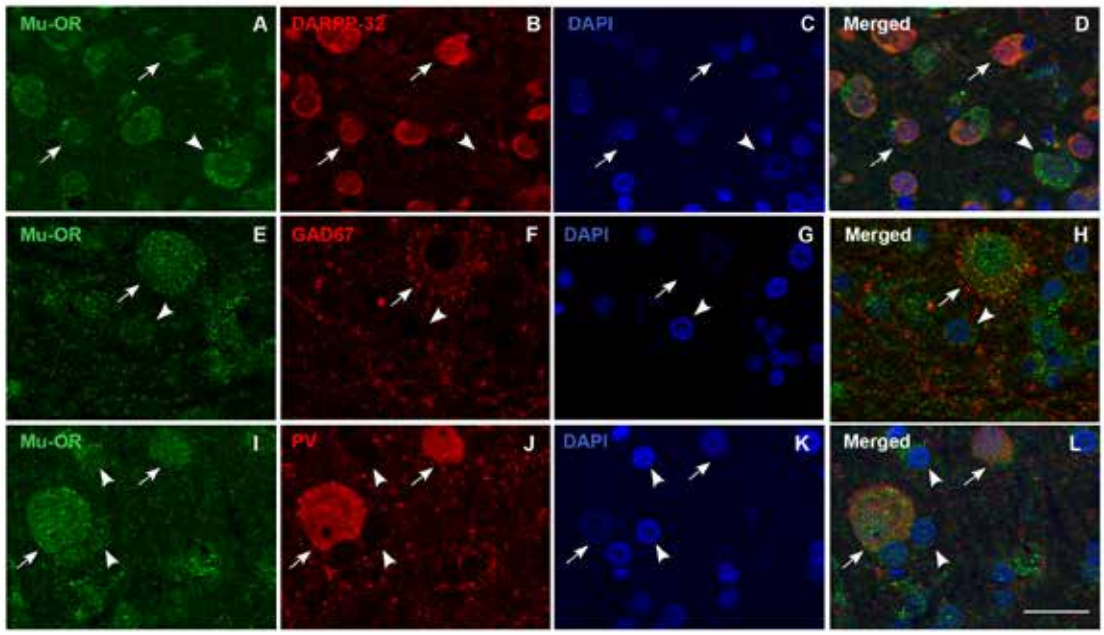


Figure 1: Both striatal (medium spiny) and pallidal neurons present in Area X express μ-ORs. (A) Striatal (medium spiny) neurons in Area X co-express μ-ORs (arrows) and the striatal neuronal marker, DARPP-32 (B, arrows). The arrowhead in (A) and (B) indicate a pallidal neuron which is positive for μ-ORs but not for DARPP-32, also seen in the merged image (D). Staining Area X with markers for pallidal neurons (GAD67 and parvalbumin) demonstrates that these inhibitory neurons in Area X co-express μ-ORs. The arrow in (E) indicates the expression of μ-ORs (green) in Area X with GAD67 (red, F) expressed by a GPe (globus pallidus externa) neuron seen in the merged image (H). A striatal neuron (arrowhead, E) expressing low levels of GAD67 (F and H) can also be seen. The lower panel (I) shows two μ-OR-labelled neurons (green, arrows) which are positive for parvalbumin (PV, red, J; merged image, L). Smaller striatal neurons in this panel (I – L) are indicated by arrowheads and are not PV-positive, DAPI in all sets of figures in the third column (C, G and K) labels neuronal nuclei. Scale bar, 20 μm.

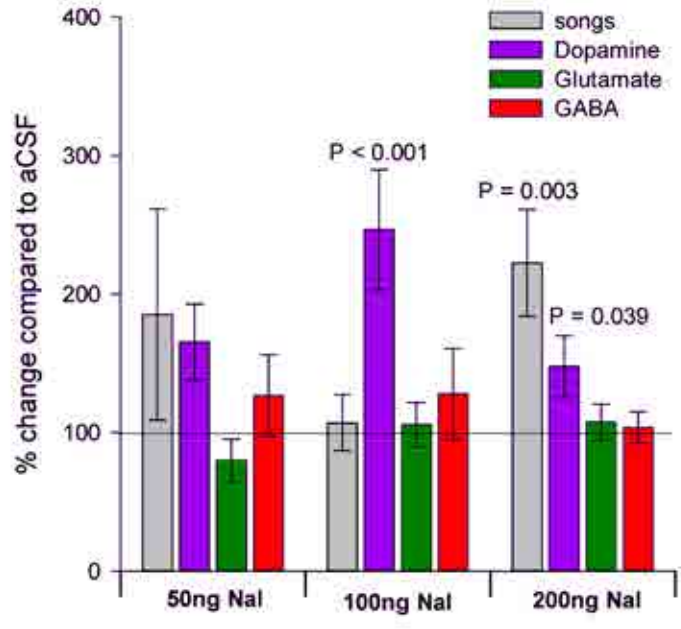


Figure 2: Effects of blocking μ-ORs in Area X on levels of neurotransmitters. A comparison of the number of FD songs and levels of different neurotransmitters after different doses of naloxone were infused into Area X. Levels of DA increased significantly compared to baseline levels when 100ng/ml of naloxone was infused into Area X. However, there were no significant changes in the number of songs accompanying this increase. In contrast, lower levels of DA were present in Area X after infusion of 200ng/ml naloxone (compared to DA levels at the 100ng/ml dose), which were accompanied by a significant increase in the number of FD songs (compared to the baseline).

Publication

1. Singh UA, Kumari M and Iyengar S (2018): Method for improving the quality of genomic DNA obtained from minute quantities of tissue and blood samples using Chelex 100 resin. Biological Procedures Online; 2018 Jun 1;20:12. doi: 10.1186/s12575-018-0077-6. eCollection 2018.

Presentations

1. S. Iyengar: Opioid Neuromodulation and the Motivation to Sing in Adult Male Zebra Finches. Invited lecture at the International Symposium on Biological Timing and Health Issues in the 21st Century (in conjunction with the IUSSTF-sponsored Indo-US Workshop and Symposium), Department of Zoology, University of Delhi, Indo-US Joint Center on Biological Timing, University of Delhi and The Indian Society for Chronobiology, February, 2017.
2. S. Iyengar: Development of the Human Auditory Cortex. Presented at the TEDx event organized by the Institute of Chemical Engineering, Mumbai, April, 2017.
3. S. Iyengar: Effects of Opioid Neuromodulation on Song Learning in Male Zebra Finches. Neurogroup meeting, Khandala, Pune, September, 2017.
4. S. Iyengar: Opioid Neuromodulation and Singing in Male Zebra Finches. XXVI International BioAcoustics Congress, Haridwar, October, 2017.
5. S. Iyengar: Opioid Modulation of Song Learning in Male Zebra Finches, 35th IAN meeting, Ravenshaw College, Cuttack, Odisha, October, 2017.
6. S. Iyengar: Neural Circuits, Singing and Song Learning in Zebra finches. Invited Lecture presented at 'The challenge to learn: New approaches to study the problem of stability vs. plasticity in the brain' Organized by the Indian National Science Academy and the German Academy of Sciences, Leopoldina, LV Prasad Eye Institute, Hyderabad, November, 2017.
7. Pundir AS, Singh UA, Ahuja N, Makhija S, Dikshit PC, Radotra B, Kumar P, Shankar SK, Mahadevan A, Roy TS, Iyengar S (2017): Establishment of Cortico-Cortical and Thalamocortical Circuits in the Human Auditory Cortex. Poster presented at the 104th Indian Science Congress, Hyderabad, 3rd - 7th Jan.

Funding

- This work was supported by a DST grant (SR/SO/AS-39/2009) "Opioid Modulation of song in Male Zebra Finches" awarded in 2010 and NBRC Core funds.
- DST Grant entitled "Effects of the δ-Opioid Receptor System on Singing and Song Learning in Zebra Finches", (EMR/2015/001422) received September 2016.

Collaborators

Prof. Neeraj Jain, NBRC.

Prof T. Velpandian, AIIMS

Hanuman Sharma, AIIMS

Dr Raghav Rajan, IISER, Pune

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

Neeraj Jain

Post Doctoral Fellows
Prem Chand
Ashok Kumar Datusalia

Research Fellows
John Thomas
Atanu Datta
Arti Kumari
Raghav Shankar

R&D Engineers
Meera Srikrishna (Until August 2017)
Arun E.V.R.

Junior Research Fellow
Dixit Sharma

Project Assistants
Kalpana Gupta (Until August 2017)
Shanah Rachel John (Until August 2017)

Technical Assistants
Mithlesh Kumar Singh
Hari Shankar

The research focus of our laboratory is to understand the organization and information processing in somatosensory and motor systems of the brain, and how the input deprivation via spinal cord injuries affects the brain regions involved in motor activity and sense of touch. We use a variety of animal model systems, including nonhuman primates, rats and mice, and techniques such as magnetic resonance imaging, (MRI) 2-photon imaging, electrophysiology, and neuroanatomy to understand the mechanistic underpinnings of effects of spinal cord injuries in different regions of the brain. Previously we have established that injuries to the dorsal columns of the spinal cord results in large-scale reorganization of the somatosensory cortex (Tandon et al., Journal of Neuroscience, 2009; Dutta et al., Brain Structure and Function, 2014), and specific changes in the movement representation in the primary motor cortex (Kambi et al., Journal of Neuroscience, 2011). Our studies in rats have also shown changes in the movement representation, such that the movements of the deefferented body parts are evoked from a larger region of the motor cortex (Tandon et al., European Journal of Neuroscience, 2013). More recently, we have investigated mechanisms of reorganization and plasticity in the cortex (Chand and Jain, Journal of Neuroscience, 2015) and medulla (Kambi et al., Nature Communications, 2014; Halder et al., Cerebral Cortex, 2017).

To further understand tactile information processing and the effects of injuries in the cortex we determined functional connectivity of the somatomotor regions of the brain using functional magnetic resonance imaging (fMRI). In area 3b of the primary somatosensory cortex, different topographic representations have different anatomical connectivity reflecting different functions of these body parts. However, previous reports have considered entire area 3b together for the functional connectivity studies. Therefore, to understand functional connectivity differences between different topographic representations in area 3b we determined resting state functional connectivity individually for different somatosensory representations. The entire area 3b was divided topographically into the face region (face 3b), the hand region (hand 3b), and the remaining medial region (med 3b) which includes trunk and lower limb representations. Resting state blood oxygenation level dependant (BOLD) signal fluctuations across these regions of interest in humans and macaque monkeys were acquired.

Resting state functional MRI scans were acquired in both anaesthetized normal macaques (n=5) and awake humans (n=23). Data was analysed following standard pre-processing steps. Functional MRI images were further processed and seed based region-to-region and region-to-brain correlation analysis was performed.

Our results show that different topographic representations in area 3b have different functional connectivity. In both the primate species, face 3b showed higher inter-areal connectivity than hand 3b and med 3b (Fig. 1 and Fig. 2). Only the face 3b showed significant connections to the second somatosensory cortex (S2) and the

ventral premotor area (PMv), whereas all the three representations showed strong functional connection with corresponding areas of the primary motor cortex or area 4 (Fig. 2). Within area 3b, strong inter-regional functional connections among the three sub-regions were observed in humans but not in macaques. In macaques, face 3b and med 3b showed bilateral functional connectivity but not the hand 3b (Fig. 3). Rather, hand 3b showed connectivity to hand region of area 4 in both the hemispheres. We also observed that the functional connections of any topographic representation from area 3b to corresponding area 4 were stronger than the within area 3b connections of these representations.

Thus our results show that the somatosensory network of entire area 3b is not uniform. Different topographic representations form distinct networks, which likely reflect differences in the functional usage of different body parts and its underlying anatomical connectivity. Further experiments are underway to determine how partial spinal cord injuries affect network properties of different representations in area 3b.

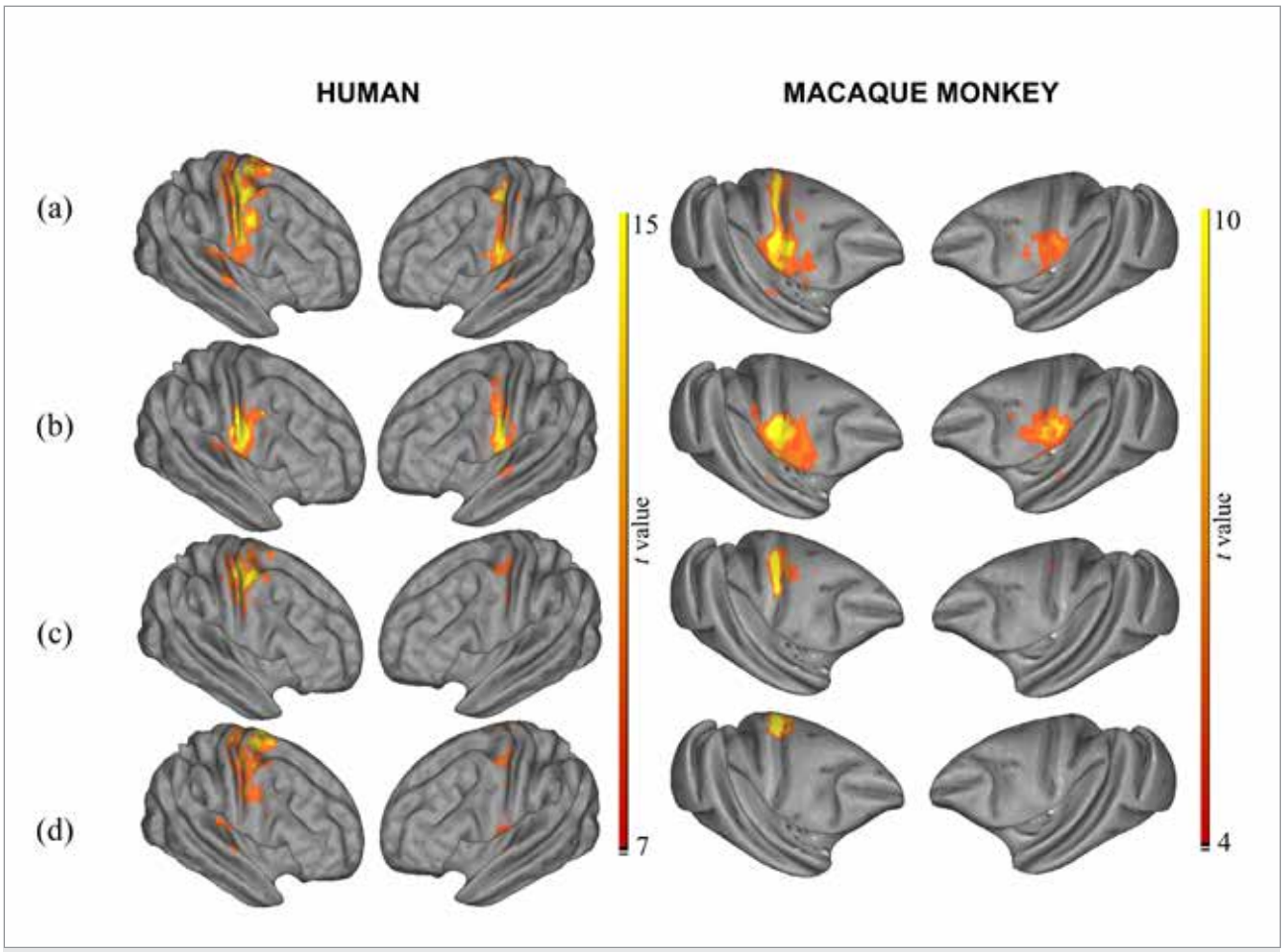


Figure 1: Functional connectivity network within somatosensory cortex of humans and macaque monkeys. Panels show bi-hemispherical view of connectivity pattern mapped on partially inflated cortical surfaces using region-of-interest (seed), which are (a) complete area 3b, (b) face representation in area 3b, (c) the hand representation and (d) rest of the medial region of area 3b. The t-values shown correspond to statistical significance of $p<0.05$ (FWE corrected) in humans, and $p<0.01$ (FDR corrected) in macaque monkeys.

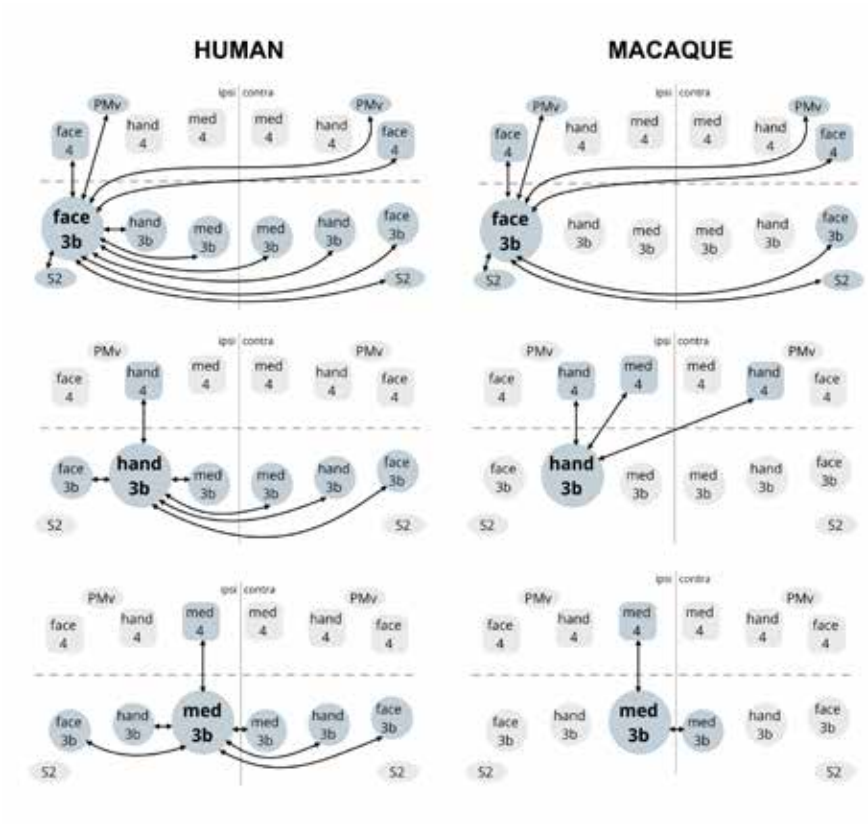


Figure 2: Highly correlated resting state functional connections of different representations in somatosensory area 3b across hemispheres in humans and macaque monkeys. Labels in circles denote area 3b representations, squares, area 4 sub-regions, and ovals other cortical areas. Darkly shaded regions shows statistically significant connectivity (one-sample t-test, p value< 10^{-2} for macaques, 10^{-5} for humans. Arrows in the schematic do not imply any directionality.

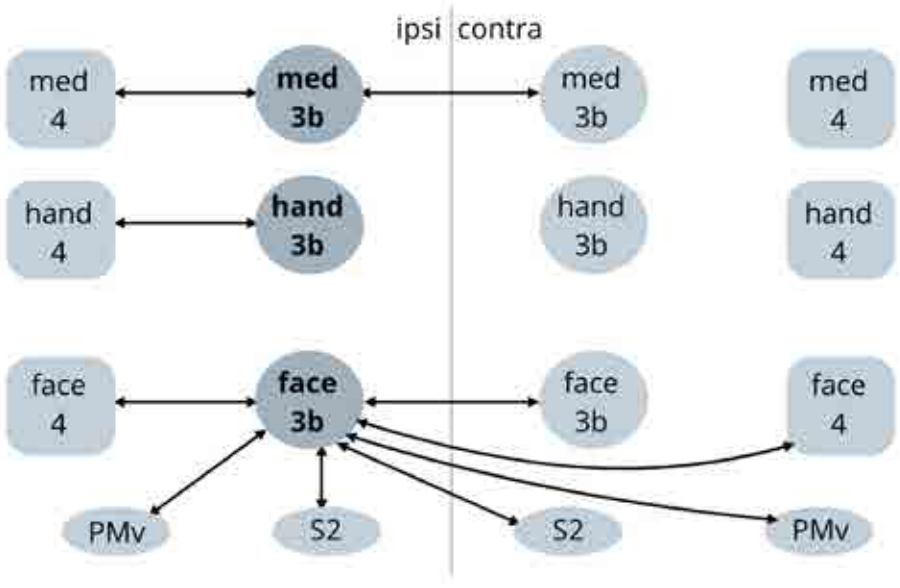


Figure 3: Functional connections of different area 3b representations that are present in both humans and macaque monkeys. Labels in the circles denote area 3b representations; in squares, area 4 representations; and in ovals, other cortical areas. One-sample t-test, p value< 10^{-2} (macaque), p value< 10^{-5} (human). Arrows in the schematic do not imply any directionality.

Publications

1. Priyabrata Haldar, Niranjan Kambi, Prem Chand and Neeraj Jain (2017) Altered expression of reorganized inputs as they ascend from the cuneate nucleus to cortical area 3b in monkeys with long-term spinal cord injuries. Cerebral Cortex 1-17. doi: 10.1093/cercor/bhx256.
2. Kamal Sharma, Neeraj Jain and Pabir K Pal (2017). Telemanipulation of a robotic arm using EEG artifacts. International Journal of Mechatronics, Electrical and Computer Technology 7: 3595-3609; DOI: IJMEC/10.225148.

Presentations

1. Neeraj Jain, Shanah Rachel John and Priyabrata Halder (2017) 'Topography in the mouse motor cortex is a mosaic'. Neuroscience 2017, Annual Meeting of the Society for Neuroscience, USA. Nov 11-15, Washington DC, USA.
2. Neeraj Jain 'Transformation of the reorganized inputs as they ascend from the brain stem nuclei to the cortex following partial spinal cord injuries' at Leopoldina-INSA Symposium "The challenge to learn: New approaches to study the problem of stability vs. plasticity in the brain", LVPEI, Hyderabad, India, November 28-29, 2017.
3. Neeraj Jain 'Cortical Plasticity Reflects Subcortical Reorganization', invited talk at Department of Psychology, University of Wisconsin–Madison, USA, November 20, 2017.
4. Neeraj Jain 'Subcortical Origins of Cortical Plasticity', in Neuroscience Seminar Series at Department of Psychology, Vanderbilt University, Nashville, USA, November 16, 2017.
5. Neeraj Jain 'Animal Models in Neuroscience Research', at the workshop on 'Handling and Care of Laboratory Animals', NBRC, Manesar, October 24-27, 2017.
6. Neeraj Jain 'Rostral Motor Area: a new area in the rat motor cortex' at 2nd NeuroGroup meeting, Khandala, Sept. 8-9, 2017.
7. Neeraj Jain 'Brain plasticity at systems level: Effects of spinal cord injury' at 'Neuroscience across scales, an International Meeting organized at National Center for Biological Sciences, Bangalore, July 17-19, 2017.
8. Neeraj Jain 'Animal models for brain research' and 'Spinal cord injuries and brain plasticity' at National workshop on 'Recent Updates on Brain Research', at SDM College of Ayurveda and Hospital, May 26-27, 2017.

Funding

- This work is supported by a grant from Department of Biotechnology, and NBRC Core funds.

Collaborator

Prof P Raghunathan, NBRC

Protein Modifications in Synaptic Plasticity and Memory

Shiv K Sharma

Research Fellows
Kautuk Kamboj
Biswaranjan Sahoo
Apurva Agrawal
Tushar Arora

Post Doctoral Fellow
Deepali Singh

Project Assistants
Deborah Daphne
Subhajit Jana

Laboratory Attendant
Narayan

The focus of my laboratory is to understand the mechanisms of memory formation, and the mechanisms that go wrong in the memory impairment conditions. Thus, my laboratory is working on two related projects. The first project relates to the changes in regulatory molecules that play critical roles in synaptic plasticity and memory. The second project is focused on Alzheimer's disease and Down syndrome. Alzheimer's disease is the most common form of dementia in the elderly population. Down syndrome is a developmental disorder that shows cognitive deficits in addition to other features. Memory deficit is observed in both disorders. We have made substantial progress in both the projects. The research personnel mentioned above are working on these projects. I will describe research progress in the first project that examines posttranslational changes in regulatory molecules which are established to play important roles in synaptic plasticity and memory formation.

One of the fundamental functions of the brain is to make memories, and recall them when needed. We know that memory plays critical roles in our daily activities. But, its importance is better appreciated in the situations when there is memory impairment. Thus, a lot of attention has been focused on understanding the processes that contribute to memory formation. My laboratory has significantly contributed to understanding of processes that are involved in synaptic plasticity and memory formation. We use multi-disciplinary approach of molecular, electrophysiological and behavioral studies to get a comprehensive view of mechanisms of memory formation. Previously, we have discussed our studies that included molecular analyses of signaling pathways, electrophysiological recordings of neuronal responses and memory tasks in behaving animals.

Neuronal synapses are able to change their strength in response to experience. This process is referred to as synaptic plasticity. Long-term potentiation (LTP) is a kind of synaptic plasticity that is reflected in a rather persistent increase in synaptic strength. LTP is widely studied as a cellular basis of memory formation. Research over several decades has shown that signaling molecules critically regulate LTP and memory. These include the molecules that bring about phosphorylation, acetylation and other modifications in proteins. Protein modifications regulate gene expression and protein synthesis also, the processes that are required for long-lasting forms of synaptic plasticity and long-lasting memory. Among the several kinases that bring about phosphorylation event, the role of extracellular signal-regulated kinase (ERK), has received considerable attention with respect to its role in synaptic plasticity and memory. ERK is one signaling molecules that regulates several processes relevant for synaptic plasticity and memory including gene expression and protein synthesis. The role of ERK in memory is evident from the fact that ERK activity is regulated by stimuli that are relevant for LTP and memory, and the fact that inhibition of ERK activity blocks LTP as well as memory formation.

Given the critical role of ERK in synaptic plasticity and memory in diverse systems, significant effort is directed towards understanding the mechanisms involved in ERK activation. However, the processes that regulate ERK activation are not fully understood. We have previously reported sustained activation of ERK by KCl-induced depolarization of hippocampal slices. We further investigated, in great detail, the processes that regulate sustained ERK activation. In another study, we investigated mechanisms of sustained ERK activation by cyclic adenosine monophosphate pathway.

We have extended our study on sustained ERK activation. These studies use hippocampal slices since hippocampus is established to be an important brain region for formation of different kinds of memories. We are examining whether activation of another kinase that also plays crucial roles in synaptic plasticity and memory, induces sustained ERK activation. We pharmacologically activate the kinase under study, and examine ERK activation immediately, or at the sustained time point, after treatment to activate the kinase under study. ERK activation is examined using antibodies which recognize ERK when it is phosphorylated and thus activated. We previously reported that activation of the kinase pathway under study led to sustained ERK activation in the hippocampal slices.

We further examined the processes that govern sustained ERK activation by the kinase pathway under study. Our results show that new RNA and protein synthesis processes play critical roles in sustained ERK activation. We have also identified a step in the protein synthesis process that critically regulates sustained ERK activation. An interesting finding is that a growth factor may play critical role in sustained ERK activation. This suggests that activation of the kinase pathway under study may lead to synthesis of a growth factor which then keeps ERK activated for a longer duration. Thus, there seems to be a feedback mechanism that leads to sustained ERK activation.

It is possible that the sustained ERK activation could play an important role in synaptic plasticity and memory formation since it could regulate processes such as gene expression and protein synthesis for a longer duration. It should be noted that these processes are critically required for long-lasting LTP and memory.

Presentations

1. Shiv Kumar Sharma Delivered a lecture at International Conference on Advances in Dementia & XXI National conference of ARDSI, 22-24 September 2017, Kolkata.
2. Shiv Kumar Sharma Delivered a lecture in the Colloquium on "Sharing resources for quality higher education and research", 14th October, 2017, Central University of Haryana.

Funding

- This work is supported by NBRC Core.

Computational Neuroscience & Neuroimaging

Neuro-cognitive Network Mechanisms Using Multimodal Neuroimaging

Arpan Banerjee

Post-doctoral fellows
Dr. Dipanjan Ray
Dr Amit Naskar
Dr Soibam Shyamchand Singh

Research Fellows
Amit Ranjan
Neeraj Kumar
Priyanka Ghosh
G. Vinodh Kumar
Anagh Pathak
Ritu Moni Borah

Project Assistants
Anirudh Vattikonda
Nilambari Hajare
Shrey Dutta
Siddharth Talwar

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, 2017 - March, 2018. The overarching goal of these projects is to develop an understanding for the neurobiological mechanisms of multisensory integration and basic sensory function.

Neurodynamic mechanisms underlying inter-individual and inter-trial variability of cross-modal perception

A widely used experimental design in multisensory integration is the McGurk paradigm that entails illusory (cross-modal) perception of speech sounds when presented with incongruent audio-visual (AV) stimuli. However, the distribution of responses across trials and individuals is heterogeneous and not necessarily everyone in a given group of individuals perceives the effect. Nonetheless, existing studies in the field primarily focus on addressing the correlation between subjective behavior and cortical activations to reveal the neuronal mechanisms underlying the perception of McGurk effect, typically in the "frequent perceivers". Additionally, a solely neuroimaging approach does not provide mechanistic explanation for the observed inter-trial or inter-individual heterogeneity. In the current study we employ high density electroencephalogram (EEG) recordings in a group of 25 human subjects that allow us to distinguish "frequent perceivers" from "rare perceivers" using behavioral responses as well as from the perspective of large-scale brain functional connectivity (FC). Using global coherence as a measure of large-scale FC, we find that alpha band coherence, a distinctive feature in frequent perceivers is absent in the rare perceivers. Secondly, a decrease in alpha band coherence and increase in gamma band coherence occur during illusory perception trials in both frequent and rare perceivers. Source analysis followed up with source time series reconstructions reveals a large scale network of brain areas involving frontal, temporal and parietal areas that are involved in network level processing of cross-modal perception. Finally, we demonstrate that how a biophysically realistic computational model representing the interaction among key neuronal systems (visual, auditory and multisensory cortical regions) can explain the empirical observations. Each system involves a group of excitatory and inhibitory Hindmarsh Rose neurons that are coupled amongst each other. Large-scale FC between areas is conceptualized using coupling functions and the identity of a specific system, e.g., visual/ auditory/multisensory is chosen using empirical estimates of the time-scale of information processing in these systems. The model predicts that the disappearance of alpha band coherence observed in rare perceivers stems from a negligible direct A-V (audio-visual) coupling however, an increase in indirect interaction via multisensory node leads to enhanced gamma band and reduced alpha band coherences observed during illusory perception. Overall, we establish the mechanistic basis of large-scale FC patterns underlying cross-modal perception (Fig 1).

Organization of effective networks along the dual stream pathways of visual information processing

Dual stream hypothesis is a pre-eminent theoretical approach to conceptualize visuo-motor information processing. Subtle variations of the model exist often leading to fundamentally divergent explanations of underlying neural mechanisms. For example, the Mishkin-Ungerlieder (MU) model suggests that the input information decides the neural pathway for processing. Position related information ('where') takes the dorsal stream comprising MT/V5 and parietal cortex whereas finer feature processing ('what') comprising color, face, etc. takes the ventral stream involving V4 and inferior temporal areas. Concomitantly, the Milner-Goodale (MG) model suggests that the task goal decides the processing pathway, with dorsal stream areas needed for visual (sensory) guidance of action that doesn't involve active perceptual processing whereas the ventral stream is recruited for perceptual object processing. No single study has evaluated the viability of each model in an overarching experimental design. Furthermore are the models subject to neuroplastic changes is an open question. We addressed these issues in an fMRI experiment involving 20 right-handed human volunteers (20-34 years, 12 females). Participants were scanned with TR=2s, TE= 35ms, flip angle =90° while each of them was performing 3 visual perception tasks and 3 visuo-motor action tasks inside a 3T MRI scanner. For, both categories, 2 tasks were designed to involve "what" (color, face) processing and 1 task required processing of "where" (position) information. The fMRI scans were repeated after seven days of the practice session outside the scanner to explore the neuroplastic changes. In all perception tasks, bilateral ventral stream areas are activated, whereas all action tasks shows prominent activations in bilateral primary visual cortices, ventral and dorsal stream regions. Unlike color and face perception, position perception elicits additional activations in dorsal stream areas. Deactivation of BOLD signals were observed in medial dorsal stream areas and in few primary visual and ventral stream regions. Analysis of reaction times established the positive effect of practice. Number of voxels activated in response tasks decreased with practice, primarily in left hemisphere.

Dynamic causal modeling analysis suggested that, during response tasks, the visual information flows from primary visual cortex to ventral and dorsal streams, and finally to motor cortical area, favouring an input based conceptualization of dual stream model. DCM also indicates that, during position perception, premotor cortex drives dorsal stream, suggesting some form of motor simulation is required for comparing the position of two dots. DCM also explains the distinctive deactivation found in the perception tasks borrowing the concepts of predictive coding framework. Thus, overall, the present study suggests the need of an updated version of the dual stream model, integrating the theoretical frameworks of mirror neurons and predictive coding theory (Fig 2)

Spatiotemporal boundaries of the P300 complex across multiple sensory modalities

P300 complex is associated with cognitive processes such as attention and memory. An oddball paradigm in which, a deviant stimulus is infrequently presented amidst a sequence of standard repetitive stimuli, typically exhibits a positive peak in the event related potential recording via electroencephalogram (EEG) at a latency of around 300ms from the onset of the stimulus. Many source localization techniques have been implemented over the years to localize the underlying neural generators of the P300 suggesting involvement of frontal, temporal and parietal regions. Although, different paradigms and sensory modalities (e.g. visual, auditory, somatosensory) have been used, the spatiotemporal boundaries of the cortical generators underlying unisensory and mulitsensory P300 remains poorly understood. Do the P300 complex for different sensory modalities (uni- or multisensory) have common cortical sources or is it generated by areas responsible for the processing of corresponding sensory modality?

We address these questions using EEG recordings of 12 human volunteers of ages from 20 to 30. 3 blocks of different combinations of sensory modalities were presented including unisensory blocks: auditory only, visual only and multisensory blocks: audio-visual. The auditory condition consists of two separate tones, one of which is a high frequency deviant stimulus and the other of a low frequency. Analogously, the visual stimuli consist of 2 classes of trials, a red triangle (deviant) and the other, a blue square (standard). Similarly, audio-visual (AV) stimuli consist of deviant videos constituting high frequency tone and a red triangle among a set of standard repetitive videos that consisted of lower frequency tone and blue square. Each condition consists of 14% trials constituting deviant trials and the rest as standard trials. Duration of the stimuli was 200ms with an ISI of 400ms. Stimuli were presented via Presentation (Neurobehavioral Systems Inc.) software and 64 channel EEG data was recorded at a sampling rate of 1 KHz. Additionally, a 3D coordinate tracking system, Polhemus was used to estimate respective electrode positions for co-registration with individual participants structural MRI data collected using a 3T Philips Achieva scanner.

Presence of P300 complex was verified using t-test between deviant and standard trials. 2 peaks of the P300 complex in visual condition (P300 b,c) and 3 peaks in the audio and AV conditions (P300 a,b,c) were identified. Moreover, the onset of the P300 complex in the AV condition was observed to be earlier compared to audio and visual conditions. Larger amplitude of audio P300 peaks were detected, while similar amplitudes were noted for visual and AV conditions. Sources of each peak were computed using eLORETA, for each subject and the overlap between the significant sources was assumed to be more probable source underlying the P300 response. Left middle temporal gyri were found to be the common sources of all the peaks across all the conditions. Additionally, an overlap was observed in the right superior temporal area for audio P300a and AV P300a, and the left lingual gyrus at visual P300b and AV P300b. Right lateralization in the occipital cortex for unisensory P300b was detected and left lateralization for multisensory P300b. A considerable overlap of sources for the P300c across multisensory and unisensory conditions was found.

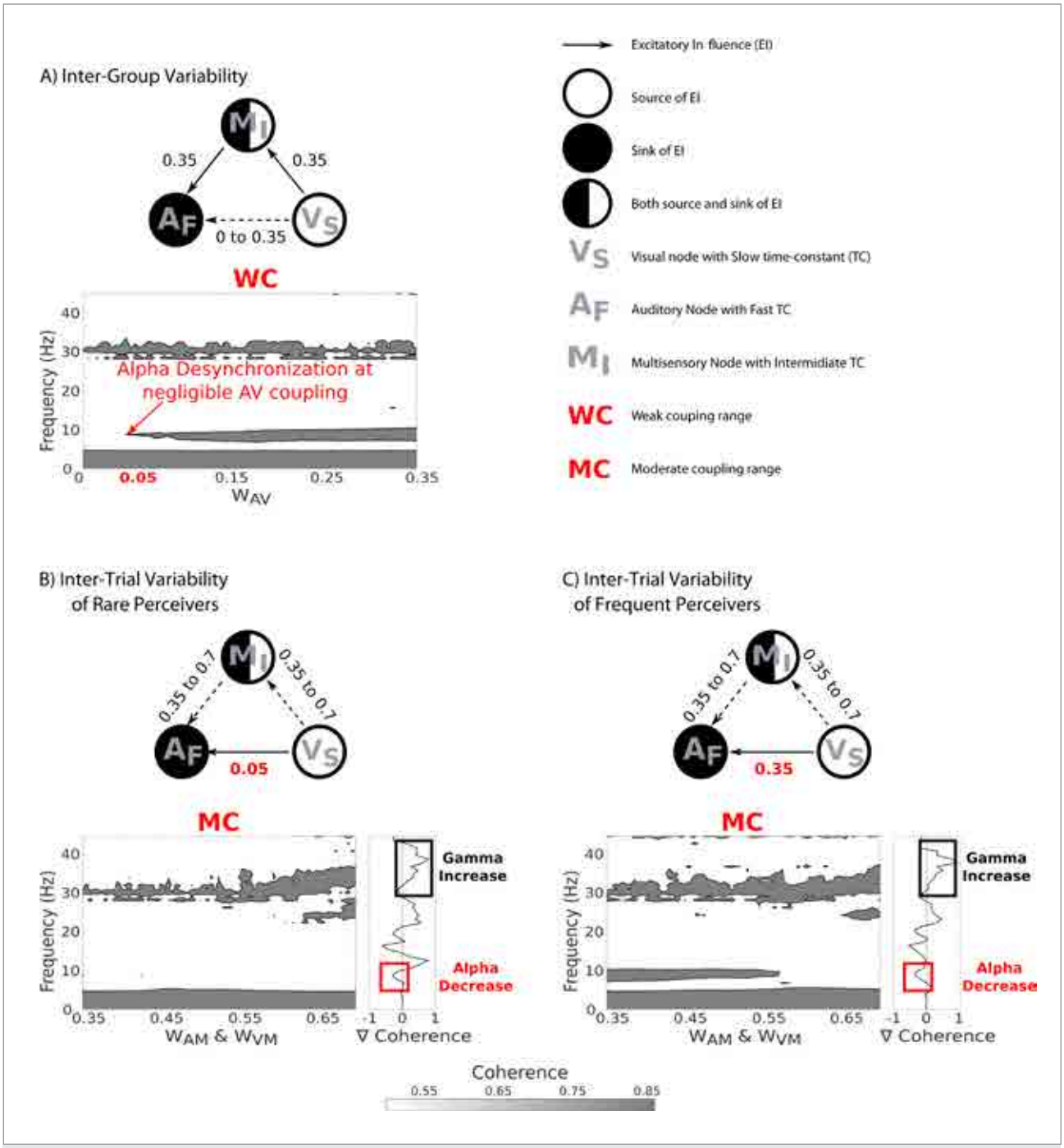


Figure 1: Mechanistic understanding of Inter-individual and inter-trial variability: a) Alpha de-synchronization characteristic of rare perceivers resulted due to negligible A-V coupling. b) & c) Enhanced gamma coherence and reduced alpha coherence observed in illusory perception are due to an increase in indirect coupling involving multisensory node irrespective of the influence of direct A-V coupling.

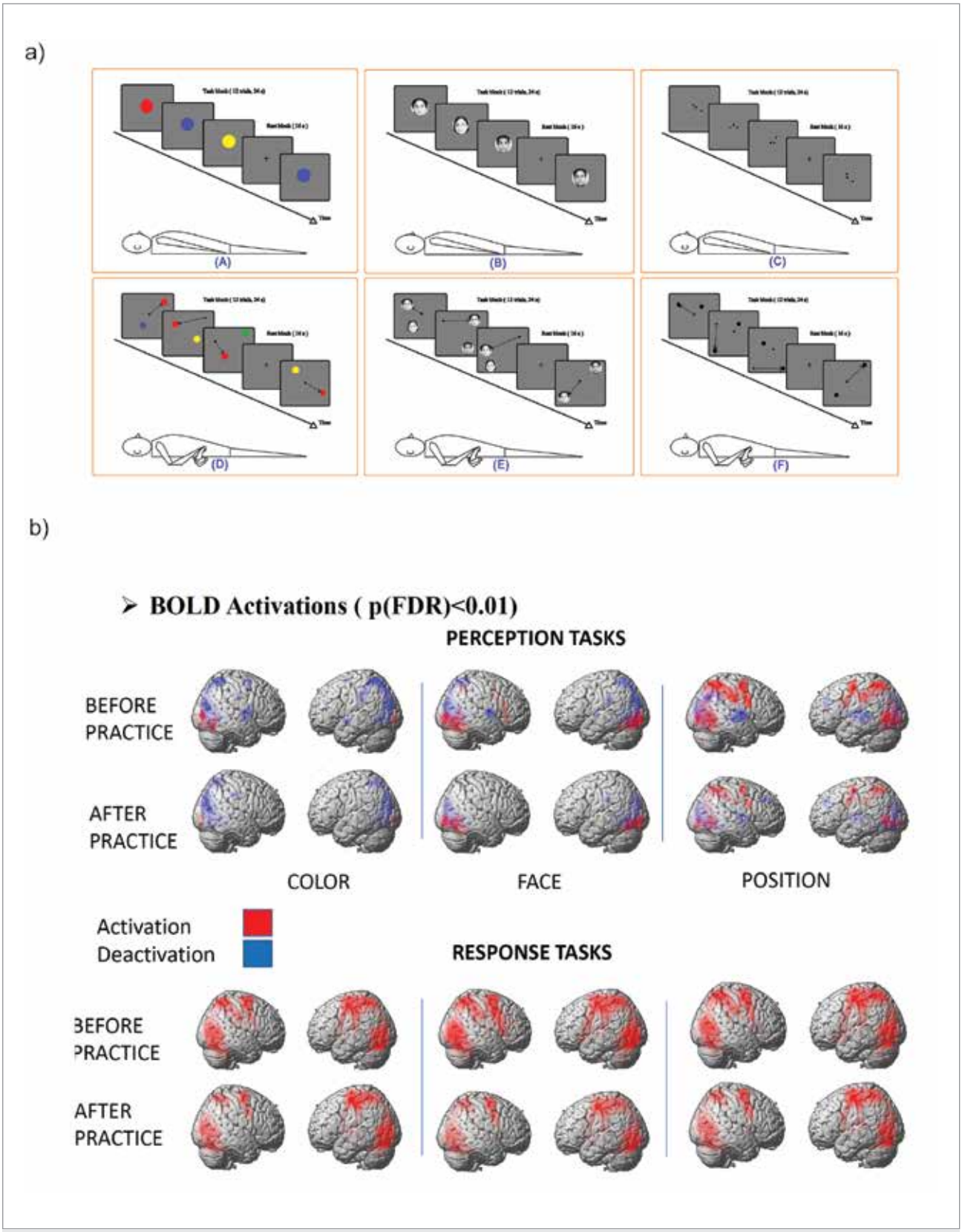


Figure 2: a) The study design to tease out the information processing pathways in dual stream of visual information processing in perception and action tasks b) Brain activation (red) and deactivation patterns (blue) in perception and action tasks.

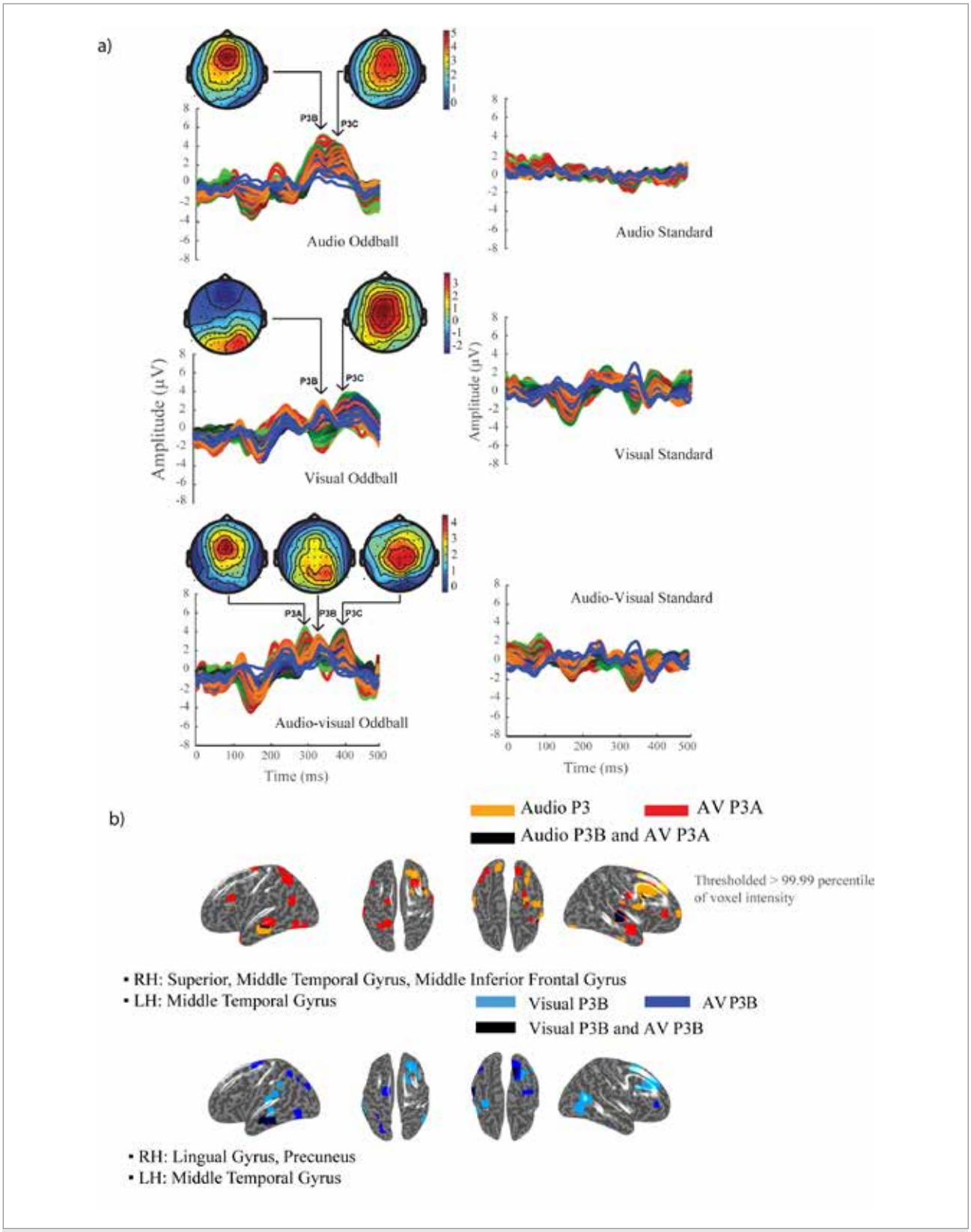


Figure 3: a) The grand average of event related potentials (ERPs) across subjects and trials for auditory, visual and auditory visual oddball and standard trials. The topoplots represent the scalp topography at peaks of important events in P300 complex in different conditions. b) Source localization maps that shows common and specific areas in audio and AV P300 complex (first row) and between visual and AV P300 complex (second row).

Publications

1. Kumar, V.G., Kumar, N., Roy, D. & Banerjee, A. (2018), Segregation and integration of cortical information processing underlying cross-modal perception, Multisensory research, 31 (5), 481-500.
2. Ray, D., Roy, D., Sindhu, B., Sharan, P. & Banerjee, A (2017). Neural Substrate of Group Mental Health: Insights from Multi-Brain Reference Frame in Functional Neuroimaging, Frontiers in Psychology 8, 1627.
3. Naik, S., Oota, S., Banerjee, A., Roy, D., Raju, S. B. (2017) Metastability of Cortical BOLD Signals in Maturation and Senescence, IEEE Conference proceedings IJCNN 2017, 4564-4570.
4. Naik, S., Banerjee, A., Raju, S. B., Deco, G. & Roy, D. (2017) Metastability in Senescence, Trends in Cognitive Sciences 21 (7), 509-521.

Presentations

1. Ray, D., Hajare, N., Banerjee A (2017): Deactivation and activation of dorsal visual information processing pathway gates perception-action coupling. Society for Neuroscience Annual meeting, Washington DC, USA.
2. Kumar, N., Jaiswal, A.K., Kumar, V.G.,, Roy, D., Banerjee, A. (2017) Entrainment of large-scale cortical networks underlie the processing of periodic auditory stimulus. Society for Neuroscience Annual meeting, Washington DC, USA.
3. Kumar, V.G.*, Dutta, S.*, Roy, D., Banerjee, A. (2017) Biophysically realistic neuronal model explains the inter-individual differences in the processing of multisensory speech. Society for Neuroscience Annual meeting, Washington DC, USA.
4. Banerjee, A at LV Prasad Eye Institue in a Indo-German Seminar funded by Leopoldina Program and DFG (Germany)., Nov 2017 (Invited Talk).
5. Banerjee, A International Center for Theoretical Sciences, Bangalore: Multisensory represntational space of cross-modal perception, July 2017 (Invited Talk).

*Authors have equal contribution

Funding

- NBRC Core
- Ramalingaswami Fellowship, Department of Biotechnology
- Cognitive Science Research Fellowship, Department of Science and Technology
- National Postdoctoral fellowship, Department of Science and Technology

Collaborators

Abhijit Sen & Bhumika Thakur, Institute for Plasma Research (IPR), Gandhinagar

Anirban Basu, NBRC

Dipanjan Roy, NBRC

Pravat K. Mandal

Early Diagnostic Biomarkers for Alzheimer's Disease from Brain Metabolic, Structural, and Behavioral Pattern Learning.

Research Scientist
Dr. Deepika Shukla
Dr. Tripti Goel

R&D engineer
Ankita Sharma
Khushboo Punjabi
Saurav Roy

Research Manager
Kanika Sandal

Neuropsychologist
Shallu Joon

Objective: To develop early diagnostic marker for Alzheimer's Disease (AD) from multi-modal imaging and neuropsychological tests. To achieve this goal, we are investigating the role of major antioxidant, glutathione (GSH) and its conformational changes for the onset AD. The role of different conformations of GSH in the various brain regions in Indian population and as well as people from other continents. We are testing the cognitive profile of healthy aging and pathologically affected brain by testing the working memory performance. We are also conducting various neuropsychological tests that are specific to cognitive reserve indicator in healthy young, and old individuals as well as AD patients.

The NeuroImaging and NeuroSpectroscopy (NINS) laboratory focuses 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 and 7.7 million additions every year (2016 WHO Dementia). An understanding of causal molecular process that transform a healthy brain to a diseased condition would help us for therapeutic advancements to cure AD.

Our lab is focusing in the study groups consisting of normal healthy control (HC), mild cognitive impaired (MCI), and AD for the following features:

- Glutathione (GSH) levels
- Brain Iron quantitation
- Working Memory Performance
- Neuropsychological test scores

This assessment of these neurochemical in quantitative terms and its correlation with disease progression is a major area of our research in our laboratory.

Investigation for the role of oxidative stress in AD:

Oxidative stress is an important event in AD process. The role of metals specifically iron as possible enhancer of oxidative stress in AD process are being investigated in our laboratory. Similarly, the antioxidants, glutathione and its role for neutralization of reactive oxygen species (ROS) are also being investigated in healthy and clinical populations.

The brain iron levels are being detected using specialized 3D MRI sequence. We have developed a MATLAB based pipeline for region specific iron susceptibility measurement. The determination of brain glutathione on these specific regions (hippocampus and frontal cortex) are being investigated using MEGA PRESS pulse sequence. Our lab has developed a novel comprehensive MATLAB-based software package called **'KALPANA'** for processing, visualization and absolute quantitation of Magnetic Resonance Spectroscopy data (under international patent).

We have found that major antioxidant glutathione exists in two conformations (Figure 1) and the potency of these conformers to scavenge the radicals is an important area to investigate with respect to AD pathology. We have already investigating the % of these conformers in healthy versus AD brains.

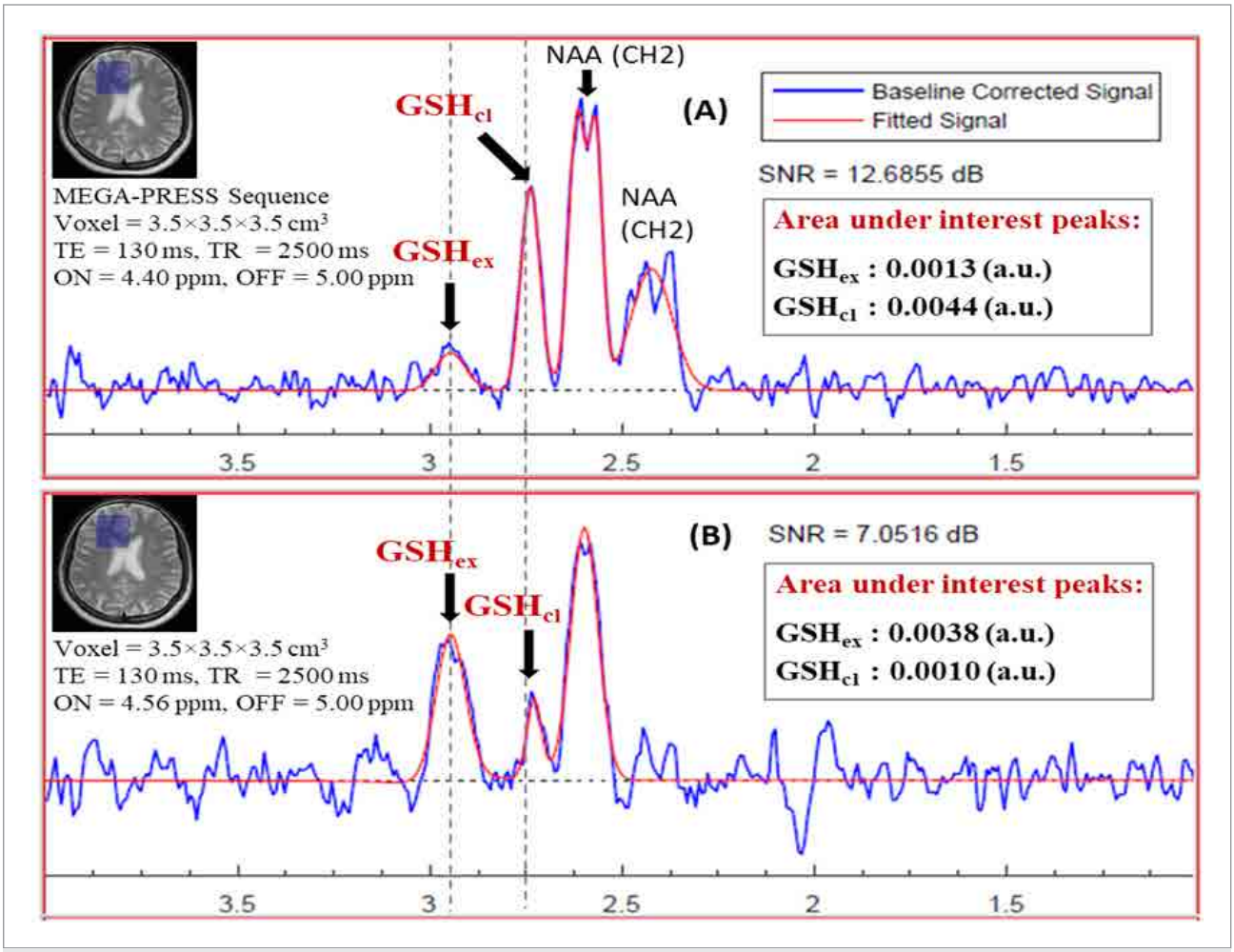


Figure 1: Detection of the two (extended and closed) in vivo GSH conformer peaks (GSHEX and GSHCL) in healthy control subject using MEGA-PRESS experiment. Data was collected using 3T Philips scanner with following parameters: TE = 130 ms, TR = 2500 ms.

Role of GABA in decline of Working Memory performance in Alzheimer's Disease

Working memory (WM) performance refers to the ability to maintain and manipulate information temporarily. In AD patients WM has been shown to decline as a function of increasing reaction times and decreasing accuracy in a working memory task. In healthy individuals, Working Memory performance has been shown to depend on the primary inhibitory neurotransmitter GABA in the Dorsolateral Prefrontal Cortex and Superior Parietal Cortex, which are the primary areas associated with WM performance. To understand the physiological link between GABA and WM performance in AD, we are using non-invasive multimodal Imaging techniques- fMRI and MRS too correlate the GABA levels measured using MEGA PRESS MRS with the performance observed in the Sternberg WM task during fMRI in healthy young, healthy old adults and AD patients.

Publications

1. Pravat K. Mandal and Deepika Shukla "Brain Metabolic, Structural and Behavioral Pattern Learning for Early Predictive Diagnosis of Alzheimer's Disease" Vol 63(3) 935–939, 2018.
2. Pravat K. Mandal, Deepika Shukla, Varan Govind, Yves Boulard and Lars Ersland "Glutathione Conformations and Its Implications for in vivo Magnetic Resonance Spectroscopy" Journal of Alzheimer Disease, 52 (2), 537-541, 2017.
3. Pravat K Mandal*, Krity Kansara and Aroma Dabas "The GABA-Working Memory Relationship in Alzheimer's Disease" Journal of Alzheimer's Disease Reports 1 43-45, 2017.
4. R Prashanth, Sumantra Dutta Roy, Pravat K Mandal, Shantanu Ghosh "High-accuracy classification of Parkinson's disease through shape analysis and surface fitting in 123I-Ioflupane SPECT imaging" IEEE journal of biomedical and health informatics, 21(3) 794-802, 2017.

Patent

The methodology which is applied in 'KALPANA' was filed for a National patent at the Indian Patent Office (IPO) on 19 January 2016 and PCT application is in progress for an International patent at the World Intellectual Property Organization (WIPO). International Patent Application No. PCT/IB2016/054978 dated 19th August, 2016. National Patent Application No. 20161100194 dated 19th January, 2016.

Presentation

1. Deepika Shukla, Manjari Tripathi and Pravat K Mandal "Pattern of Glutathione Conformation (Closed form) from Frontal and Hippocampal Regions in Three Healthy Age Groups using Non-Invasive Magnetic Resonance Spectroscopy, Society of Biological Psychiatry meeting, New York, 2018.

Funding

- Indo-Australia Biotechnology Funding
- Department of Biotechnology, Government of India
- Department of Information Technology, Government of India
- Department of Science and Technology, Government of India

Collaborators

1. Prof. (Dr.) Manjari Tripathi, MD, DM,Department of Neurology, All India Institute of Medical Science (AIIMS), New Delhi.
2. Dr. Lars Ersland, Professor, Dept. of Clinical Engineering, Haukeland University Hospital, Bergen, Norway.
3. Dr. Ashley Bush,Head, Oxidation Biology Unit - Melbourne Dementia Research Centre, Florey Institute of Neuroscience and Mental Health, Melbourne, Victoria, Australia.
4. Dr. Peter Barker, Professor, Dept. of Radiology and Radiological Sciences, Johns Hopkins, Baltimore, Maryland, USA.

Dipanjan Roy

Reorganization of Multiscale Brain Network Dynamics in Healthy Aging, Development and Disease Using Multimodal Imaging

Research Fellows
Vanshika Singh
Abhishek Singh Narvaria
Azman Akhter

Post-Doctoral Fellows
Dr. Subham Kumar
Dr. Moumita Das

Project Assistants
Fahd Yazin, Bikash Sahoo

Our Lab is interested in understanding multi scale brain network dynamics using various imaging (fMRI, EEG, MEG) modalities to understand what gives rise to perception, different forms attention, learning and higher order cognition and their alteration with abnormal development and aging. One of the experimental paradigm that we are interested in known as the resting state - when the wakeful brain neither accomplishes explicit tasks nor is exposed to external stimuli – the brain is organized in distinct networks of correlated activity. Fluctuations of these resting-state networks (RSN) influence human behavior and cognition as has recently been demonstrated. The RSNs, including the default mode network (DMN) are highly reproducible across different healthy individuals and are considered to underlie fundamental and intrinsic functions such as self-referential cognitive processes, maintenance of memory and cognitive processes during attention. Moreover, across wide range of experimental works related to working memory task, visual learning task, tactile stimulation task has found that the activity in this set of brain regions are high when the mind is not engaged in specific behavioral tasks and low during focused attention on the external sensory processing. Hence in this project, we aim to investigate the DMN suppression and its functional role in health and disease, whose direct impact would span several disciplines, including cognitive neuroscience, pharmacological neuroimaging, clinical neuroscience, and theoretical neuroscience. We investigate three outstanding open problems in cognitive neuroscience (a) Mechanisms that underlies default mode activation and suppression, (b) Interactions between default mode activations and suppressions with the remaining goal directed brain networks observed during resting state, (c) Information processing capacity or complexity in the default mode and cognitive functional brain networks. To this end, we use high throughput diffusion tensor imaging

Large scale Brain network investigations to understand mechanistically suppression in default mode networks during resting state

Diffusion tensor imaging allow us to estimate structural connectivity (SC) from individual subjects using our own connectome processing pipeline. Resting state fMRI on healthy aging human data is acquired during rest and also under cohorts of conditions. Further, these datasets are already made available from open source neuroinformatics platform Human Connectome Project (HCP), and integrated with open source neuroinformatics platform such as The Virtual Brain (TVB). Using such open source neuroinformatics platform we have characterized intrinsic resting state Blood Oxygen Hemodynamic response (BOLD) dynamics, functional connectivity between multiple brain areas assessed by fMRI across healthy subjects. We anticipated an increased functional connectivity in the DMN paralleled by decrease in Frontal-Parietal network (FPN) implicated in working memory, planning, decision making. Secondly, we modelled mechanistically using a biophysically realistic brain network model composed of several brain areas to generate synthetic BOLD resting state dynamics. Third, we investigated how the degree of intrinsic BOLD activity (temporal change), functional connectivity (change spatial map) in the DMN and FPN networks are sensitive to disruption via biophysically altering the cortical short-range as well long-range inhibition. This multimodal approach using non-invasive human neuroimaging along with biophysically detailed large scale computational model will establish links between neurotransmitter imbalance in the organization of large-scale anti-correlated neural systems, cognition, and symptoms (broadly speaking cognitive impairment) associated with neurocognitive and neuropsychiatric disorders in humans.

There were two recent significant publications from our lab; (a) the

first one addresses a fundamental problem in basic neuroscience of relating structural connections in the brain with the functional connections and links and their applications in healthy aging. (b) The second one addresses the gene expression profiles and identification specific sets of gene pool in the protein-protein interaction network using systems biology approach that differentiates between healthy normal aging versus Alzheimer's Disease.

Relating brain structure and function through machine intelligence to address maturation and aging

This work addresses a fundamental problem of Cognitive Neuroscience of what processes sculpts functional connectivity in the brain on a relatively fixed anatomical connectivity. Using machine learning approach this work for the first time make prediction of subject specific functional connectivity with high accuracy surpassing what can be explained within existing frameworks. Further, learning latent variables and parameters in this framework could be used to characterize age-specific developmental reorganization in the brain structure and function.

We propose the multiple kernel learning model as a variant of Reaction-diffusion (RD) systems wherein the regional mean activities diffuse on the graph determined by anatomical pathways (SC). Recent models incorporate the random-walk stochastic process on network of connected components and model the process as an RD system. Atasoy and colleagues embed anatomical constraints in terms of the graph Laplacian matrix of the SC matrix in the Wilson-Cowan equations to explain the macro-scale excitatory and/or inhibitory interactions of the regional activities. These excitatory and/or inhibitory interactions result in the formation of complex functional patterns such as RSNs. We extend our model and explain the formation of FC through RSNs. We hypothesize that the cumulative mean activities of all the regions is generated by intra-regional micro-scale dynamics which diffuses inter-regionally on the structural connectome. We propose a physical model that implicitly captures the pairwise functional interactions between ROIs by explicitly associating them with their extent of influence through the diffusion kernels on the SC.

In summary, on the model continuum, the proposed MKL model lies somewhere between simple linear, diffusion models and complex non-linear drift diffusion models. Consequently, we compared our simulation results predicting BOLD functional connectivity using the proposed model with models at either end of the complexity spectrum. The experimental results showed that the correlation structure of BOLD functional resting state brain networks is significantly well captured by our model. Prediction accuracy of the MKL model for the 23 test subjects is close to 0.70 whereas that of the non- linear model comes second best at 0.52 and that of the SDK model around 0.37. We conducted a series of tests that perturbed the inputs to the model as well as permuted the learned parameters. The test results attest to the robustness of the proposed model. Interestingly the model not only captures the variability of scales across participants but also demonstrates a possible application in characterizing age-related differences in learning optimal parameters for the accurate estimation of FC. Even in the face of considerable amount of variability present in the data, the proposed MKL model is still able to predict subject-specific FCs with high accuracy. Beyond this, functional connectivity subsumes the influence of different regions across scales and age groups providing a viability of learned parameter being a useful for classification purposes for other domains of application in health and disease. Overall, our method might be considered the missing link in the estimation and improvement of predicting subject-specific resting-state functional connectivity that remained elusive so far for complex non-linear and linear models. Given the strength of the analytical approach and tractability, the proposed model could be a suitable method for predicting task-based functional connectivity across different age groups.

Integrative network analysis of young, ageing and Alzheimer's disease

Ageing is a major risk factor associated with Alzheimer's disease (AD), a neurodegenerative disorder contributing to rapid decline in cognitive function and ultimately dementia. There is a growing need for understanding the relationship between ageing and AD to identify shared and unique hallmarks associated with the disease progression in a region and cell-type specific manner. Although genomic studies on AD have been performed extensively, the molecular mechanism of disease progression is still not clear. The major objective of our study is to obtain a higher-order network-level understanding of ageing and AD, and their relationship using the hippocampal gene expression profiles of young (20-50yrs), ageing (70-99yrs) and AD (70-99yrs). We combined the weighted gene co-expression network and weighted protein-protein interaction network-level approaches to study the progression from young to ageing to AD. In the unsupervised co-expression network analysis, we found that modules-specific to astrocytes, endothelial cells and microglial cells are upregulated and significantly correlate with both ageing and AD. The modules- specific to neurons, mitochondria and endoplasmic reticulum are downregulated and significantly correlate with AD than ageing. The oligodendrocytes module does not show significant correlation with neither aging nor disease. Further, we identified ageing- and AD-specific interactions/subnetworks by integrating the gene expression with a human protein-protein interaction network. The analysis shows that the transition from ageing to AD might be driven by the increase in number of nodes and interactions in AD that mostly alter the degree of existing nodes of ageing subnetwork. We found dysregulation of protein kinases and transcription factors in ageing and AD. Further, we found several genes that encode proteins with neuroprotective function in ageing to be part of the downregulated AD subnetwork. Our study highlights that simultaneously analyzing ageing and AD will help to understand the pre-clinical and clinical phase of AD and aid in developing the treatment strategies.

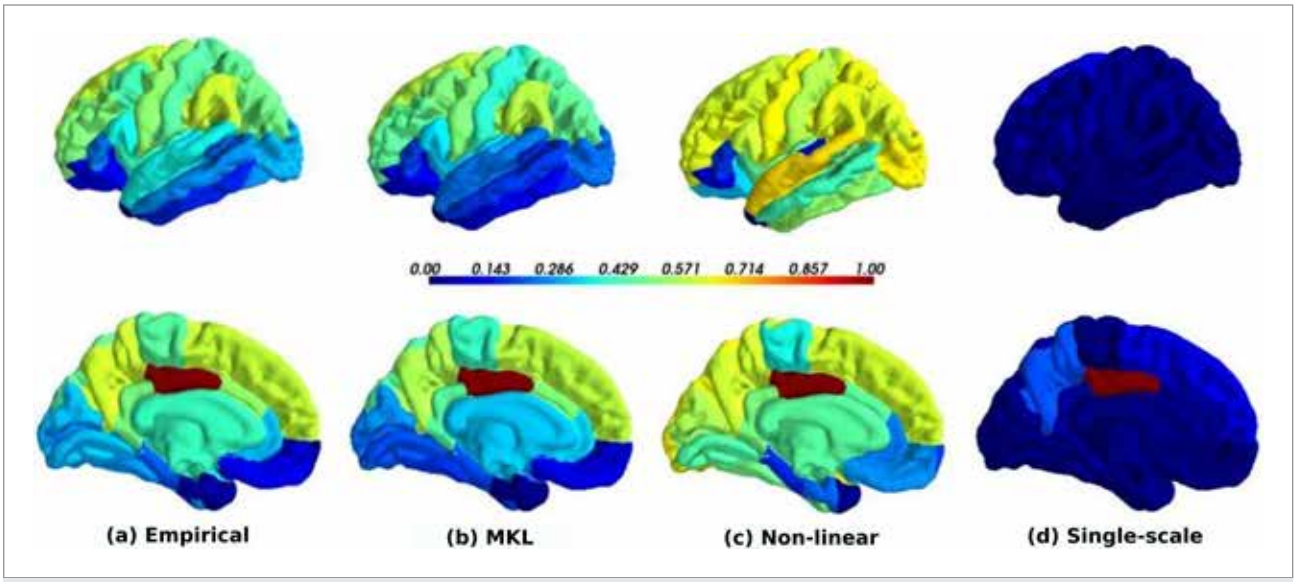


Figure 1: Results of Seed-based Correlation. Mean correlation maps resulting from considering the left Posterior Cingulate Cortex as a seed region and then calculating the seed-based correlations of all other regions. These maps are rendered on the left lateral sagittal view in the top sub-figures (a–d) and on the medial sagittal surface in the bottom sub-figures (e–h). While sub-figures (a) and (e) depict the maps for Empirical FC, the maps from the predicted FCs of MKL model are in (b) and (f); those of DMF in (c) and (g); and those of SDK in (d) and (h), respectively. Captions in the top row mention the model name and those in the bottom row indicate the mean correlation value on the test subjects. As can be observed, the correlation maps of MKL model seem to have greater correspondence with those of the mean empirical FC. Moreover, as depicted by the contrasts in the colors, MKL model is able to distinguish between the correlations at a better resolution than the other two models.

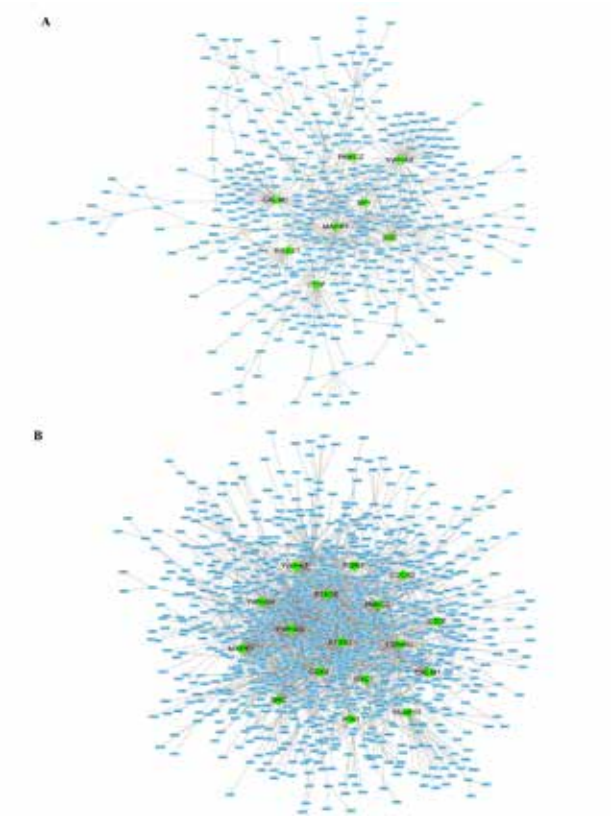


Figure 2: The upregulated (A) ageing and (B) AD subnetworks. The significant interactions of young vs ageing, and young vs AD obtained using edge betweenness network measure is shown. Genes/nodes with significant interactions are shown in green colour.

Publications

1. Vinay Lanke, S.T.R. Moolamalla, Roy D.*, P.K.Vinod* "Integrative network analysis hippocampus gene expression profiles identifies network alteration in ageing and Alzheimer's disease" Frontiers in Aging Neuroscience DOI: 10.3389/fnagi.2018.00153(2018) * shared senior authorship.
2. Surampudi, S.G., Naik, S., Surampudi, R.B., Jirsa, V.K., Sharma, A. and Roy, D.* "Multiple Kernel Learning Model for Relating Structural and Functional Connectivity in the Brain" Scientific Reports, Nature Publishing Group 8(1), p.3265. doi:10.1038/s41598-018-21456-0 (2018).
3. Ray, D., Roy, D., Sindhu, B., Sharan, P., & Banerjee, A. (2017). Neural Substrate of Group Mental Health: Insights from Multi-Brain Reference Frame in Functional Neuroimaging. Frontiers in psychology, 8, 1627.
4. G. Vinodh Kumar; Neeraj Kumar; Roy, D. and Arpan Banerjee Segregation and Integration of Cortical Information Processing Underlying Cross-Modal Perception Multisensory Research, Volume 31, Issue 5, pages 481–500 2017 DOI: 10.1163/22134808-00002574.
5. Harlalka V, Bapi RS, Vinod PK, Roy D (2018) Age, Disease, and Their Interaction Effects on Intrinsic Connectivity of Children and Adolescents in Autism Spectrum Disorder Using Functional Connectomics. Brain Connect. 2018 Aug 29. doi: 10.1089/brain.2018.0616.

Opinion and perspective

1. Naik, S., Banerjee, A., Bapi, R. S., Deco, G., & Roy, D. (2017). Metastability in senescence. Trends in cognitive sciences, cell press 21(7), 509-521.
2. Roy, D., & Pammi, V. C. (2017). Promises and pitfalls of relating alteration of white matter pathways causing improvement in cognitive performance. Cognitive neuroscience, 8(2), 120-122.

Book Chapter

[1] An EEG-Based Image Annotation System Viral Parekh, Ramanathan Subramanian, Roy, D., and C.V. Jawahar Springer Nature Singapore Pte Ltd. 2018 R. Rameshan et al. (Eds.): NCVPRIPG 2017, CCIS 841, pp. 1–11, 2018. https://doi.org/10.1007/978-981-13-0020-2-27

Conference Proceedings

[1] Naik, S., Subbareddy, O., Banerjee, A., Roy, D.*, & Bapi, R. S.* (2017, May). Metastability of cortical BOLD signals in maturation and senescence. In Neural Networks (IJCNN), 2017 International Joint Conference on (pp. 4564-4570). IEEE. (shared senior authorship).

Presentation

1. Indian Association of Neurosciences 35th meeting Session Chair Emergent functional architecture from structure 30th October 2017.
2. Invited speaker One day symposium in Network Biology IIIT Delhi, 28th August 2017.
3. Invited speaker Workshop on Language, Mind and Brain IIT Patna 19 -21 August 2017.
4. Invited speaker Summer School in Neuroimaging (SSNI 2017) IIIT Hyderabad 16 - 21 June 2017.

Funding

- Role of Default Mode Network in Cognitive functions BT/RLF/Re-entry/07/2014 Department of Biotechnology (DBT) Ramalingaswami fellowship (Initiated in 2016 for five years)
- Oscillatory Network Dynamics in Perceptual Learning SR/CSRI/21/2016 Department of Science and Technology (DST) Initiated in 2017 and for three years
- Dementia Science Program: Incidence/Prevalence/Risk analysis of dementia and basic research thereof. Ageing process in normality and dementia Department of Biotechnology starting from 2018, for three years

Award

1) Ramalingaswami re-entry fellowship Department of Biotechnology (DBT).

Collaborators

Arpan Banerjee, Anirban Basu NBRC

Avinash Shrama, Vinod Pallakad IIIT Hyderabad

Bapi Raju University of Hyderabad

Gustavo Deco UPF Barcelona

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

Viktor Jirsa (Director) CNRS and Institute of Systems Neurosciences and Epilepsy Unit Marseilles, France.

Randy McIntosh (Director Baycrest Centre Canada and leader The Virtual Brain Neuroinformatics platform).

Wired for Musical Rhythm? – A diffusion MRI Based Study of Musical Talent

Nandini Chatterjee Singh

Post Doctoral Fellow
Jeffrey M Valla

Project Assistants
Jacob Antony Alappatt
Archith Rajan

Background

The origin of musical expertise has long been a fascination of lay and academic audiences alike. While one view suggests that experts are "born", in that innate ability is the determining factor in performance achievement (i.e. "Nature") the opposing view is that experts are "made" and training overshadows any effects of innate ability to determine the ultimate level of performance (i.e. "Nurture"). While much is known about how musical training influences brain structure and organization, past studies have primarily compared musicians with non-musicians. As a consequence, individual differences associated with music perception abilities, without the influence of musical training are not very well understood. Recently, white matter organization has emerged as a sensitive marker for subtle differences in behavior. Diffusion Weighted Imaging (DWI) is an extensively used in-vivo technique that uses the properties of diffusion of water molecules to infer underlying variations in white matter microarchitecture in the brain.

We proposed that some non-musicians, even without musical training, could possess neural architecture that is primed with unrealized musical potential, and musicians with years of musical training may not have aptitudes commensurate with their self-reported "professional" status. Thus, even with years of musical training and degrees, a musician may not be as proficient as assumed ("Sleeping Musicians") whereas even without any musical training, a non-musician could show superior musical proficiency ("Musical Sleepers") since an absence of musical training does not essentially mean an absence of musical ability (Law and Zentner,2012). The primary objective of this study was to test for individual differences in musical perception skills and their relation to white matter architecture in an adult population with heterogeneous musical backgrounds.

Methods

Twenty-nine adult participants (16 male, age 24.7y ± 3.66) completed the Profile of Music Perception Skills -Short form (PROMS-S) .The PROMS-S is a test of music perception skills across multiple dimensions such as Melody, Pitch Rhythm, Tempo, Timbre and Tuning. Performance on the PROMS-S is measured using d-prime (d') scores. Participants also completed high angular resolution diffusion imaging (HARDI) scans (64 directions with b=2000s/mm and one b=0 image) on a 3T Philips Achieva scanner with a 8-channel head coil. Diffusion images were preprocessed using standard FSL's tools and included eddy current correction by registering to the b0 volume, brain extraction and fitting a diffusion tensor We used a multi-metric approach using tract-based spatial statistics (TBSS) to calculate whole-brain diffusion maps of MD (Mean Diffusivity), AD (Axial Diffusivity), RD (Radial Diffusivity), FA (Fractional Anisotropy) and MO (Mode of Anisotropy). In order to investigate the relation between musical perception abilities and microstructural properties of various white matter tracts, 5 general linear models were used with total d' scores as the independent variable and age as a nuisance variable and each of MD, RD, AD, FA and MO as dependent variables. Additionally, a 3 fiber crossing fiber model was also fitted to the diffusion data in the statistically significant regions to attain deeper insights into the fiber integrity in these regions. Non-parametric permutation statistics (5000 permutations) with threshold-free cluster enhancement (TFCE) was performed for all the voxel-wise analyses. Results were considered significant at $p<0.05$, TFCE-corrected for multiple comparisons.

Results and Conclusion

PROMS-S total d' scores did not show significant correlations with FA, MD, RD or AD maps. However, MO – a measure sensitive to the presence of crossing fibers was negatively correlated with the total d' scores in the genu and body of the corpus callosum extending to anterior parts of the right corona radiata ($p<0.05$, TFCE-corrected,

Figure 1). The crossing fibers analysis revealed a positive correlation for partial volumes of secondary fiber populations (F2 and F3 at p<.05, TFCE corrected) with the total d' scores and also the sub-scores of temporal features like Accent, Embedded rhythm and Tempo (F2 and F3 at p<.05, TFCE corrected).

The TBSS analyses revealed departure from linear anisotropy in parts of the corpus callosum (CC) in individuals with better music perception skills, strongly indicating the possibility of more than one dominant fiber population. We investigated this using a multi-compartment model that models three distinct anisotropic compartments (F1, F2, F3) with distinct orientations for each fiber component. The results of this model confirmed an increase in partial volumes of secondary fiber populations in individuals with increased musical perception ability suggesting thereby that a certain type of neural architecture (e.g. presence of crossing fibers in the CC) might provide an advantage for the perception of musical features. Even after controlling for musical training, correlation of F2 and F3 fibres with musical sub-scores specifically temporal sub-scores (tempo, accent, embedded rhythm) indicates that it is the secondary fibre structure that is responsible for differences in music perception ability specifically in the temporal domain.

If the neuroarchitecture underlying high rhythmic aptitude is independent of musical training, then Nature may outweigh Nurture where temporal aspects of musical aptitude are concerned. Thus, we might ask: are we wired for rhythm? We hope more studies which include genetics with larger populations in larger cohorts would shed light on the effects of musical aptitude and musical training.

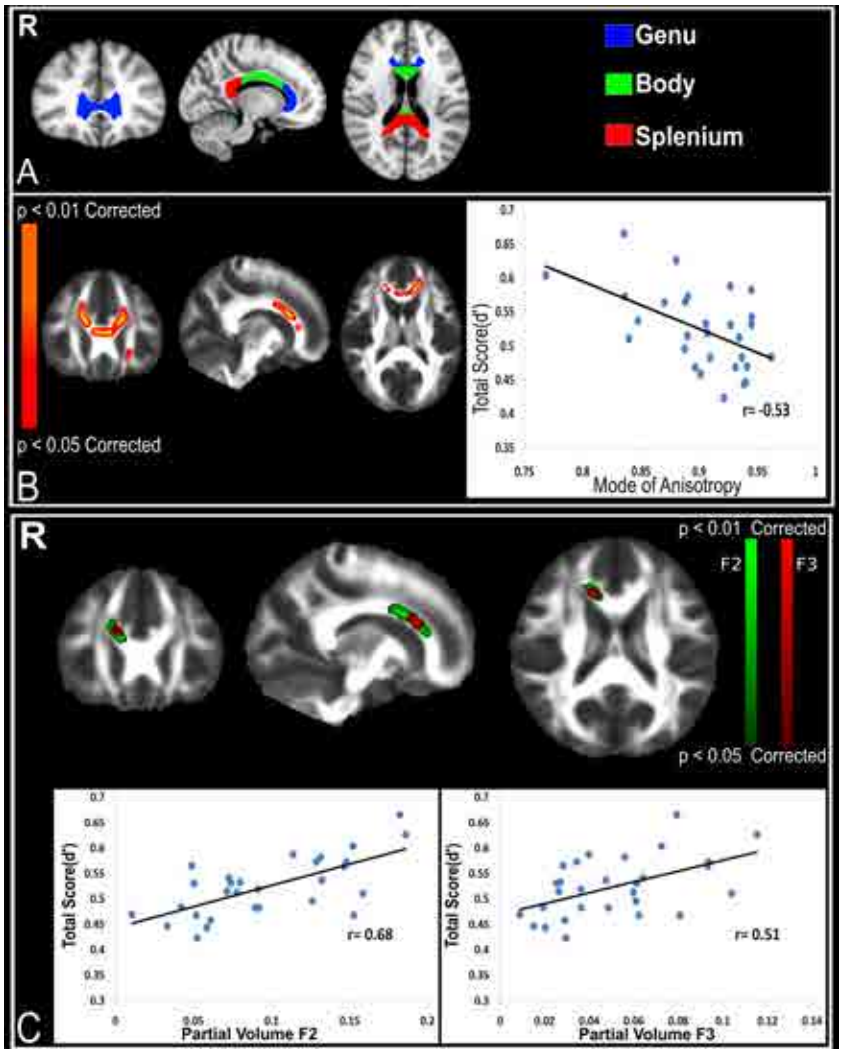


Figure 1: A. Representative labelling of the parts of corpus callosum. **B**. TBSS results showing a negative linear association of Mode of Anisotropy with the total d' score in the corpus callosum (genu and body) and parts of anterior corona radiata (p< 0.05, TFCE corrected). The correlations between the measures in these regions are also shown (r= -0.53, p=0.003) **C**. TBSS results showing a positive linear association between the total PROMS-S scores and the partial volumes of secondary fiber populations F2 and F3. The significant clusters (p< 0.05, TFCE corrected) for F2 (green) and F3 (red) are shown. The correlations between the measures in these regions are also shown below (F2: r = .68, p = .52 x 10-4, F3: r = .51, p = .004).

The Role of Oral Language in Learning to Read Akshara Based Orthographies

Nandini Chatterjee Singh

Research & Development Engineer
T. Sumathi

Background

A vast variety of Indic languages use the akshara based writing system and past research focused on reading in such systems has primarily explored how the structure of the writing system influences reading in akshara based languages. However, relatively little research has focused on the role of oral language, in learning to read in akshara based orthographies. It is well known that the successful acquisition of reading in any language is jointly explained by spoken language and its writing system. A third factor that will also impact reading skill and later reading comprehension is vocabulary or oral language skill. Past studies on decoding in akshara orthographies have been unable to establish a clear pattern for oral language in reading acquisition. While in the early grades the relative contribution of decoding skills is higher, language comprehension skills become increasingly important after decoding is proficient. We therefore propose that an investigation of word recognition in an akshara system in young children should include an assessment of the relative roles of vocabulary and phonological processing. In light of the consistency of akshara-sound consistency, coupled with the visuo-spatial complexity of the akshara orthography, we hypothesized that for beginning readers, akshara recognition should take precedence over phonological processing and oral fluency in explaining word recognition. However, as children achieve akshara recognition skills, we speculated that oral vocabulary skills and phonological processes would independently contribute to word recognition.

Here we examine how the relative contributions of features of oral language and writing systems modulate word recognition in Devanagari, an akshara-based orthography.

Participants

The data presented in this study were part of a larger scale survey of literacy skills conducted in primary and middle schools in the cities and neighboring districts of the National Capital Region (New Delhi and its surrounding areas) and the city of Allahabad located in the state of Uttar Pradesh in the northern part of India. The Marathi data were collected from Mumbai and Pune in the western part of India. Hindi is the dominant language in areas in and around New Delhi while Marathi is the dominant language of Maharashtra to which both Mumbai and Pune belong. Consent for the study was obtained from parents of the children as per the norms prescribed by the Human Ethics Committee of the National Brain Research Centre.

Data were collected from 28 schools. In these schools, formal literacy instruction for Hindi and Marathi began in grade 1, between the ages of 5-6 years. As per the education policy, many of the schools were also required to introduce English in grade 1. Data were collected from children across grades 1-5 (Grades 1-2 n=75, Mage=7.1, SD=0.8; Grades 3-5 n=155, Mage =9.6, SD=1.1). The analysis presented here describes the children who displayed no reading difficulties and formed a chronological group from each grade. An exhaustive battery of ine tests comprising of picture naming, phonological processing, vocabulary and literacy as detailed in the Dyslexia Assessment for Languages of India (DALI) was administered for every child participating in the study.

Results

In order to ascertain sub-skills which might theoretically play a causal role in determining reading performance in word and non-word reading, we first examined correlations between various behavioral skills and reading performance. Bivariate correlations across all measures were performed and revealed several significant trends as shown in Figure 1. Fluency skills of semantic and verbal fluency were all highly correlated. Phonological skills of syllable replacement and rhyming also showed a strong significant correlation. Correlations between measures of fluency

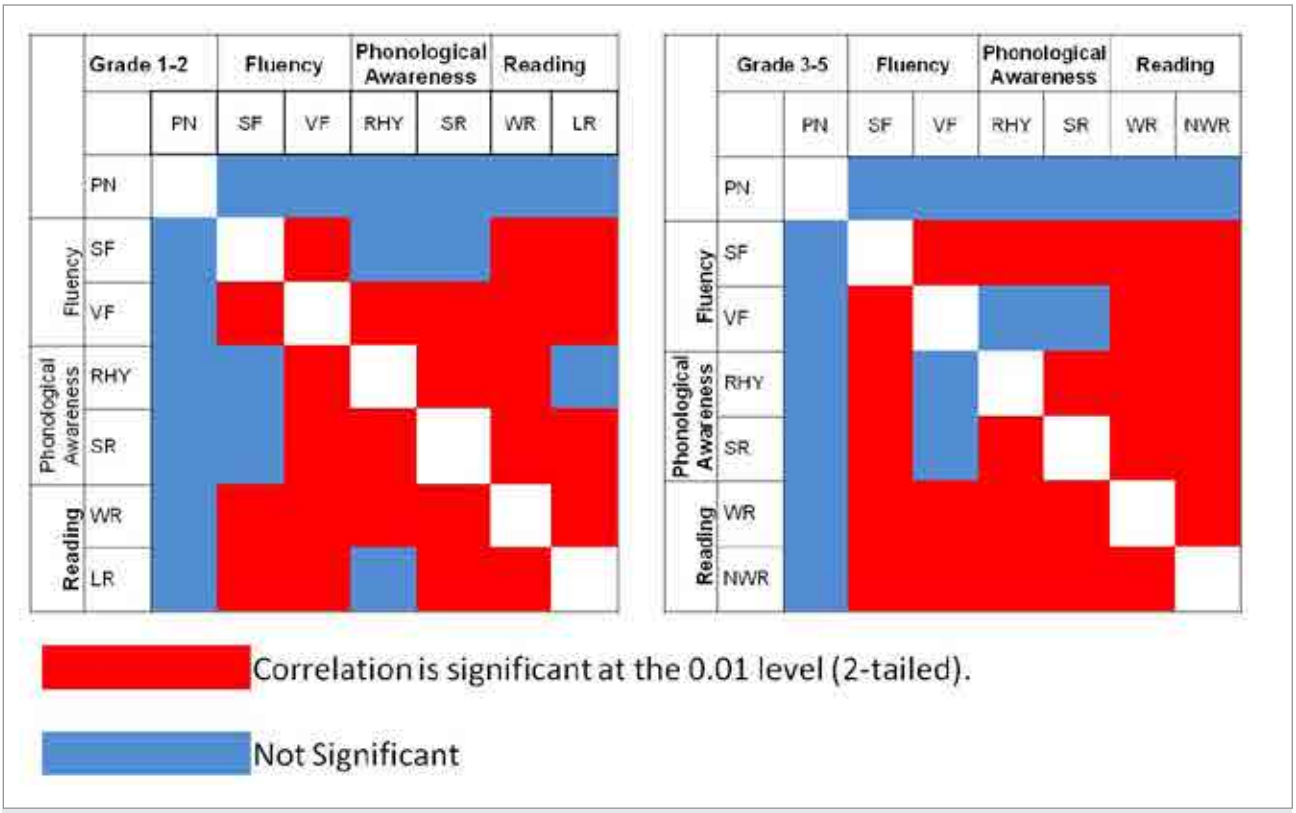


Figure 1: Correlation trend in Grades 1-2 and Grades 3-5

Note. PN – Picture Naming , SF – Semantic Fluency, VF – Verbal Fluency, LR – Letter Reading, WR – Word Reading, NWR– Non Word Reading

and phonological processing suggested that while fluency and phonological processing both explained word reading, phonological processing might be a stronger correlate as compared to fluency.

The correlational analyses clearly established that akshara reading, phonological processing, and fluency were moderately associated with reading and decoding outcomes in Devanagari. Stepwise regression analyses revealed that both phonological awareness (PA) and fluency were significant predictors of Devanagari decoding.

Conclusions - The most consistent finding of our study was the finding that vocabulary emerged as the most consistent independent correlate for word reading in Devanagari. Given the transparent nature of the akshara-sound mapping, the finding that phonological awareness was a strong predictor for reading was not surprising. The finding that PA explained both word and non-word reading almost equally confirms its role in decoding in consistent orthographies.

With regard to fluency, a noteworthy finding was its role in explaining the variance in word reading but little change in the prediction of non-word reading performance. In recent years a large body of work has revived an interest in the role of oral language in reading acquisition.

Funding – Cognitive Science Initiative, Department of Science and Technology, Government of India

Publications

1. "Wired for musical rhythm? – A diffusion MRI based study of normative musical perception skills" (under review).
2. The role of phonological processing and oral language in the acquisition of reading skills in Devanagari, Handbook of Literacy in Akshara Orthography, (accepted). (2018) Springer Publishing.
3. The brain on Music, Nandini Chatterjee Singh and Hymavathy Balasubramanium, Resonance, March (2018).
4. Reading Research and Practice : Indian Perspective, R. Malatesha Joshi, Pooja R. Nakamura and Nandini Chatterjee Singh, New Directions for Child and Adolescent Development, Vol. 158., 2017 | DOI: 10.1002/cad.20222.
5. Microstructural anatomical differences between bilinguals and monolinguals, Nandini C Singh, A. Rajan, Ar. Malagi, K. Ramanujam et al, 2017, Bilingualism and Cognition https://doi.org/10.1017/S1366728917000438.

Presentations

1. Nandini C. Singh "Wired for musical rhythm? – A diffusion MRI based study of normative musical perception skills", Brain Modes-2017, December 11-14, Delhi, 2017.

Funding

- Research grant on, 'The neurobiology of dyslexia:integrating brain and behaviour, NBRC and RML Hospital, Cognitive Science Initiative, Department of Science and Technology, Govt. of India.

Collaborators

Apurva Shah, Madhura Ingalhalikar (Symbiosis Institute of Technology, Pune),

Megha Sharda (University of Montreal, Canada)

Publications, Patents & Presentations

Publications

1. Kumari, P., Balakumar, S., and Banerjee, S. (2017) Modulation of hippocampal synapse maturation by activity-regulated E3 ligase via non-canonical pathway. Neuroscience, 19;364:226-241. doi: 10.1016/j.neuroscience.2017.08.057.
2. Kim, J.W., Seung, H, Kim, K.C., Gonzales, E.L. Oh, H.A., Yang, S.M., Ko, M.J., Han, S.H., Banerjee, S., Shin, C.Y. (2017) Agmatine rescues autistic behaviors in the valproic acid-induced animal model of autism. Neuropharmacology 113(Pt A):71-81. doi: 10.1016/j.neuropharm.2016.09.014. Epub 2016 Sep 14.
3. S Mahanti, A Majhi, R Adhikary, S Ghosh, A Basu, and B Bishayi (2017) Exogenous Interleukin-10 and ciprofloxacin treatment reduces inflammation and helps to improve cognitive behavior in acute and chronic restrain stressed mice infected with Eschericia coli. Indian Journal of Biochemistry & Biophysics 54: pp 241-257.
4. A Verma, P Tripathi, N Rai, A Basu, A Jain, V Atam, M Agarwal, and R Kumar (2017) Long-Term Outcomes and Socioeconomic Impact of Japanese Encephalitis and Acute Encephalitis Syndrome in Uttar Pradesh, India. Int J Infect. 4(4):e15607.
5. S C Philkhana, A Verma, G R. Jachak, B Hazra, A Basu* and D S Reddy (2017) Identification of new anti-inflammatory agents based on nitrosporeusine natural products of marine origin. Eur Journ of Med Chemistry Jul 28;135:89-109 [* joint corresponding author].
6. B.K. Singh, N. Vatsa, V. Kumar, S. Shekhar, A. Sharma and N.R. Jana. Ube3a deficiency inhibits amyloid plaque formation in APPswe/PS1δE9 mouse model of Alzheimer's disease. Human Molecular Genetics (doi:10.1093/hmg/ddx295), 2017.
7. I. Jamal, V. Kumar, N. Vatsa, S. Shekhar, B.K. Singh, A. Sharma and N.R. Jana. Rescue of altered HDAC activity recovers behavioural abnormalities in a mouse model of Angelman syndrome. Neurobiology of Diseases, 105, 99-108, 2017.
8. K. Debnath, N Pradhan, B.K. Singh, Nihar R. Jana* and Nikhil R. Jana* Poly(trehalose) Nanoparticles Prevent Amyloid Aggregation and Suppress Polyglutamine Aggregation in a Huntington's Disease Model Mouse. ACS Applied Materials & Interfaces, 9(28), 24126-24139, 2017. *Both are corresponding author.
9. P. Majumder, K. Roy, B.K. Singh, N.R. Jana and D. Mukhopadhyay. Cellular levels of Grb2 and cytoskeleton stability are correlated in a neurodegenerative scenario. Disease models & mechanisms, 10 (5), 655-669, 2017.
10. R. Kumar, D. K. Jangir, G. Verma, S. Shekhar, P. Hanpude, S. Kumar, R. Kumari, N. Singh, N. S. Bhavesh, N. R. Jana, T. K. Maiti. S-nitrosylation of UCHL1 induces its structural instability and promotes α-synuclein aggregation. Scientific Reports, 7, 44558, 2017.
11. Atrayee Basu, Shirshendu Dey, Dharmendra Puri, Nilanjana Das Saha, Vidur Sabharwal, Pankajam Thyagarajan, Prerna Srivastava, Sandhya Koushika, Anindya Ghosh-Roy (2017). Axonal fusion restores the gentle touch sensation lost due to neuronal injury. Proc Natl Acad Sci U S A 2017 November, 114 (47) E10206-E10215. https://doi.org/10.1073/pnas.1704372114.
12. Sheikh T, Gupta P, Gowda P, Patrick S and Sen E. Hexokinase 2 and nuclear factor erythroid 2-related factor 2 transcriptionally coactivate xanthine oxidoreductase expression in stressed glioma cells. Journal of Biological Chemistry 2018, 293(13) 4767-4777.
13. Gowda P, Patrick S, Singh A, Sheikh T and Sen E. Mutant IDH1 disrupts PKM2--catenin-BRG1 transcriptional network driven CD47 expression. Molecular and Cellular Biology, 2018, 38: 9.
14. Gupta P, Sheikh T, Sen E. SIRT6 regulated nucleosomal occupancy affects Hexokinase 2 expression. Exp Cell Res. 2017; 357(1):98-106.
15. Ahmad F, Patrick S, Sheikh T, Sharma V, Pathak P, Malgulwar PB, Kumar A, Joshi SD, Sarkar C, Sen E. TERT-EZH2 network regulates lipid metabolism and DNA damage responses in glioblastoma. J Neurochem. 2017, 143(6):671-683.
16. Ankita Singh, Ellora Sen. Reciprocal role of SIRT6 and Hexokinase 2 in the regulation of autophagy driven monocyte differentiation. Exp Cell Res. 2017, 360(2):365-374.
17. Majumdar A, Ahmad F, Sheikh T, Bhagat R, Pathak P, Joshi SD, Seth P, Tandon V, Tripathi M, Saratchandra P, Sarkar C, Sen E. miR-217-casein kinase-2 cross talk regulates ERK activation in ganglioglioma. J Mol Med (Berl). 2017, 95(11):1215-1226.

18. E. Sen, A Majumdar, F. Ahmad, T. Sheikh, R. Bhagat, P. Pathak, S.D Joshi, P. Seth, V. Tandon, M. Tripathi, P. Saratchandra and C. Sarkar (2017). miR-217 - Casein Kinase-2 crosstalk regulates ERK activation in Ganglioglioma. Journal of Molecular Medicine 95(11):1215-1226.

19. A. Ahmad Naik, N. Patro, P. Seth and I.K. Patro (2017). Intra-generational protein malnutrition impairs temporal astrogenesis in rat brain. Biology Open Jul 15;6(7):931-942.

20. Srivastava C, Irshad K, Dikshit B, Chattopadhyay P, Sarkar C, Gupta DK, Sinha S, Chosdol K. FAT1 modulates EMT and stemness genes expression in hypoxic glioblastoma. Int J Cancer. 2018 Feb 15;142(4):805-812. doi: 10.1002/ijc.31092. Epub 2017 Oct 17. PMID: 28994107.

21. Naskar T, Faruq M, Banerjee P, Khan M, Midha R, Kumari R, Devasenapathy S, Prajapati B, Sengupta S, Jain D, Mukerji M, Singh NC, Sinha S.Ancestral Variations of the PCDHG Gene Cluster Predispose to Dyslexia in a Multiplex Family. EBioMedicine. 2018 Feb;28:168-179. doi: 10.1 016/j. ebiom.2017.12.031. Epub 2018 Jan 9.PMID: 29409727.

22. Khan L, Kumar R, Thiruvengadam R, Parray HA, Makhdoomi MA, Kumar S, Aggarwal H, Mohata M, Hussain AW, Das R, Varadarajan R, Bhattacharya J, Vajpayee M, Murugavel KG, Solomon S, Sinha S, Luthra K. Cross-neutralizing anti-HIV-1 human single chain variable fragments(scFvs) against CD4 binding site and N332 glycan identified from a recombinant phage library. Sci Rep. 2017 Mar 23;7:45163. doi: 10.1038/ srep45163.

23. Kumar S, Kumar R, Khan L, Makhdoomi MA, Thiruvengadam R, Mohata M, Agarwal M, Lodha R, Kabra SK, Sinha S, Luthra K.CD4-Binding Site Directed Cross-Neutralizing scFvMonoclonals from HIV-1 Subtype C Infected Indian Children. Front Immunol. 2017 Nov 15;8:1568. doi: 10.3389/fimmu.2017.01568. e Collection 2017. PMID; 2918785.

24. Adlakha Y.K. and Seth P. (2017). The Expanding Horizon of MicroRNAs in Cellular Reprogramming. Progress in Neurobiology Jan 148:21-39.

25. Adlakha Y.K. and Swaroop A. (2018). Determination of Mitochondrial Oxygen Consumption in the Retina Ex Vivo: Applications for Retinal Disease. Methods in Molecular Biology 1753:167-177.

26. Singh UA, Kumari M and Iyengar S (2018): Method for improving the quality of genomic DNA obtained from minute quantities of tissue and blood samples using Chelex 100 resin. Biological Procedures Online; Accepted, March 17, 2018.

27. Priyabrata Haldar, Niranjan Kambi, Prem Chand and Neeraj Jain (2017) Altered expression of reorganized inputs as they ascend from the cuneate nucleus to cortical area 3b in monkeys with long-term spinal cord injuries. Cerebral Cortex 1-17. doi: 10.1093/cercor/bhx256.

28. Kamal Sharma, Neeraj Jain and Pabir K Pal (2017). Telemanipulation of a robotic arm using EEG artifacts. International Journal of Mechatronics, Electrical and Computer Technology 7: 3595-3609; DOI: IJMEC/10.225148.

29. Kumar, V.G., Kumar, N., Roy, D. & Banerjee, A. (2018), Segregation and integration of cortical information processing underlying cross-modal perception, Multisensory research, 31 (5), 481-500.

30. Ray, D., Roy, D., Sindhu, B., Sharan, P. & Banerjee, A (2017). Neural Substrate of Group Mental Health: Insights from Multi-Brain Reference Frame in Functional Neuroimaging, Frontiers in Psychology 8, 1627.

31. Naik, S., Oota, S., Banerjee, A., Roy, D., Raju, S.B. (2017) Metastability of Cortical BOLD Signals in Maturation and Senescence, IEEE Conference proceedings IJCNN 2017, 4564-4570.

32. Naik, S., Banerjee, A., Raju, S.B., Deco, G. & Roy, D.(2017) Metastability in Senescence, Trends in Cognitive Sciences 21 (7), 509-521.

33. Pravat K. Mandal and Deepika Shukla "Brain Metabolic, Structural and Behavioral Pattern Learning for Early Predictive Diagnosis of Alzheimer's Disease" Vol 63(3) 935–939. (2018).

34. Pravat K. Mandal, Deepika Shukla, Varan Govind, Yves Boulard and Lars Ersland "Glutathione Conformations and Its Implications for in vivo Magnetic Resonance Spectroscopy" Journal of Alzheimer Disease, 52 (2), 537-541 -2017.

35. Pravat K Mandal*, Krity Kansara and Aroma Dabas "The GABA-Working Memory Relationship in Alzheimer's Disease" Journal of Alzheimer's Disease Reports 1 43-45 (2017).

36. R Prashanth, Sumantra Dutta Roy, Pravat K Mandal, Shantanu Ghosh "High-accuracy classification of Parkinson's disease through shape analysis and surface fitting in 123I-Ioflupane SPECT imaging" IEEE journal of biomedical and health informatics, 21(3) 794-802 (2017).

37. Vinay Lanke, S.T.R. Moolamalla, Roy D.*, P.K.Vinod* "Integrative network analysis hippocampus gene expression profiles identifies network alteration in ageing and Alzheimer's disease" Frontiers in Aging Neuroscience DOI: 10.3389/ fnagi.2018.00153(2018) * shared senior authorship.

38. Surampudi, S.G., Naik, S., Surampudi, R.B., Jirsa, V.K., Sharma, A. and Roy, D.* "Multiple Kernel Learning Model for Relating Structural and Functional Connectivity in the Brain" Scientific Reports, Nature Publishing Group 8(1), p.3265. doi:10.1038/ s41598-018-21456-0 (2018)

39. Ray, D., Roy, D., Sindhu, B., Sharan, P., & Banerjee, A. (2017). Neural Substrate of Group Mental Health: Insights from Multi-Brain Reference Frame in Functional Neuroimaging. Frontiers in psychology, 8, 1627.

40. Segregation and Integration of Cortical Information Processing Underlying Cross-Modal Perception G. Vinodh Kumar; Neeraj Kumar; Roy, D. and Arpan Banerjee Multisensory Research, Volume 31, Issue 5, pages 481–500 2017 DOI:

10.1163/22134808-00002574.

41. Harlalka V, Bapi RS, Vinod PK, Roy D (2018) Age, Disease, and Their Interaction Effects on Intrinsic Connectivity of Children and Adolescents in Autism Spectrum Disorder Using Functional Connectomics. Brain Connect. 2018 Aug 29. doi: 10.1089/brain.2018.0616.
42. Naik, S., Banerjee, A., Bapi, R. S., Deco, G., & Roy, D. (2017). Metastability in senescence. Trends in cognitive sciences, cell press 21(7), 509-521.
43. Roy, D., & Pammi, V. C. (2017). Promises and pitfalls of relating alteration of white matter pathways causing improvement in cognitive performance. Cognitive neuroscience, 8(2), 120-122.
44. Naik, S., Subbareddy, O., Banerjee, A., Roy, D.*, & Bapi, R. S.* (2017, May). Metastability of cortical BOLD signals in maturation and senescence. In Neural Networks (IJCNN), 2017 International Joint Conference on (pp. 4564-4570). IEEE. (shared senior authorship).
45. Nandini C Singh "Wired for musical rhythm? – A diffusion MRI based study of normative musical perception skills" (under review).
46. Nandini C Singh The role of phonological processing and oral language in the acquisition of reading skills in Devanagari, Handbook of Literacy in Akshara Orthography, (accepted). (2018) Springer Publishing.
47. The brain on Music, Nandini Chatterjee Singh and Hymavathy Balasubramanium, Resonance, March (2018).
48. Reading Research and Practice : Indian Perspective, R. Malatesha Joshi, Pooja R. Nakamura and Nandini Chatterjee Singh, New Directions for Child and Adolescent Development, Vol. 158., 2017 | DOI: 10.1002/cad.20222.
49. Microstructural anatomicaldifferences between bilinguals and monolinguals, Nandini C Singh, A. Rajan, Ar. Malagi, K. Ramanujam et al, 2017, Bilingualism and Cognition https://doi.org/10.1017/S1366728917000438.

Editorial

50. B Hazra, S Chakraborty, and A Basu (2017) miR-301a mediated immune evasion by Japanese encephalitis virus. Oncotarget Vol. 8, (No. 53), pp: 90620-90621

Book Chapter

51. K Dutta, and A Basu (2018) Overview on Japanese Encephalitis in South and Southeast Asia. In Neglected Tropical Diseases –South Asia. ed. Sunit K Singh. Springer–Science.
52. M. Tewari, H.S Pandey and P. Seth (2017). Using Human Neural Stem Cells as a Model to Understand the "Science of Ashwagandha". In: Science of Ashwagandha: Preventive and Therapeutic Potentials. Springer-Nature, Eds - Sunil C. Kaul and Renu Wadhwa; pp 319-344.
53. An EEG-Based Image Annotation System Viral Parekh, Ramanathan Subramanian, Roy, D., and C.V. Jawahar Springer Nature Singapore Pte Ltd. 2018 R. Rameshan et al. (Eds.): NCVPRIPG 2017, CCIS 841, pp. 1–11, 2018. https://doi.org/10.1007/978-981-13-0020-2-27.

Patents

1. Placental Like Alkaline Phosphatase (PLAP) Promoter Mediated Cell Targeting S Sinha, I Khan, K Ahmad, K Chosdol and P Chattopadhyay. (Provisional Indian Patent No 1400/DEL/2013. Filed on 10 May, 2013, PCT/IB2014/061350 dated May 10, 2014, US Patent Granted - Application No.: 14/722,361 filed on September 03, 2015 (jointly by DBT, AIIMS and NBRC). US Patent granted, 16 Jan 2018.
2. Pravat K. Mandal: The methodology which is applied in 'KALPANA' was filed for a National patent at the Indian Patent Office (IPO) on 19 January 2016 and PCT application is in progress for an International patent at the World Intellectual Property Organization (WIPO). International Patent Application No. PCT/IB2016/054978 dated 19th August, 2016. National Patent Application No. 20161100194 dated 19th January, 2016.

Presentations

1. Banerjee, S., Samaddar, S., and Balakumar, S. Creative Destruction: Localized control of dendritic protein synthesis by selective degradation of miRNAs. EMBO meeting on "RNA localisation and local translation" Barga, Italy. July 2017.
2. Banerjee, S., Balakumar, S., Samaddar, S., and Basu, B. Harmony or conflict: Interplay between constructive and destructive mechanisms modulating synaptic plasticity. Molecular & Cellular Cognition Society (Asia) Annual Meeting. Singapore. August 2017.
3. Banerjee, S., Kumari, P., and Balakumar, S. Regulatory of mechanism of synapse formation by non-canonical function of polyubiquitination. Indian Society for Neurochemistry Annual Meeting. Varanasi. September 2017.
4. Banerjee, S., Kumari, P., and Balakumar, S. Regulatory of mechanism of synapse formation by non-canonical function of ubiquitination. Minisymposium on "Regulatory mechanisms of functional synapse development, remodeling and repair" at Indian Academy of Neuroscience Annual Meeting. Cuttack. October 2017.
5. Samaddar, S., Balakumar, S., and Banerjee, S. Think global act local: The role of miRNA turnover in modulating local translation at the synapse. Janelia Farm – HHMI Junior Scientists Workshop on Neuronal Cell Biology. Ashburn, USA. May 2017.
6. A Basu (2018) Host pathogen interaction in Japanese Encephalitis Virus infection: from pathogenesis to therapy. Prof S S Katiyar Endowment Lecture of the Indian Science Congress Association, Manipur University, 16-20th March, 2018.
7. A Basu (2018) Host pathogen interaction in Japanese Encephalitis Virus infection: from bench to bedside. Bioscience and Bioengineering, IIT-Jodhpur, 16th February 2018.
8. A Basu (2018) Japanese Encephalitis Virus infection: Pathobiology and therapy. Dept. of Microbiology, Institute of Home Economics, 10-11th January, 2018.
9. A Basu (2017) Host pathogen interaction in Japanese Encephalitis Virus infection: from bench to bedside Sreenivasaya Memorial Award -SBC (I), JNU, 16-19th November, 2017.
10. A Basu (2017) Neural Stem/Progenitor cells shows versatility in their Response following Japanese encephalitis virus infection. Bioscience and Biomedical Engineering, IIT-Indore, 27th July, 2017
11. N. Vatsa and N.R. Jana. Understanding the role of microRNA in Angelman Syndrome pathogenesis using mouse model. IAN 2017, Bhubaneswar, October, 2017.
12. S. Shekhar and N.R. Jana. Topotecan, a topoisomerase-1 inhibitor retards the disease pathogenesis in a mouse model of Huntington's disease. IAN 2017, Bhubaneswar, October, 2017.
13. V. Kumar and N.R. Jana. Simvastatin ameliorates behavioral deficits in Angelman syndrome model mouse. IAN 2017, Bhubaneswar, October, 2017.
14. N. R. Jana. Rescue of altered protein homeostasis in a mouse model of Huntington's disease. IAN 2017, Bhubaneswar, October, 2017.
15. N. R. Jana. UBE3A and its link with autism and autism spectrum disorder. IBRO meeting, BHU, Varanasi, April, 2017.
16. N. R. Jana. Altered protein homeostasis and neuronal dysfunction in Huntington's disease. International Symposium on Neurodegenerative Disorders (ISND2017), NIMHANS, Bengaluru, March, 2017.
17. N. R. Jana. Popular lectures given in many undergraduate colleges, (Midnapore College, Goaltore College, RNLK Women's College in West Bengal) and Universities (Amity University, Jamia Hamdrad University, Dibrugarh University and Tezpur University) and IBRO-2017 and IAN-2016 meeting.
18. Anindya Ghosh Roy "Microtubule organization in C. elegans neurons" in 'Current Trends in Intracellular Transport and Molecular Motors' (CTITMM) between Dec 21-23, 2017 at IIT-Bombay.
19. Anindya Ghosh Roy "Microtubule organization in touch neuron" 2nd India C elegans meeting held in NII-Delhi during 23rd to 26th Feb 2018.
20. Anindya Ghosh Roy "Restoration of Functional Connectivity After Neuronal Injury" in Wellcome Researcher Meetings: Cell and Developmental Biology at Warwick Conference Centre,

London during 15-16 March 2018.

21. Ellora Sen. IL-1 induced cell death under glucose deprivation is dependent on SIRT6-Hexokinase 2 cross talk (Invited Talk). 5th Annual Meeting of the International Cytokine & Interferon Society (ICIS) Kanazawa, Japan, 2017.
22. Ankita Singh and Ellora Sen. Hexokinase 2 crosstalk in monocyte differentiation. (Poster). 5th Annual Meeting of the International Cytokine & Interferon Society (ICIS) Kanazawa, Japan, 2017.
23. Fahim Ahmad, Shruti Patrick, Vikas Sharma, Pathak P, Anupam Kumar, Shanker Datt Joshi, Chitra Sarkar and Ellora Sen. (Poster). Regulation of lipid metabolism in gliomas bearing TERT promoter mutation. Keystone Symposia Conference E4: Integrating Metabolism and Immunity, Dublin, Ireland, June 2017.
24. Ellora Sen. Interplay of inflammatory and metabolic networks in glioma progression. Indian Association of Cancer Research, Kolkata, February 2018.
25. Pruthvi Gowda, Shruti Patrick, Ankita Singh, Touseef Sheikh and Ellora Sen. Involvement of β-catenin transcriptional network in CD47 expression and phagocytosis of IDH1R132H glioma cells. Indian Association of Cancer Research, Kolkata, February 2018.
26. Ellora Sen. Therapeutic challenges in brain tumors. Extension Lecture Govt. College for Girls, Gurugram, February 2018.
27. Ellora Sen. Tumor heterogeneity: Influence on therapeutic response Lady Brabourne College, Kolkata, February 2018.
28. Ellora Sen. Inflammation-metabolism crosstalk in glioma: Deconstructing the network. Advanced Centre for Treatment, Research & Education in Cancer ACTREC, Navi Mumbai November, 2017.
29. Ellora Sen. Triathlon in glioma: Metabolism - inflammation - epigenetics interplay. University of Hyderabad November, 2017.
30. Ellora Sen. Interplay between Metabolism and inflammation: Perspective on cancer dynamics. Institute of Life Sciences, Bhubaneswar October, 2017.
31. Ellora Sen. Metabolic reprogramming in Glioma: Influence of epigenetic landscape. 31st Annual Conference of Society for Neurochemistry, India (SNCI), Benaras Hindu University, Dept. of Zoology, September, 2017.
32. Ellora Sen. Metabolism, inflammation and epigenetics in glioma: Connecting the dots. Institute of Medical Sciences, Molecular Biology Unit, Benaras Hindu University, September, 2017.
33. P. Seth (Invited Speaker), "A novel model for understanding virus induced neurodegeneration" at the 10th NIPER Symposium on Nano-based Therapies for Neurodegenerative Diseases at National Institute of Pharmaceutical Education and Research (NIPER), Raebareli, March 27-28, 2018.
34. P. Seth (Invited Speaker), "What we know and what we need to know about virus induced neurodegeneration" at the Faculty Development Program of Delhi Technical University, New Delhi, India, March 14, 2018.
35. P. Seth (Plenary Speaker), "Human Neural Stem Cells as Models to Understand NeuroAIDS" at World NeuroCongress-2017, Aligarh Muslim University, Aligarh, India, Dec 9-10, 2017.
36. P. Seth (Invited Speaker), "Role of glia mediated neuronal damage in HIV neuropathogenesis", a meeting on Challenges in Clinical Neuroscience: from bench to bed side, at AIIMS-Bhubneshwar, Bhubneshwar, India, November 1, 2017.
37. P. Seth (Invited Speaker), "Cellular and Molecular Mechanisms of HIV-1 Neuropathogenesis", 35th Annual meeting of Indian Academy of Neurosciences (IAN-2017), at Ravenshaw University, Cuttack, India, October 29-31, 2017.
38. P. Seth (Director Nominee), "Human neural stem cells – Cell based assays for CNS disorders", Brain Storming meeting for - Alternatives to Animals – Cell Based Assays, organized by ICMR, at NIOP New Delhi, India, October 11, 2017.
39. P. Seth (Guest Lecturer), "Insights into mechanisms of neurodegeneration in HIV-1/AIDS", at Era University, Lucknow, India, October 3, 3017.
40. P. Seth (Invited Speaker), "Astrocyte mediated neuronal damage in HIV-1 neuropathogenesis - how friends turn foe", at Society of Neurochemistry Conference - 2017, Banaras Hindu University, Varanasi, India, September 20-22, 2017.
41. P. Seth (Invited Faculty) at the IBRO/APRC Neuroscience School, "Human Neural Stem Cells as Model Systems to Understand Neurodegeneration", organized at Banasthali University, Banasthali, Rajasthan, India, August 21-26, 2017.
42. P. Seth (Invited Faculty) at the IBRO/APRC Neuroscience School "Molecular insights into HIV-1 neuropathogenesis", organized at National University of Singapore, Singapore, July 3-7, 2017.
43. P. Seth (Invited Speaker), "Neural Stem cells as a model to understand virus induced neurodegeneration", Central Inter-Disciplinary Research Facility, Mahatma Gandhi Medical College and Research Institute, Pondicherry, India, June 20, 2017.
44. P. Seth (Invited Speaker), "Use of Human Neural Stem Cells as a Model to Understand Neurodegenerative Disorders", hands-on workshop on Molecular Biology Techniques & Stem Cells in Human Health and Diseases at Amity Institute of Molecular Medicine and Stem Cell Research (AIMMSCR), Amity University NOIDA, India, June 12-16, 2017.
45. Subrata Sinha Molecular diagnostics and cancer assessment in the clinic. Biotechnology in Health care: Challenges and Opportunities. Jamia Hamdard University, New Delhi. 19 March 2017.
46. Subrata Sinha Combining genetics and cell biology in the study

of dyslexia Amity University, NOIDA Campus, New directions in Cell Signalling, 21 April 2017.

47. Subrata Sinha Improved specificity by recombinant antibody targeting and tumor specific transcription. Inaugural talk. Gene therapy for curing rare genetic disorders. JNU, New Delhi 16 September 2017.
48. Subrata Sinha Dyslexia genetics opens a window to brain development and stem cell differentiation. Invited Talk MS University, Baroda, September 2017.
49. Subrata Sinha Studies in familial dyslexia help in identifying novel neurodevelopmental pathways; Keynote lecture. 31st Annual Conference of the Society of Neurochemistry; Banaras Hindu University, Varanasi 20 September 2017.
50. Subrata Sinha A study of familial dyslexia identifies a novel long non coding RNA essential for human neural progenitor cell differentiation. RNA Meet 2017. Banaras Hindu University, Varanasi 28, October 2017.
51. Subrata Sinha Translational neuroscience and its applications. Opening Talk, as President, Indian Academy of Neurosciences. XXXV Annual Meeting of the Indian Academy of Neurosciences, Ravenshaw College, Cuttack, Odisha, 29 October 2017.
52. Subrata Sinha Family studies in dyslexia: windows to neurobiology World Neurocongress Aligarh Muslim University, 9 December 2017.
53. Naskar T , Faruq M, Kumari R, Khan M, Midha R, Devasenapati S, Prajapati B, Mukerji M, Singh N C and Sinha S India| EMBO Symposia titled "Big Data in biomedicine" held from 25-27 February, 2018 at Delhi, India Whole exome sequencing and genome-wide genotyping in a multiplex family identified novel genetic loci on chromosome 5 for dyslexia. (Best Poster Awarded).
54. Swaroop S, Sengupta N, Adlakha YK, and Basu A. HSP60 plays a regulatory role in IL-1b induced microglial inflammation via TLR4-p38 MAPK axis at International Society of Neuroscience meeting, Paris, France, August 20-24, 2017.
55. Adlakha YK, Shimada-Ishii H, Ratnapriya R, Brooks M, Gieser L, Meral Gunay-Aygun, Jacobson SG and Swaroop A. Transcriptome profiling of developing human retinal organoids at Keystone Symposia "Transcriptional and epigenetic regulation of stem cells" Olympic Valley, CA, USA, January 8-12, 2017.
56. S. Iyengar: Opioid Neuromodulation and the Motivation to Sing in Adult Male Zebra Finches. Invited lecture at the International Symposium on Biological Timing and Health Issues in the 21st Century (in conjunction with the IUSSTF-sponsored Indo-US Workshop and Symposium), Department of Zoology, University of Delhi, Indo-US Joint Center on Biological Timing, University of Delhi and The Indian Society for Chronobiology, February, 2017.
57. S. Iyengar: Development of the Human Auditory Cortex. Presented at the TEDx event organized by the Institute of Chemical Engineering, Mumbai, April, 2017.
58. S. Iyengar: Effects of Opioid Neuromodulation on Song Learning in Male Zebra Finches. Neurogroup meeting, Khandala, Pune, September, 2017.
59. S. Iyengar: Opioid Neuromodulation and Singing in Male Zebra Finches. XXVI International BioAcoustics Congress, Haridwar, October, 2017.
60. S. Iyengar: Opioid Modulation of Song Learning in Male Zebra Finches, 35th IAN meeting, Ravenshaw College, Cuttack, Odisha, October, 2017.
61. S. Iyengar: Neural Circuits, Singing and Song Learning in Zebra finches. Invited Lecture presented at 'The challenge to learn: New approaches to study the problem of stability vs. plasticity in the brain' Organized by the Indian National Science Academy and the German Academy of Sciences, Leopoldina, LV Prasad Eye Institute, Hyderabad, November, 2017.
62. Pundir AS, Singh UA, Ahuja N, Makhija S, Dikshit PC, Radotra B, Kumar P, Shankar SK, Mahadevan A, Roy TS, Iyengar S (2017): Establishment of Cortico-Cortical and Thalamocortical Circuits in the Human Auditory Cortex. Poster presented at the 104th Indian Science Congress, Hyderabad, 3rd - 7th Jan.
63. Neeraj Jain, Shanah Rachel John and Priyabrata Halder (2017) 'Topography in the mouse motor cortex is a mosaic'. Neuroscience 2017, Annual Meeting of the Society for Neuroscience, USA. Nov 11-15, Washington DC, USA.
64. Neeraj Jain 'Transformation of the reorganized inputs as they ascend from the brain stem nuclei to the cortex following partial spinal cord injuries' at Leopoldina-INSA Symposium "The challenge to learn: New approaches to study the problem of stability vs. plasticity in the brain", LVPEI, Hyderabad, India, November 28-29, 2017.
65. Neeraj Jain 'Cortical Plasticity Reflects Subcortical Reorganization', invited talk at Department of Psychology, University of Wisconsin – Madison, USA, November 20, 2017.
66. Neeraj Jain 'Subcortical Origins of Cortical Plasticity', in Neuroscience Seminar Series at Department of Psychology, Vanderbilt University, Nashville, USA, November 16, 2017.
67. Neeraj Jain 'Animal Models in Neuroscience Research', at the workshop on 'Handling and Care of Laboratory Animals', NBRC, Manesar, October 24-27, 2017.
68. Neeraj Jain 'Rostral Motor Area: a new area in the rat motor cortex' at 2nd NeuroGroup meeting, Khandala, September 8-9, 2017.
69. Neeraj Jain 'Brain plasticity at systems level: Effects of spinal cord injury' at 'Neuroscience across scales, an International Meeting organized at National Center for Biological Sciences, Bangalore, July 17-19, 2017.
70. Neeraj Jain 'Animal models for brain research' and 'Spinal cord

injuries and brain plasticity' at National workshop on 'Recent Updates on Brain Research', at SDM College of Ayurveda and Hospital, May 26-27, 2017.

71. Shiv Kumar Sharma Delivered a lecture at International Conference on Advances in Dementia & XXI National conference of ARDSI, 22-24 September 2017, Kolkata.
72. Shiv Kumar Sharma Delivered a lecture in the Colloquium on "Sharing resources for quality higher education and research", 14th October, 2017, Central University of Haryana.
73. Ray, D., Hajare, N., Banerjee A (2017): Deactivation and activation of dorsal visual information processing pathway gates perception-action coupling. Society for Neuroscience Annual meeting, Washington DC, USA.
74. Kumar, N., Jaiswal, A.K., Kumar, V.G.,, Roy, D., Banerjee, A. (2017) Entrainment of large-scale cortical networks underlie the processing of periodic auditory stimulus. Society for Neuroscience Annual meeting, Washington DC, USA.
75. Kumar, V.G.*, Dutta, S.*, Roy, D., Banerjee, A. (2017) Biophysically realistic neuronal model explains the inter-individual differences in the processing of multisensory speech. Society for Neuroscience Annual meeting, Washington DC, USA. (*Authors have equal contribution).
76. Banerjee, A at LV Prasad Eye Institue in a Indo-German Seminar funded by Leopoldina Program and DFG (Germany)., Nov 2017 (Invited Talk).
77. Banerjee, A International Center for Theoretical Sciences, Bangalore: Multisensory represntational space of cross-modal perception, July 2017 (Invited Talk).
78. Dipanjan Roy, Indian Association of Neurosciences 35th meeting Session Chair Emergent functional architecture from structure 30th October 2017.
79. Dipanjan Roy, Invited speaker One day symposium in Network Biology IIIT Delhi, 28th August 2017.
80. Dipanjan Roy, Invited speaker Workshop on Language, Mind and Brain IIT Patna 19 -21 August 2017.
81. Dipanjan Roy, Invited speaker Summer School in Neuroimaging (SSNI 2017) IIIT Hyderabad 16 - 21 June 2017.
82. Deepika Shukla, Manjari Tripathi and Pravat K Mandal "Pattern of Glutathione Conformation (Closed form) from Frontal and Hippocampal Regions in Three Healthy Age Groups using Non-Invasive Magnetic Resonance Spectroscopy, Society of Biological Psychiatry meeting, New York 2018.
83. Nandini C. Singh "Wired for musical rhythm? – A diffusion MRI based study of normative musical perception skills", Brain Modes-2017, December 11-14, Delhi, 2017.

Externally Funded Research Projects

Externally Funded Research Projects

List of Extra Mural projects as on date 31.03.2018(for the financial year 2017-18)

Name of P.I.	Project S.No.	Name of Project	Name of the Implementing Agency	Date of Sanction of Project	Original Sanctioned Cost (Rs. In Lakh)	Date of Completion
Dr. Neeraj Jain	1	Mechanisms of Adult Brain Reorganization	D.B.T.	28.05.2014	35.74	27.05.2018
Dr. Anirban Basu	2	Identification and Characterization of brain cellular membrane components acting as receptors as receptors for japanese encephalitis virus	C.S.I.R.	21.11.2014	15.00	20.11.2017
	3	MicroRNA mediated regi;ation of neural stem/progenitor cell fate in neurotropic flaviviral infection	D.B.T.	29.12.2017	77.07	28.12.2020
	4	Understanding the therapeutic role of adult stem cell derived exosome in combating virus induced neurodegenerative disease	D.B.T.	20.03.2018	25.50	19.03.2021
	5	MicroRNAs as a potential therapeutic target in Neuro tropic viral infection(Tata Innovation fellowship)	D.B.T.	01.05.2015	27.00	31.04.2018
Dr. Ellora Sen	6	Understanding inflammation driven regulation of macrophages function: Implications in glioblastoma progression(National Bioscience Award)	D.B.T.	25.11.2014	15.00	24.11.2017
	7	Inflammation regulated metabolic reprogramming Implications in tumor progression(UOE)	D.B.T.	30.03.2015	172.9	29.03.2018
Dr. Nandini C. Singh	11	The neurobiology of dyslexia: integrating brain and behavior	D.S.T.	22.11.2017	43.08	21.11.2020

Externally Funded Research Projects

	12	A longitudianal study to responsiveness to song based stimuli in children with autism behavior and diffusion tensor Imaging(National Women Bioscientists Awards)	D.B.T.	12.11.2013	25.00	11.11.2018
Dr. Soumya Iyangar	13	Effects of the δ- opioid receptor system on singing and song learning in Zebra Finches	D.S.T.(SERB)	23.09.2016	37.43	22.09.2019
Dr. Pankaj Seth	14	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	20.54	19.03.2021
	15	Insights into role of a dyslexia linked long non-coding RNA(lncRNA) in human neural stem cell	D.S.T.	18.07.2017	65.24	17.07.2020
Dr. Dipanjan Roy	16	Oscillatory network dynamics in perceptual learning	D.S.T.	23.08.2017	50.55	22.08.2020
Dr. Pravat kumar Mandal	17	Characterizing biomarkers of Alzheimer's disease :A longitudianal multii modal brain imaging study (Brain imagining)	D.B.T.	25.09.2013	120.68	24.09.2018
	18	National Programme On Perception Engg.Phase II	D.E.I.T.	20.12.2013	86.40	19.12.2017
	19	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	27.00	31.03.2018
	20	Construction of an indian population specific brain template	C.S.I.R.	11.05.2016	26.12	10.05.2019
	21	Unravelling the causes of stroke and cognitive decline in general population A cross-Cultural perspective (DBT Netherland Grant)	D.B.T.	21.04.2016	73.66	20.04.2022
	22	Novel Imaging Diagnostics for Alzheimer's Disease	D.B.T.	24.01.2018	151.26	23.01.2021
Dr. Nihar Ranjan Jana	23	Neurotherapy development of a new screening platform for the discovery of novel therapeutics to cure neurodegenerative disease	D.S.T.	08.03.2018	33.45	07.03.2021
	24	Tata Innovation Fellowship	D.B.T.	22.01.2014	18.00	21.01.2017

Dr. Sourav Banarjee	25	CRISPRi system : A toolbox to investigate novel regulatory mechanisms of synapse formation by long non-coing RNAs"	D.B.T.	11.01.2016	74.19	10.01.2019
	26	Regulation of energy metabolism by miRNA-mediated control of neurogenesis	D.B.T.	21.02.2015	78.09	20.02.2018
	27	Ramalingaswamy fellowship 2011-12	D.S.T.	07.06.2012	74.50	06.06.2017
Dr. Subrata Sinha	28	Epilepsy Project(M.E.G.)	D.B.T.	11.02.2011	2776.76	10.02.2018
	29	Neuroscience education research fellowships in clinical neuroscience and Neuro-informatics & Computatinal neuroscience	D.B.T.	27.09.2012	620.00	26.09.2017
	30	Dist infromation Centre(DIC)	D.B.T.	01.04.2013	72.40	31.03.2017
	31	Dementia Programme	D.B.T.	14.09.2007	37.50	31.03.2017
Dr. Arpan Banerjee	34	Neuro -Cognitive networks underlying goal Directed Behavior	D.B.T.	28.11.2013	82.00	27.11.2018
	35	How do vision guide speech perception (IYBA-2013)	D.B.T.	21.05.2014	38.81	20.05.2017
Dr. Anindya Ghosh Roy	36	Wellcome Trust/DBT Indian Alliance	D.B.T.	01.12.2013	321.93	30.11.2018
Director NBRC	37	Dementia Programme	D.B.T.	30.12.2017	928.35	29.12.2022
Dr. Yogita K Adlakha	38	Innovation in science pursuit for inspired Research(INSPIRE)	D.S.T.	01.07.2014	35.00	31.06.2019
Dr. Aparna Dixit	39	Deciphering the role of the mulifaceted kinase CDK5 in itractable epilepsy	D.S.T.	21.10.2014	27.21	20.10.2017
Dr. Dipanjay Ray	40	A critical assessment of the dual stream models of visual information processing	D.S.T.	02.06.2015	18.56	01.06.2017
Poonam Meena	41	Post Doctoral Fellowship	SERB	08.08.2016	14.40	07.08.2018
Dr. Akansha Jalota	42	Post Doctoral Fellowship	SERB	15.11.2016	19.20	14.11.2018
Dr. Soibam Shayamchand	43	Post Doctoral Fellowship	SERB	03.05.2017	19.20	02.05.2019
Sailu Ibrahim	44	TWAS-DBT Fellowship	D.B.T.	26.12.2017	2.01	31.03.2018
Dr. Rolland kipre	45	C V Raman In fellowship	D.B.T.	24.01.2018	2.85	23.01.2019
Dr. Prem Chand	46	Effect of handedness on recovery of forepaw in rats with spinal cord injury	D.S.T.	11.07.2017	17.6	10.07.2019

Distinctions, Honors and Awards

Distinctions, Honors & Awards

Faculty

Dr. Anirban Basu

- Prof S S Katiyar Endowment Lecture of The Indian Science Congress Association (ISCA)-2018.
- Elected as a Fellow of the Indian Academy of Sciences (IASc)-2018
- Sreenivasaya Memorial Award of Society of Biological Chemist (India)-2017.

Dr. Ellora Sen

- Milstein Travel Award International Cytokine & Interferon Society (ICIS), 2017.

Dr. Pankaj Seth

- Nominated and Elected as Fellow, of The National Academy of Sciences (India) (2017).
- Nominated and Elected as Member of the Guha Research Conference (2017).

Dr. Dipanjan Roy

- Ramalingaswami re-entry fellowship Department of Biotechnology (DBT).

Students

Shalini Swarup International Society of Neurochemistry (ISN) travel award to attend ISN-ESN Biennial Meeting, Paris, 20-24th August, 2017.

Sriparna Mukherjee SFN-IBRO Travel award to attend Annual meeting of Society for Neuroscience, 11-15th November, 2017, Washington DC.

Sarbani Samaddar, a Ph.D. student received fellowship from Janelia Farm-HHMI to present her research in Junior Scientists Workshop on Neuronal Cell Biology, May 2017.

Course-Work

M.Sc. 2016

Ms. Kasturi Biswas: M.Sc. student, has been awarded first rank upon completion of Course-Work during the year 2016-17 and a certificate was given to her on the 14th Foundation Day, the 16th December 2017.

Ms. Tapasya Pal: M.Sc. student, has been awarded second rank upon completion of Course-Work during the year 2016-17 and a certificate was given to her on the 14th Foundation Day, the 16th December 2017.

Ph.D. 2016

Mr. Sibaram Behera: Ph.D. student, has been awarded first rank upon completion of Course-Work during the year 2016-17 and a certificate was given to him on the 14th Foundation Day, the 16th December 2017.

Ms. Tripti Joshi: Ph.D. student, has been awarded second rank upon completion of Course-Work during the year 2016-17 and a certificate was given to her on the 14th Foundation Day, the 16th December 2017.

Ph.D. Degrees Awarded

S/No	Name of the Student
1.	Dr. Priyabrata Halder
2.	Dr. Himakshi
3.	Dr. Imran Jamal
4.	Dr. Avantika Mathur
5.	Dr. Pushpa Kumari

M.Sc. Degrees Awarded

S/No	Name of the Student
1.	Mr. Priyabrata Halder
2.	Ms. Shruti F Nagaral
3.	Mr. Gaurav Sharma
4.	Ms. Himali Arora
5.	Ms. Meenakshi Bhaskar
6.	Mr. Neeraj Kumar
7.	Ms. Sanskriti
8.	Mr. Utsav Mukherjee
9.	Ms. Himakshi
10.	Mr. Imran Jamal
11.	Ms. Avantika Mathur

Academic Programs

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.

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 ₹ 25,000/- per month for Junior Research Fellows and ₹ 28,000/- per month for Senior Research Fellows.

M.Sc. in Neuroscience

NBRC is one of the first Institutes in the country to develop an integrated multidisciplinary teaching programme in Neurosciences.

During the academic year 2015-16 NBRC reintroduced the M.Sc. (Neuroscience) programme to develop trained manpower having a broad overview of different aspects of Neuroscience.

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

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

Summer Training and Short-term Programmes

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

NBRC Facilities

Distributed Information Centre (DIC)

The Distributed Information Centre (DIC) department of National Brain Research Centre is entrusted with managing the overall ICT infrastructure and communication networks of the Institute apart from aiding in R&D activities. The department focuses on providing Scientific Services related to Computational facility to the Scientists as well as promoting e-Governance activities of the institute. It is also a DIC Centre under the BTISNET initiative of Department of Biotechnology. The Centre also manages the campus network (data and voice traffic), communications links (Network and PSTN), Institute's Datacentre, hosting core network and application servers, software development, ICT Modernization, e-Governance initiatives, technical support to users, common computing facility etc. The details of 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 itself. The network is supplemented with secure firewall and unified threat management appliances for network safety, intrusion detection system, gateway level antivirus, VPN facility, managing IT policy and detailed auditing / logging etc. The campus network is a fully 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 thus provides visiting scientists and researchers seamless secure wireless access in all participating institutions across the world.

The campus converged network of the institute is connected with National Knowledge Network (NKN), the last mile link to NKN-Delhi POP is on 1Gbps optical fibre link provided by BSNL. 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 were 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; they are housed and maintained in the mini-datacenter facility. In essence the institute currently has four numbers of fully utilized 42U server racks in the datacenter facility. The various service running on these server can be classified as under :

a. Web-servers for the institute website (http://www.nbrc.ac.in) and other website like http://neuroscienceacademy.org.in. In addition, various web-servers related to ongoing computational projects and applications of various scientific groups is also hosted and managed in the central facility.

b. E-mail servers for institute mailing along with list servers.

c. DNS servers for the official and hosted domains.

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

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

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

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

h. Central Storage servers along with backup servers handling storage requirements of the users and laboratories for online central storage and data processing.

i. 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.

D) Other Facilities & Services

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

b. *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 have been provided with GOV. IN email ids on NIC platform for better availability.

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 are managed through central NMS device for aiding into the security 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.

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.Cg–Mapttm1 (EGFP)KltTg(MAPT)8cPdav/J (Alzheimer disease model)
- B6.129P2-Gsk3btm1Dgen/J (Alzheimer disease model)
- B6129P2Pvalb< 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 Ssttm2.1(cre)Zjh/J
- B6.Cg-Gt(ROSA)26Sortm6(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 1181 online journals through the DBT e-Library Consortium (DeLCON), 3 specialized journals, and 122 freely accessible online journals. It also maintains digital archives and news clips about the Centre and subscribes to Newspapers and News Letters. The collection of the NBRC Library is growing day-by-day along with new developments in research and knowledge in the field of Neuroscience and related areas. To provide optimum service to all users, the NBRC library is currently digitizing its list of collections using the LSEASE software, to which all users will have full access. A barcode technology has also been installed for accurate and speedy circulation and the management of all library documents. The new software will also help in efficient library operations viz. administration, acquisition, circulation, serial control, cataloguing and information retrieval. The Library has set up 22 Computers with Internet facility to provide services for use of researchers and students in the NBRC Common room and has been providing electronic access to the subscribed journals through the campus portal. The NBRC Library also provides Inter Library Loan Services to NBRC's 48 networked centres all over India. Researchers at different centres send their requirement for research material or journal articles through email to NBRC Library at library@nbrc.ac.in which are then downloaded and sent to them free of cost. By library staff The library entertains an average of approximately 450 requests for articles and this number is increasing every year. The NBRC Library regularly evaluates its information services to ensure that the Institution's requirements are met. It promotes resource sharing and cooperation activities among libraries by providing an efficient and reliable means of resource sharing, that is, the inter library loan for the maximum use of resources, by providing copies of documents which are not available to researchers at centres outside the institute.

Main Activities Of NBRC Library

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

DBT's Electronic Library Consortium (DeLCON)

DeLCON Consortium: A National Library Consortium For Life Sciences & Biotechnology Hosted And Administered By NBRC And Sponsored By Department Of Biotechnology

The DBT Electronic Library Consortium (DeLCON)' is major project of the Department of Biotechnology (DBT) to bring qualitative change in the research institutions. It was launched in January 2009 with 10 DBT member institutions (including DBT H.Q. & ICGEB) 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 institutional community. It facilitates access to high quality e-resources to the faculty, 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 to 17 more DBT Institutions in the 2nd phase of extension in the year 2010, and additional 7 members were added in the 3rd phase in the Year 2011. In the year 2012, DBT merged all the phases and it became a single 'DeLCON Consortium' with 33 members. Since 2013 the total membership is 34. The 'DeLCON Consortium' provides current as well as archival access to more than 1181 core peer-reviewed journals and one bibliographic database (SCOPUS Database) in different disciplines from 21 foreign publishers and some of the aggregators.

The DeLCON comprised of following 33 member institutions in 2011:

DeLCON Members (2009) - Phase-I

- National Brain Research Centre (NBRC), Manesar
- Department of Biotechnology (DBT), New Delhi
- National Institute of Plant Genome Research (NIPGR) – New Delhi
- National Institute of Immunology (NII) – New Delhi
- National Centre for Cell Science (NCCS) – Pune
- Institute of Life Sciences (ILS) – Bhubaneshwar
- Institute of Bioresources and Sustainable Development (ISBD) – Imphal
- Centre for DNA Fingerprinting and Diagnostics (CDFD) – Hyderabad
- Rajiv Gandhi Centre for Biotechnology (RGCB) – Thiruvananthapuram
- International Centre for Genetics Engineering and Biotechnology (ICGEB), New Delhi

DeLCON Members (2010) - Phase -II

- The Wellcome Trust-DBT India Alliance, Hyderabad (further excluded in the year 2011)
- Dibrugarh University (DU), Assam
- Assam University (AU), Silchar
- North Eastern Regional Institute of Science & Technology (NERIST), Arunachal Pradesh
- North East Institute of Science & Technology (NEIST), Assam
- Mizoram University (MizU), Mizoram
- D. M. College of Science (DMC), Manipur
- Sikkim University (SU), Gangtok
- College of Veterinary Science, Assam Agricultural University (CVSAAU), Guwahati
- St. Anthony's College (SAC), Meghalaya
- Biotechnology Industry Research Assistance Program (BIRAP), New Delhi
- Guwahati University (GU), Assam
- Manipur University (ManU), Imphal
- College of Veterinary Science & Animal Husbandry Central Agricultural University (CVSAHCAU), Mizoram
- Rajiv Gandhi University (RGU), Arunachal Pradesh
- Nagaland University (NU), Nagaland

- North-Eastern Hill University (NEHU), Shillong

DeLCON Members (2011) - Phase-III

- Indian Institute of Technology Guwahati (IITG), Guwahati, Assam
- National Agri-Food Biotechnology Institute (NABI), Mohali, Punjab
- National Institute of Biomedical Genomics (NIBHG), Kalyani, Kolkata
- Regional Centre for Biotechnology (RCB), Gurgaon
- Tezpur University (TU), Tezpur, Sonitpur, Assam
- Transnational Health Science & Technology Institute, Gurgaon
- Sikkim State Council of Science and Technology (SSCST), Gangtok, Sikkim

DeLCON Members From Year 2012

In the year 2012, DBT merged the all phases I, II & III and made it as a single 'DeLCON Consortium'. DBT also merged two colleges under their universities. St. Anthony's College (SAC), Meghalaya, merged with North Eastern Hill University, Shillong, and D. M. College of Science (DMC), Manipur, merged with Manipur University. The two other DBT cluster institutions, Regional Centre for Biotechnology (RCB), Gurgaon, and Transnational Health Science & Technology Institute (THSTI), Gurgaon, were merged as the Biotech Science Cluster. Moreover, the Biotechnology Industry Research Assistance Programme (BIRAP), New Delhi was replaced by National Institute of Animal Biotechnology, (NIAB), Hyderabad.

Current Delcon Membership, Since The Year 2013, Is Given Below As DBT Institution & North East Regional (NER) Institutions DBT Institutions

1. Department of Biotechnology (DBT), New Delhi
2. National Brain Research Centre (NBRC), Manesar
3. National Institute of Plant Genome Research (NIPGR), New Delhi
4. National Institute of Immunology (NII), New Delhi
5. National Centre for Cell Science (NCCS), Pune
6. Institute of Life Sciences (ILS), Bhubaneshwar
7. Institute of Bioresources and Sustainable Development (ISBD), Imphal
8. Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad
9. Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvananthapuram
10. International Centre for Genetics Engineering and Biotechnology (ICGEB), New Delhi
11. National Agri-Food Biotechnology Institute (NABI), Mohali, Punjab
12. National Institute of Biomedical Genomics (NIBMG), Kalyani, Kolkata DBT's Electronic Library Consortium (DeLCON) NBRC Annual Report 2016-17 129
13. National Institute of Animal Biotechnology (NIAB), Hyderabad
14. Regional Centre for Biotechnology (RBC), Faridabad, as a part of NCR Biotech Science Cluster (BSC)
15. Transnational Health Science & Technology Institute (THSTI), Faridabad, as a part of NCR Biotech Science Cluster (BSC)
16. Biotechnology Industry Research Assistance Council (BIRAC), New Delhi

North Eastern Region (NER) Institutions

17. Dibrugarh University, Assam
18. Assam University, Silchar
19. North Eastern Regional Institute of Science & Technology, Arunachal Pradesh
20. North East Institute of Science & Technology, Assam
21. Mizoram University, Mizoram
22. D. M. College of Science (DMC), Manipur*
23. Sikkim University, Gangtok
24. College of Veterinary Science, Assam Agricultural University, Guwahati
25. Guwahati University, Assam
26. Manipur University, Imphal
27. College of Veterinary Science & Animal Husbandry Central Agricultural University, Mizoram
28. Rajiv Gandhi University, Arunachal Pradesh
29. Nagaland University, Nagaland
30. North-Eastern Hill University (NEHU), Shillong
31. St. Anthony's College (SAC), Meghalaya*
32. Indian Institute of Technology Guwahati, Assam
33. Tezpur University, Tezpur, Sonitpur, Assam
34. 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 Covered 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
- American Association for Cancer Research (AACR) http://www.aacr.org 9
- American Chemical Society (ACS) http://pubs.acs.org 47
- Annual Reviews (AR) http://www.annualreviews.org 23
- American Society for Biochemistry and Molecular Biology (ASBMB) http:/// www.jbc.org 2
- American Society For Microbiology (ASM) http:// www. asm.org/ 21
- Cold Spring Harbor Laboratory Press (CSHL) http:// www. cshl.edu 4
- Taylor & Francis (T&F) http://www.informaworld.com 40
- Lippincott William & Wilkins/ Wolter Kluwer / OVID http://ovidsp.ovid.com 11
- Marry ANN Liebert (MAL) http://www.liebertonline.com 92
- Nature Publications http:// www.nature.com 37
- Oxford University Press (OUP) http://www. oxfordjournals. org 22
- Springer India http://www. springerlink.com 342
- Society for General Microbiology (SGM) http:// mic. sgmjournals.org 3
- American Society for Hematology (ASH) http:// bloodjournals.hematologylibrary.org 1
- Wiley-Blackwell http:// www3.interscience.wiley.com/ cgi-bin/home 85
- Elsevier Science (Science Direct) http:// www. sciencedirect.com 433
- American Society of Plant Biologist (ASPB) http://www. aspb. org/ 2
- American Association of Immunologist (AAI) http:// www.aai.org/ 1
- Scopus Database http:// www.scopus.com 1 Database
- The New England Journal of Medicine (NEJM) http:// www.nejm.org 1
- Proceedings of National Academy of Sciences (PNAS) http://www.pnas.org 1

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 cover-up 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

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. 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 and MRS. In addition to understanding brain function and clinical research, the center also is closely interacting with leading imaging centers within the country and across the globe.

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

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

Clinical studies on patients with Alzheimer's Disease, Parkinson's Disease, Autism and Brain Tumours, as well as monitoring of aging in normal healthy brain, are being performed extensively in the National Neuroimaging facility. Understanding the basic neurobiology of various sensory and cognitive functions using non-invasive neuroimaging tools are also undertaken by several labs in NBRC.

Translational & Clinical Neuroscience Unit

The unit is located at the Government General Hospital, Gurgaon 122 001.

Investigation facilities:

The following facilities are available to the patients of the unit 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 expertise of the following faculty are available at the NBRC Unit:

Consultant Clinical Associate Professor, Neurology: Dr Rajnish Kumar

Consultant Clinical Assistant Professor, Neurology: Dr. Kunal Bharani

Clinical Psychologist: Priyanka Kaushik

Clinic Assistant: Hanuman Singh and Pawan Kumar

Translational research aims to provide the benefits of our understandings of disease pathology basic research with a purpose of patient care. The translational and clinical neuroscience unit was established based on the concept of mutually benefitting the patient and basic research laboratory with an aim to share knowledge "From the Bench to the Bedside and back to the Bench". The Clinical Research Unit of NBRC offers the full spectrum of clinical neuroscience: Neurology, Neuropsychology, Neuropsychiatry, Neurosurgery, Behavioral therapy, Psychology, and Psychometry. The unit has a morning outpatient facility, at the Government General Hospital, each of the consultant clinical faculty is available on one of the designated days of the week. The NBRC Unit has integrated well with the Civil hospital medical team and there is an increasing number of referrals from other in-house departments and local hospitals. If a patient of the unit requires indoor treatment or observation, then, with courtesy of Neuropsychiatrists and Specialist Clinicians of internal medicine of the General Hospital, the patient is taken care of. The neurologists were also assisted by a resident medical officer, Dr. Tamanna Yadav for screening and recording of patients.

The out-patients facility caters to medical needs of patients from Gurgaon and neighbouring areas which keeps the neuro OPD quite crowded, and on some days the footfall of patients exceeds 50-60. The facility has an impressive follow up of patients, that is about 75%. Male to female ratio is almost equal. Patient age groups range from pediatric to adult and elderly. 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 and epilepsy.

Patients attending the OPD at Civil Hospital come from old Gurgaon township and the villages and towns in the surrounding districts of Haryana, while some come from neighbouring states as Rajasthan, Delhi, Uttaranchal, Himachal Pradesh, Punjab and Uttar Pradesh.

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), or Vardhaman Medical College (Safdarjung Hospital), New Delhi or to other tertiary hospital as per the choice of the patient, if he/she so desires.

Outpatient (OP) case records in neurology are maintained from the outset, aside from relevant entry into the patient OP case sheets, which the patients keep in their possession. A comprehensive Neurology case sheet has been formulated and formatted by Distributed Information Centre of NBRC in consultation with

attending neurologists. We are undertaking to prospectively enter all the medical data of new patients, to create computer database with relevant patient data along with any planned imaging/molecular/ neurophysiological studies at the NBRC labs, thus creating a well documented "clinical window" for our research institute. 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.

Due to the extreme shortage of Neuropsychiatric manpower in the northern regions of the country, the Directorate General of Health Sciences, Government of Haryana, has taken initiative towards Post-Graduate Educational Program in Psychiatry (DNB, Diplomate of the National Board) at the hospital, facilitating our Unit to have a seminal productive academic output.

For proper functioning and further clinical support, the NBRC Unit at the Hospital receives the cooperation of the Ministry of Health - Government of Haryana, and the Deputy Commissioner - Gurgaon, as well as from the Chief Medical Officer & Civil Surgeon and Principal Medical Officer of the Hospital. The translational and clinical research unit of NBRC is great advantage for the local patients and is much appreciated.

Centre of Excellence (CoE) for Epilepsy Research

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

Scientific Faculty: AIIMS- Delhi

Prof. P Sarat Chandra,
Prof. Manjari Tripathi,
Dr. Jyotirmoy Banerjee,

Scientific Faculty: NBRC

Dr. Pravat Mandal,
Dr. Neeraj Jain, Director (Additional Charge)

MEG Technologists:

Mr. Kamal Bharti

Centre of Excellence for Epilepsy (COE) is collaborative project between National Brain Research Centre (NBRC) and All India Institute of Medical Sciences (AIIMS) established under the aegis of Department of Biotechnology (Government of India). This one of the few centres in the world which brings together a premier medical science institute and a dedicated neuroscience research centre to study difficult-to-treat epilepsy. The main aim of the centre is to develop a cure for drug-resistant epilepsy by bridging the gap between clinical and basic research which is mediated by the close coordination between NBRC and AIIMS. For a comprehensive study the AIIMS component of the centre is using magnetic resonance imaging (MRI), electroencephalography (EEG), video EEG, as well as functional imaging techniques like positron emission tomography (PET) and single photon emission tomography (SPECT) to locate the epileptogenic area. The NBRC component of the centre is using non-invasive protocol of magnetoencephalography (MEG) for the localization of epileptogenic focus. These well-established epileptogenic zones surgically removed during epilepsy surgery serves as ideal model to study the mechanism of epileptogenesis in patients with DRE. Quantification of abnormalities in these tissues is performed by RNAseq/microarray analysis for gene expression abnormalities and cellular electrophysiological experiments to study the changes in the synaptic transmission and the shift of electrical properties of the neurons. Correlation of the radiological and electrophysiological parameters with the molecular/cellular properties of neurons to study epileptogenesis is the hallmark of this multi-disciplinary centre.

MEG source localization for delineating the epileptogenic networks (MEG Facility):

Magnetoencephalography source localization (SL) added information towards delineating the epileptogenic networks and helped final decision making in epilepsy-surgery. To this end definite focal clusters on ictal-MEG data was analysed and single equivalent current dipole (ECD model) along with SL was performed. Clinical history, long-term video-EEG (VEEG) monitoring, epilepsy-protocol MRI, FDG-PET, ictal-SPECT and interictal-MEG were discussed at the multispeciality epilepsy Surgery Case-conference (ESC). Patients were grouped as VEEG localization and MRI-lesion concordant (Group-A), discordant (Group-B), and no MRI-lesion (Group-C). We observed that the difference between numbers of patients cleared for surgery without and with MEG data was statistically significant ($p = 0.04$); but the difference in those cleared for phase II monitoring was not ($p = 1.00$) as shown in figure 1. MEG influenced decisions on possibility of surgery in 75 % and converted decisions of phase II monitoring in 20 % patients to electrocorticography-guided lesionectomy.

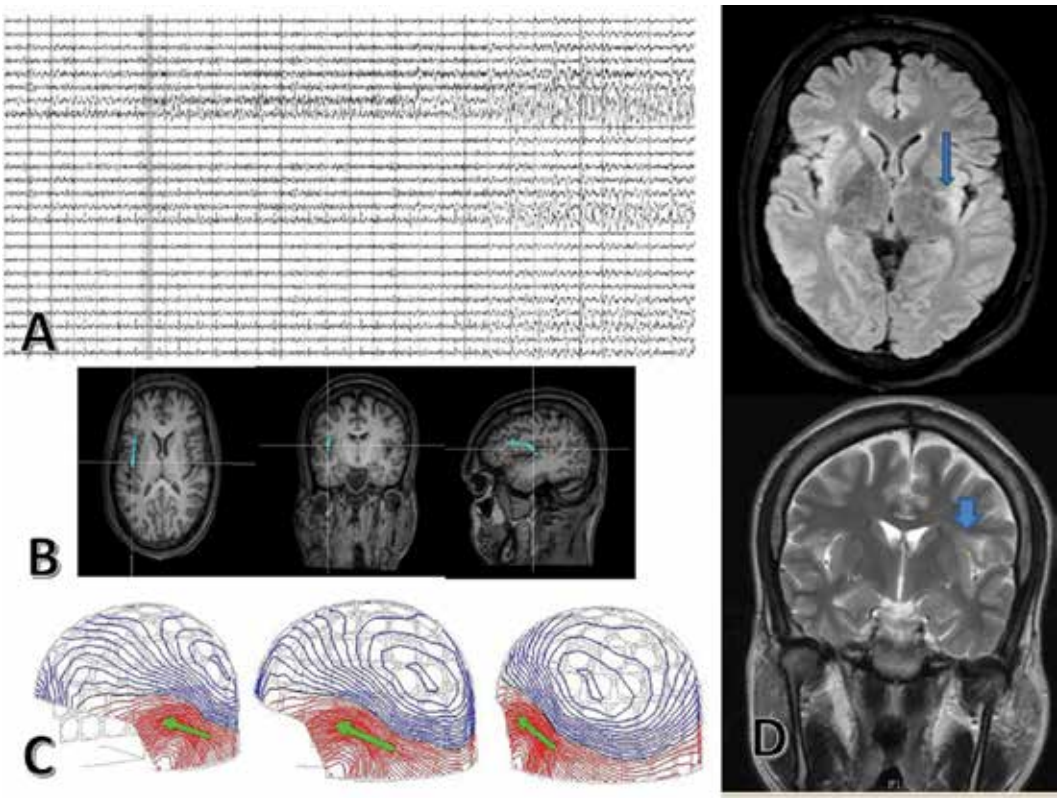


Figure 1

Publication:

1: Srivastava A, Dixit AB, Paul D, Tripathi M, Sarkar C, Chandra PS, Banerjee J. Comparative analysis of cytokine/chemokine regulatory networks in patients with hippocampal sclerosis (HS) and focal cortical dysplasia (FCD). Sci Rep. 2017 Nov 21;7(1):15904.

2: Dwivedi R, Ramanujam B, Chandra PS, Sapra S, Gulati S, Kalaivani M, Garg A,Bal CS, Tripathi M, Dwivedi SN, Sagar R, Sarkar C, Tripathi M. Surgery for

Drug-Resistant Epilepsy in Children. N Engl J Med. 2017 Oct 26;377(17):1639-1647.

3: Chaudhary K, Ramanujam B, Kumaran SS, Chandra PS, Wadhawan AN, Garg A,

Tripathi M. Does education play a role in language reorganization after surgery in drug refractory temporal lobe epilepsy: An fMRI based study? Epilepsy Res.2017 Oct;136:88-96.

4: Ray S, Tripathi M, Chandra SP, Chakravarty K. Protocols in contemporary

epilepsy surgery-a short communication. Int J Surg. 2017 Aug;44:350-352.

5: Dixit AB, Banerjee J, Tripathi M, Sarkar C, Chandra PS. Synaptic

roles of

cyclin-dependent kinase 5 & its implications in epilepsy. Indian J Med Res. 2017 Feb;145(2):179-188.

6: Banerjee J, BanerjeeDixit A, Srivastava A, Ramanujam B, Kakkar A, Sarkar C,Tripathi M, Chandra PS. Altered glutamatergic tone reveals two distinct resting state networks at the cellular level in hippocampal sclerosis. Sci Rep. 2017 Mar 23;7(1):319.

7: Banerjee Dixit A, Sharma D, Srivastava A, Banerjee J, Tripathi M, Prakash D,Sarat Chandra P. Upregulation of breast cancer resistance protein and major vault protein in drug resistant epilepsy. Seizure. 2017 Apr;47:9-12.

8: Kumar S, Ramanujam B, Chandra PS, Dash D, Mehta S, Anubha S, Appukutan R, Rana MK, Tripathi M. Randomized controlled study comparing the efficacy of rapid and slow withdrawal of antiepileptic drugs during long-term video-EEG monitoring. Epilepsia. 2018 Feb;59(2):460-467.

Funding:

"Centre of Excellence for Epilepsy Research" a collaborative project between NBRC & AIIMS, funded by Department of Biotechnology, Ministry of Science & Technology, India.

Lectures, Meetings & Workshops

Lectures, Meetings & Workshops

Invited Speakers at NBRC

Sr. No.	Name of the Speaker	Title of the Lecture	Date
1.	Jyotirmoy Banerjee Center of Excellence for Epilepsy, National Brain Research Centre (NBRC)	Understanding the alteration in synaptic activity associated with drug-resistant epilepsy (DRE): A cellular electrophysiological approach	April 27, 2017
2.	Dr Arun Singh PhD, Department of Neurology Neuromodulation Research Center University of Minnesota 2001 6th St SE Minneapolis-55455, MN, USA	The role of striatal mechanisms in advanced stage of parkinsonism	May 9, 2017
3.	Dr. Dipanjan Roy Center of Behavior and Cognitive Science (CBCS), University of Allahabad	Reorganization of resting state connectivity across the Lifespan	May 22, 2017
4.	Dr. Subhash Sinha Research Associate Professor, Laboratory of Molecular and Cellular Neuroscience, The Rockefeller University	Novel Tools and Targets for developing Therapies of the Alzheimer's Disease	June 8, 2017
5.	Prof K K Deepak Department of Physiology In-Charge, Autonomic Function Lab, Executive Editor, Indian J Physiology & Pharmacology AIIMS, New Delhi	Activating mind through breath: The yogic way of brain stimulation	June 21, 2017
6.	Dr Andrew Holmes Chief, Laboratory of Behavioral and Genomic Neuroscience National Institute on Alcohol Abuse and Alcoholism Rockville, MD, USA	Deciphering neural circuits of anxiety to identify new anti-anxiety medications	July 14, 2017
7.	Dr Alok Kumar Ramalingaswamy Fellow Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh	Secondary Injury mechanisms contribute to pathophysiology of traumatic brain injury and linking to chronic neurodegeneration: clinical and therapeutic implications	July 17, 2017
8.	Dr. Sathees Raghavan IISc Bangalore	DNA Double-strand Break Repair in Human Genome: The Good, The Bad and The Unknown	July 24, 2017
9.	Prof Mriganka Sur, Newton Professor of Neurosciences, Director, Simons Center for the Social Brain, MIT, USA	The neural architecture of cognition	August 17, 2017

10.	Dr Ravi Bansal Professor of Research, Department of Pediatrics & Electrical Engineering, University of Southern California	In Vivo Evidence for Neuroplastic Changes in Gray and White Matter of Persons with Depressive Illness	August 28, 2017
11.	Ganesh Bagler Center for Computational Biology, IIIT-Delhi, New Delhi	Controllability of C. elegans brain network	September 7, 2017
12.	Achira Roy Seattle Children's Hospital & Research Institute, Seattle	Modelling human PI3K-related brain malformations and epilepsy – time, cause and treatment	September 20, 2017
13.	Dr Deepika Suri Postdoctoral Research Fellow Department of Psychiatry, Columbia University, New York, USA	Adolescent shaping of dopaminergic circuit activity and impulsive behavior	September 18, 2017
14.	Dr. Ramesh Kandimalla Texas Tech University	Reduced dynamin-related protein 1 protects against phosphorylated Tau and Aβ induced mitochondrial dysfunction, synaptic damage, dendritic spine loss, failure in auto/mitophagy in Alzheimer's disease mouse models.	October 17, 2017
15.	Dr Sikha Saha Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds	A novel in vitro blood brain barrier model	November 9, 2017
16.	Dr. Anand Swaroop National Eye Institute, National Institutes of Health (NIH), USA	Retinal Development, Organoids and Design of Therapies for Neurodegenerative Disease	November 29, 2017
17.	Dr. Sorab N. Dalal Principal Investigator ACTREC, Tata Memorial Centre, Navi Mumbai	Regulation of centrosome duplication by 14-3-3 proteins	December 8, 2017
18.	Prof. Kamal Sen Boston University	Unraveling Cortical Mechanisms of Spatial Processing for Solving the Cocktail Party Problem	January 8, 2018
19.	Dr. Swagata Dey Department of Biological Sciences, Tata Institute of Fundamental Research, Mumbai	Modalities of Kinesin-2 mediated axonal transport in Drosophila melanogaster and their implications	February 1, 2018
20.	Dr. D Balasubramanian Distinguished Scientist and Director Emeritus, Prof Brien Holden Eye Research Centre	Advances in the stem cell applications to the eye -our research at LVPEI	February 7, 2018
21.	Dr Srikanth Padmala University of Maryland USA	Interactions between emotion, motivation and cognition in the human brain	March 19, 2018
22.	Dr. Prabuddha Kundu Executive Director, Premas Biotech.	Build your own Biotech Company: the building blocks.	March 13, 2018
23.	Dr. Souvik Modi Department of Neuroscience, Physiology and Pharmacology University College London	Designer nanoprobes to investigate cellular function	March 26, 2018
24.	Dr Sharmila Nair Departments of Medicine, Molecular Microbiology, Pathology & Immunology St. Louis, MO 63110	Host Genetic and Metabolic determinants that prevent immunopathology during bacterial and viral infections	March 23, 2018
25.	Dr Deepak Kaushik Hotchkiss Brain Institute, University of Calgary, Canada	Drivers and mechanisms of inflammation in multiple sclerosis	March 20, 2018
26.	Dr.Bhairav Mehta Case Western Reserve University, USA	Novel Approaches for Quantitative MR Imaging and their Potential Applications	March 22, 2018
27.	Dr Varun Sethi Neurology Registrar, National Hospital for Neurology and Neurosurgery (UCLH), London, UK	Being guided by Imaging in Multiple Sclerosis	March 28, 2018

Workshop on Handling and Care of Laboratory Animals at National Brain Research Centre.

NBRC organized ***"workshop for Handling and care of laboratory Animals" during October 24th – 27th, 2017.***

The objective of workshop was to provide hands-on training to improve quality of research conducted on animals and also to disseminate basic facts and principles including knowledge, skills and attitude that are essential for the humane use and care of animals namely mice, rats and rabbits used for research. Resource persons from all over the India renowned for their expertise and significant research contributions were invited to deliver lectures on the topic of their expertise. The major themes of the workshop included Laboratory animals and its environment, Nutrition, Cryopreservation, Diseases of laboratory animals, Laboratory animal welfare and ethics, Anaesthesia, Surgical techniques and analgesia in Lab animals. Practical in handling and restraining of mice, rat and rabbit, Administration of substances, collection of body fluids, pain anaesthesia and peri-operative care and Demo for live animal imaging were also part of the workshop. This workshop was attended by participants from universities/institutes/industry from all over India as well as from neighboring countries (i.e. Nepal and Nigeria).

Brain Modes 2017

This year National Brain Research Centre, Manesar hosted the 10th annual BrainModes meeting on 'A multimodal brain: Spatiotemporal network mechanisms and models', from 11th-14th December 2017. BrainModes is a yearly meeting that brings together leading computational and experimental neuroscientists from around the world to discuss cutting-edge neuroscience methods, theories, and applications aimed at understanding complex brain signals. The conference had a distinct mathematical flavor. It addresses questions related to the understanding of mental diseases through a mathematical prism. The focus of this year's meeting was to understand spatiotemporal network mechanisms and models in health and disease. A major talking point within this framework is 'brain oscillations'. Talks focused on understanding different kinds of oscillations and how they may be involved in perceptual decision-making, multimodal perception and how perception changes in brain pathologies like schizophrenia & epilepsy. Another thrust area for this year's meeting was on modeling neuro-imaging data using tools borrowed from physics and mathematics, such as nonlinear dynamics and Bayesian probability theory.

NBRC 14th Foundation Day- 16th December, 2017

The National Brain Research Centre celebrated its 14th foundation day with pomp and gaiety on 16th December 2017. 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 the chief guest Dr. Karl Friston who spoke on the topic 'I am therefore, I think'. The provocative title turns Descartes' famous promulgation on its head by asserting that all living organisms search for evidence for their own existence and in doing so, generate action and perception. 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.

13th B. Ramamurthi Memorial Lecture

National Brain Research Centre conducted the annual B Ramamurthi Memorial lecture in memory of late Prof B. Ramamurthi. Prof. Ramamurthi is one of the founding fathers of neurosurgery in India. Notwithstanding his extremely busy professional life as a neurosurgeon, Prof Ramamurthi explored all avenues to promote neuroscience education and research in India. Prof Ramamurthi served on various committees of the highest policy-making bodies like the ICMR, DST, DBT and Health Ministry.

The 13th B. Ramamurthi lecture was delivered on February 7th, 2018, by Prof. D Balasubramanian, Ph.D. Distinguished Scientist and Director Emeritus, Prof Brien Holden Eye Research Centre. The lecture entitled - "Advances in the stem cell applications to the eye - our research at LVPEI" gave us a glimpse of the amazing work done at LV Prasad Eye Institute. He spoke about the Translational Research in biochemistry and the applications of stem cells in the eye to treat disorders in the eye. The highly informative lecture was followed by interactive session with students and faculty of NBRC.

NBRC Workshops on DALI for Teachers and Psychologists to Screen and Identify Children with Dyslexia.

Three comprehensive capacity-building workshops were conducted between April 2017 to March 2018 to train teachers and psychologists on the Dyslexia Assessment For Languages of India (DALI), developed by NBRC. The first of these was held in Mumbai as part of Specific Learning Disability Conclave organised by Maharashtra Dyslexia Association from 26-29th October 2017. Nearly 100 teachers and 50 psychologists from different parts of India were trained on DALI. The workshop in Mumbai was conducted by Prof. Nandini C Singh, Dr. Geet Oberoi, Orkids New Delhi and Prof. Bhoomika Kar from Centre for Behavioural and Cognitive Science, Allahabad University. The second set of workshops was held on May 10 2018, at Department of Education, Govt. of Delhi and attended by 60 psychologists from the National Capital Region. as part of Government of Delhi's project SMILE for its public schools.

The third workshop was held at Ram Manohar Lohia Hospital on 12th May 2018 and conducted by Dr. Nandini Chatterjee Singh. Approximately 30 psychologists and psychiatrists and developmental paediatricians participated in a comprehensive workshop on using DALI for the assessment for dyslexia. Prof. Smita Deshpande and her team organised and facilitated the workshop. The workshop was held under the auspices of the joint DST project between Dr. Nandini C Singh and Dr. Smita Dehpande on the Neurobiology of Dyslexia – behaviour and functional neuroimaging.

Participants were provided hand-on training on DALI in Hindi. DALI is the Dyslexia Assessment for Languages of India. DALI is the first indigenous screening assessment tool to identify Dyslexia in India languages. It was developed by Nandini Chatterjee Singh at the National Brain Research Centre and has been standardised and validated across nearly 4500 children. It is currently available in Hindi, Marathi, Kannada and English and is currently being extended to Tamil, Telugu and Bengali. The screening tools developed under DALI for teachers was also included by Dr. Geet Oberoi in 12 training for Dept. of Education for teachers of Delhi Govt. Schools and 1 in Nagaland.

General & Academic Administration – A Profile

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.
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 etc. The Administration achieved excellence in execution of the following activities at NBRC:

- ❖ The annual cultural festival of NBRC, 'TANTRIKA 2017' was organized within the campus which included a variety of cultural and sports events. Students, officers, and staff of NBRC participated in the event. On 13th September, 2017, a special guest lecture by Dr. Gagandeep Kang, Executive Director, Translational Health Science Technology Institute (THSTI), Faridabad was organized.
- ❖ Provided necessary logistics in conducting international and national conferences/seminars organized in the campus as well outside the campus.
- ❖ Made major imports from different countries in terms of equipment and other consumables with meticulous planning and adhered to a precise schedule.
- ❖ The 14th Foundation Day of NBRC was held on 16th day of December, 2017. 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. Karl Friston, Wellcome Principal Fellow, Institute of Neurology, London, UK delivered the lecture to the students and scientific community at Indian National Science Academy, 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 in spirit. All RTI applications received during 2017-18 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 in 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 in 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 implemented.

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

Institutional Governance Structure & People at NBRC

Members of NBRC Society

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

Prof. K. VijayRaghavan (upto Feb, 2018)
Secretary
Department of Biotechnology
C.G.O Complex
New Delhi – 110 003

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

Dr. Soumya Swaminathan
Director-General
Indian Council of Medical Research
New Delhi – 110 029

Dr. Sandip K. Basu
JC Bose Chair Professor
National Institute of Science Commination & Information Resources (NISCAIR)
14,Satsang Vihar Marg
New Delhi – 110 067

Ms. Gargi Kaul
JS&FA
Department of Biotechnology
Lodhi Road, CGO Complex
New Delhi – 110 003

Director General CSIR
Institute of Genomics & Integrative Biology, Mall Road, Near Jubilee Hall
Delhi – 110 007

Dr. Suman Govil
Advisor
Department of Biotechnology
Lodhi Road, CGO Complex
New Delhi

Dr. M. Gourie Devi
Director (Retd.)
Flat –11, Doctors Apartments
Vasundhara Enclave
Delhi – 110 096

Dr. L. M. Patnaik
CSA Department
Indian Institute of Science
Bangalore - 560 012

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

Prof. Subrata Sinha (upto 28.12.2017)
Director
National Brain Research Centre
Manesar – 122 052, Haryana

Prof. Neeraj Jain
Director (Additional Charge) (w.e.f. 29.12.2017)
National Brain Research Centre
Manesar-122 052, Haryana

Members of NBRC Governing Council

Prof. K. VijayRaghavan (Chairman) (Ex-officio) upto Feb, 2018
Secretary
Department of Biotechnology
Lodhi Road, CGO Complex
New Delhi – 110 003

Prof. Ashutosh Sharma (Ex-Officio) (Chairman) w.e.f. 1.3.2018
Secretary, Department of Science & Technology (DST),
Technology Bhawan, New Mehrauli Road
New Delhi – 110 016

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

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

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

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

Professor G. Mehta, FNA, FRS
Bhartia Chair School of Chemistry University of Hyderabad
Hyderabad 500 046

Dr. Chitra Sarkar,
Department of Pathology,
All India Institute of Medical Sciences (AIIMS)
New Delhi – 110 029.

Prof. Seyed E. Hasnain,
Vice Chancellor
Jamia Hamdard University
Hamdard Nagar, Delhi 110062

Ms. Gargi Kaul (Ex-officio)
Joint Secretary & Financial Advisor,
Department of Biotechnology,
Lodhi Road, CGO Complex
New Delhi – 110 003

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

Dr. Suman Govil (Ex-officio)
Advisor
Department of Biotechnology,
Lodhi Road, CGO Complex,
New Delhi – 110 003.

Dr. Sanjeev Jain, (Special Invitee)
Professor & HOD,
Shri B.R. Jain
Department of Psychiatry, NIMHANS, Bangalore

Mr. C. P. Goyal (Ex-officio)
JS (Admin),
Department of Biotechnology,
Lodhi Road, CGO Complex,
New Delhi – 110 003

Prof. Subrata Sinha (Ex-officio) upto 28.12.2017
Director
National Brain Research Centre
Manesar – 122 052, Haryana

Prof. Neeraj Jain
Director (Additional Charge) (w.e.f. 29.12.2017)
National Brain Research Centre
Manesar-122 052, Haryana

Members of NBRC Finance Committee

Prof. K. VijayRaghavan (Chairman) upto Feb, 2018
Secretary
Department of Biotechnology
Lodhi Road, CGO Complex
New Delhi – 110 003

Prof. Ashutosh Sharma (Ex-Officio) (Chairman) w.e.f. 1.3.2018
Secretary, Department of Science & Technology (DST),
Technology Bhawan, New Mehrauli Road
New Delhi – 110 016

Ms. Gargi Kaul
Joint Secretary & Financial Advisor
Department of Biotechnology
Lodhi Road, CGO Complex
New Delhi – 110 003

Prof. Dinakar M. Salunke
Director
International Centre for Genetic Engineering & Biotechnology
Aruna Asaf Ali Marg
New Delhi

Prof. Seyed E. Hasnain,
Vice Chancellor
Jamia Hamdard University
Hamdard Nagar, Delhi - 110 062

Prof. Subrata Sinha (upto 28.12.2017)
Director
National Brain Research Centre,
Manesar-122 052, Haryana

Prof. Neeraj Jain (Chairman) (w.e.f. Jan, 2018)
Director (Additional Charge)
National Brain Research Centre
Manesar-122 052, Haryana

F&AO
National Brain Research Centre
Manesar-122 052, Haryana

Members of NBRC Building Committee

Dr. Suman Govil (Chairperson)
Senior Adviser
Department of Biotechnology
CGO Complex, Lodhi Road
New Delhi - 110 003

Prof. Subrata Sinha (upto 28.12.2017)
Director
National Brain Research Centre
Manesar -122 052

Prof. Neeraj Jain
Director (Additional Charge) (w.e.f. 29.12.2017)
National Brain Research Centre
Manesar-122 052, Haryana

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

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

Prof. Sidhartha Satpathy
HOD
Hospital Administration, AIIMS
New Delhi

Members of NBRC Scientific Advisory Committee

Prof. P.N. Tandon (Chairperson)
President,
NBRC Society

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

Prof. K. VijayRaghavan, (upto Feb, 2018)
Secretary,
Department of Biotechnology,
CGO Complex, Lodi Road, New Delhi – 110 003

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),
Uppal Road, Hyderabad

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

Prof. Dinakar M. Salunke,
Executive Director,
Regional Centre for Biotechnology,
180, Udhyog Vihar Phase I, Gurgaon – 122 016

Prof. Siddhartha Roy,
Director,
Indian Institute of Chemical Biology (IICB),
4 Raja S.C. Mullick Road, Kolkata - 700 032

Prof. Jyotsna Dhawan,
Scientist,
Institute for Stem Cell Biology and Regenerative Medicine (inStem),
NCBS, TIFR,
GKVK, Bellary Road, Bangalore - 560 065

Prof. Rohit Manchanda,
Professor,
Biomedical Engineering Group,
School of Biosciences and Bioengineering,
IIT Bombay, Mumbai - 400 076

Prof. B.N. Mallick,
Professor,
Deptt. 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,
Deptt. of Chemical Sciences,
TIFR, Homi Bhabha Road, Colaba, Mumbai - 400 005

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

Dr. Chitra Sarkar,
Department of Pathology,
All India Institute of Medical Sciences (AIIMS),
Ansari Nagar, New Delhi - 110 029

Prof. Ajoy Kumar Ray,
Vice-Chancellor,
Bengal Engineering & Science University,
Shibpore, Howrah - 711 103, West Bengal

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

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

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

Ex-officio Member

Dr. Suman Govil,
Adviser,
Department of Biotechnology,
CGO Complex, Lodi Road, New Delhi – 110 003

Members of Academic Council

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

Prof. Sudha Bhattacharya
School of Environmental Sciences
Jawaharlal Nehru University,
New Delhi

Prof. Ishan Patro
School of Studies in Zoology / Neuroscience
Jiwaji University,
Gwalior

Prof. Gurcharan Kaur
Department of Biotechnology
Guru Nanak Dev University,
Amritsar

Prof. Subrata Sinha (upto 28.12.2017)
Director,
National Brain Research Centre
Manesar, Haryana

Prof. Soumya Iyengar
National Brain Research Centre
Manesar, Haryana

Prof. Anirban Basu
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. Yoganarasimha Doreswamy
National Brain Research Centre
Manesar, Haryana

Prof. Nihar Ranjan Jana
National Brain Research Centre
Manesar, Haryana

Dr. Sourav Banerjee
National Brain Research Centre
Manesar, Haryana

Prof. Pravat K. Mandal
National Brain Research Centre
Manesar, Haryana

Dr. Arpan Banerjee
National Brain Research Centre
Manesar, Haryana

Prof. Pankaj Seth
National Brain Research Centre
Manesar, Haryana

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

Prof. Shiv K. Sharma
National Brain Research Centre
Manesar, Haryana

Prof. Nandini C. Singh
Professor (on deputation to UNESCO-MGIEP, New Delhi)

Member Of Board Of Studies

Prof. Subrata Sinha (upto 28.12.2017)
Director,
National Brain Research Centre
Manesar, Haryana

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

Prof. Krishnamurthy Natarajan
Director,
Ambedkar Centre for Biomedical Research, University of Delhi,
New Delhi

Prof. Chitra Sarkar
Department of Pathology
All India Institute of Medical Sciences,
New Delhi

Prof. Soumya Iyengar
National Brain Research Centre
Manesar, Haryana

Prof. Anirban Basu
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

Prof. Nihar Ranjan Jana
National Brain Research Centre
Manesar, Haryana

Dr. Yoganarasimha Doreswamy
National Brain Research Centre
Manesar, Haryana

Prof. Pravat K. Mandal
National Brain Research Centre
Manesar, Haryana

Dr. Sourav Banerjee
National Brain Research Centre
Manesar, Haryana

Prof. Pankaj Seth
National Brain Research Centre
Manesar, Haryana

Dr. Arpan Banerjee
National Brain Research Centre
Manesar, Haryana

Prof. Shiv K. Sharma
National Brain Research Centre
Manesar, Haryana

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

Prof. Nandini C. Singh
Professor on deputation to UNESCO-MGIEP
New Delhi

Scientific Staff

Scientists

Prof. Subrata Sinha, Director, (upto 28.12.2017)

Prof. Neeraj Jain, Scientist – VII

Prof. Nihar Ranjan Jana, Scientist – VII

Prof. Pravat Kumar Mandal, Scientist – VI

Prof. Pankaj Seth, Scientist – VI

Prof. Shiv Kumar Sharma, Scientist – VI

Prof. Nandini C. Singh, Scientist-VI
(on deputation UNESCO-MGIEP), New Delhi

Dr. Ellora Sen, Scientist – VI

Prof. Soumya Iyengar, Scientist – VI

Prof. Anirban Basu, Scientist – VI

Dr. Ranjit Kumar Giri, Scientist – VI

Dr. Yoganarasimha Doreswamy, Scientist – V

Dr. Sourav Banerjee, Scientist – V

Dr. Arpan Banerjee, Scientist – IV

Dr. Anindya Roy Ghosh, Scientist – IV

Dr. Dipanjan Roy, Scientist – IV, (w.e.f. 28.07.2017)

Mr. Mahender Kumar Singh, Information Scientist

DST-INSPIRE Faculty

Dr. Yogita Kapil Adlakha

Ph.D. Students

Mr. Apoorv Sharma

Mr. Sandeep Kumar

Mr. Bharat Prajapati

Mr. Brijesh Kumar Singh

Mr. John Thomas

Mr. Kautuk Kamboj

Mr. Biswaranjan Sahoo

Mr. Indrajith R. Nair

Ms. Pushpa Kumari (Till 26/02/2018)

Ms. Shalini Swaroop

Mr. Shashi Shekhar Kumar

Mr. Touseef Ahmad Sheikh

Mr. Tushar Arora

Mr. S Balakumar

Mr. G Vinodh Kumar

Ms. Arti Kumari

Mr. Dharmendra Puri

Ms. Mukta Kumari

Mr. Raghav Shankar

Md. Tipu Khan

Mr. Amit Ranjan

Ms. Priyanka Ghosh

Ms. Sarbani Samaddar

Ms. Shruti Patrick

Mr. Surajit Chakraborty

Ms. Bindu

Mr. Shiladitya Laskar

Mr. Sibaram Behera

Mr. Sonam Kumar (Till 31/07/2017)

Ms. Tripti Joshi

Mr. Abhishek Singh Narvaria

Mr. Barathan G (Till 09/02/2018)

Ms. Deepti Dama

Mr. Hanuman Singh (Till 20/12/2017)

Mr. Jithin D Nair

Mr. Karthick R

Ms. Komal (Till 16/08/2017)

Ms. Nisha Chetana Sastry

Ms. Sakshi Sharma (Till 09/02/2018)

Ms. Shivangi Sharma

Ms. Sunanda Sharma

Mr. Sushanta Majumder

Ms. Vanshika Singh

Ms. Himali Arora

Ms. Meenakshi Bhaskar

Mr. Neeraj Kumar

Integrated Ph.D. Students

Ms. Guncha Bhasin

Ms. Shankhamala Sen

Ms. Uzma Din

Ms. Chitra Mohinder Singh Singal

Ms. Utkarsha A Singh

Ms. Pooja Parishar

Mr. Apurva Agrawal

Mr. Atanu Datta

Mr. Naman Vatsa

Mr. Hriday Shanker Pandey

Mr. Abhishek Kumar Verma

Mr. Vikas Pareek

Ms. Reshma Bhagat

Mr. Vipendra Kumar

Ms. Atrayee Basu

Ms. Priyanka

Mr. Gourav Sharma

Ms. Harjot Kaur

Mr. Pruthvi S.G

Ms. Shelly Pal

Mr. Shubham Krishna

M.Sc. Students

Mr. Gaurav Sharma (Till 31/07/2017)

Ms. Himali Arora (Till 31/07/2017)

Ms. Meenakshi Bhaskar (Till 31/07/2017)

Mr. Neeraj Kumar (Till 31/07/2017)

Ms. Sanskriti (Till 31/07/2017)

Mr. Utsav Mukherjee (Till 31/07/2017)

Mr. Anagh Pathak

Ms. Kasturi Biswas

Ms. Kirti

Ms. Ritu Moni Borah

Ms. Sreyashi Chandra

Ms. Tapasya Pal

Ms. Varsha Ramakrishna

Ms. Vini Tiwari

Mr. Azman Akhter

Ms. Guneet Kaur

Ms. Kirti Saluja

Mr. Masood Ahmad Wani

Ms. Pallavi Singh

Mr. Ranjit Pradhan

Research Fellows

Dr. Mahar Fatima (From 29/09/2016 till 19/04/2017)

Dr. Brijesh Kumar Singh (From 06/01/2018 till 30/06/2018)

Research Associates

Dr. Prem Chand, PDF

Dr. Chetan Kumar Yadav, Research Associate-3

Dr. Vivek Kumar Tripathi, Research Associate-3 (Till 12/05/2017)

Dr. D. Subhashree, Research Associate-2

Dr. Jeffrey Michael Valla, Research Associate-2

Dr. Anuradha Murugesan, Research Associate-1 (Till 03/01/2018)

Dr. Sandeep Kumar, Research Associate-2

Dr. Bibhabasu Hazra, Research Associate-3

Dr. Dipanjan Ray, Research Associate-3

Ms. Deepali Singh, Research Associate-1

Mr. P. Premkumar, Research Associate-1

Dr. Sonika, Research Associate-1

Dr. Romita Thounaojam, Research Associate-1

Dr. Navinder Kumar, Research Associate-1

Dr. Moumita Das, Research Associate-1

SERB-National Post Doctoral Fellows

Dr. Akansha Jalota

Dr. Suvadip Mallick

Dr. Amit Naskar

Dr. Poonam (Till 01/05/2017)

Dr. Ashok Kumar Datusalia

Dr. Soibam Shyamchand Singh

Project Assistants

Ms. Kalpana Gupta (Till 21/08/2017)

Ms. Shanah Rachel John (Till 04/08/2017)

Mr. Alok Nath Mohapatra

Mr. Giri Raj Kishore Sharma

Ms. Tanya Singh (Till 19/09/2017)

Mr. Jacob Antony Alappatt (Till 07/07/2017)

Ms. Pankajam T (Till 14/07/2017)

Ms. Kanza Saleem

Ms. Mena Fatma (Till 31/08/2017)

Ms. Hajare Nilambari Anil

Mr. Shrey Dutta

Ms. Deborah Daphne P (Till 24/08/2017)

Ms. Monika (Till 30/06/2017)

Mr. Archith Rajan

Ms. Titash Mukherjee

Mr. Irshad Akbar

Ms. Hymavathy B.

Mr. Siddharth Talwar

Ms. Anuradha Mehta

Ms. Sujata Dev

Ms. Revathi M

Mr. Nandu Raj P

Ms. Asha S C

Ms. Keerthana. P

Mr. Vivek P. Krishnan

Ms. Sonia

Mr. Subhajit Jana

Mr. Utsav Mukherjee

Ms. Vaishali

Dr. Fahd M Yasin

Ms. Ritu Nayak

Ms. Madhura S Rao

Ms. Nicky Singh

Mr. Bikash Chandra Sahoo

Ms. Aditi Charak

Mr. Jayakrishnan U

Project Employees

Mr. V.P. Subramanyam Rallabandi, Senior Research Officer (Computer Engineering) (Till 05/06/2017)

Ms. Shammi More, Senior R&D Engineer (Till 18/04/2017)

Mr. Rajiv Ramaswamy, Senior Research Fellow (Till 22/05/2017)

Ms. T. Ammaponnu Sumathi, R&D Engineer

Mr. Kamal Bharti, Technologist (MEG)

Mr. Vibhin V., Technologist (MEG)

Ms. Ruchika Mittal, Data Entry Coordinator

Mr. Sanjeev Bhardwaj, Manager (MEG) (Till 30/11/2017)

Mr. Manjit, Lab Attendant (MEG)

Mr. Rakesh Yadav, Nursing Orderly (MEG)

Dr. Aparna Dixit, Assistant Professor (MEG) (Till 01/09/2017)

Dr. Jyotirmoy Banerjee, Associate Professor (MEG) (Till 29/05/2017)

Mr. Ashok Kumar, Nurse (MEG)

Mr. Gaurav Singh, Technician (MEG)

Mr. Vivek Singh, Technician (MEG)

Mr. Om Prakash Jakhar, Nurse (MEG)

Mr. Tony C. Paikada, Nurse (MEG) (Till 27/12/2017)

Ms. Mini Mohan, Nurse (MEG)

Mr. Sushil Kumar Gupta, Technical Assistant (Libray) (Till 30/05/2017)

Ms. Devina Sharma, Junior Research Fellow (Till 01/09/2017)

Mr. Arun E V R, Senior Research Fellow

Ms. Meera Srikrishna, R&D Engineer (Till 31/08/2017)

Ms. Anindita Mandal, Human Ethics Coordinator (Till 31/05/2017)

Mr. Ashok Kumar Datusalia, Research Associate (Till 03/04/2017 F.N.)

Ms. Krity Kansara, Senior R&D Engineer (Till 04/05/2017)

Ms. Ankita Singh, Research Associate (Till 06/10/2017)

Ms. Aroma Dabas, Data Analyst-1 (Till 12/06/2017)

Mr. Sukhvir Singh Pundir, Technical Associate (Computer / IT)

Mr. Prem Chand, Accounts Administrative Assistant (DeLCON)

Ms. Ragini, Lab Technical Assistant

Ms. Bhanupriya Chouhan, R&D Engineer (Till 22/06/2017)

Dr. Siya Sherif, Research Scientist (Till 28/04/2017)

Mr. Budhaditya Basu, Junior Research Fellow (Till 01/09/2017)

Ms. Ananya Ghosh, Junior Research Fellow (Till 28/03/2018)

Ms. Ankita Sharma, R&D Scientist

Ms. Deepika Shukla, Research Scientist

Mr. Krishan Sharma, Technician A

Mr. Dixit Sharma, Junior Research Fellow

Ms. Teesta Naskar, ICMR-SRF

Ms. Sriparna Mukherjee, DST-INSPIRE Fellow Senior Research Fellow

Dr. Uday Pratap, Research Associate

Mr. Prasann Jeet, Lab Attendant

Mr. Ibrahim Olabayode Saliu, DBT-TWAS Sandwich Postgraduate Fellowship

Ms. Shalini, Technical Assistant

Mr. Neeraj Kasana, Technical Assistant
Ms. Lahoti Ritu Kamalkishor, R&D Engineer
Ms. Khushboo Vinod Punjabi, R&D Engineer
Dr. Anwesha Banerjee, Senior R&D Engineer
Dr. Gueyraud Rolland Kipre, Doctoral Fellowship
Ms. Shallu, Neuropsychologist
Ms. Anshika Goel, Junior R&D Engineer
Mr. Praful P Pai, R&D Engineer-1
Ms. Tripti Goel, Research Scientist
Ms. Kanika Sandal, Research Manager
Mr. Saurav Roy, R&D Engineer

Technical Staff

Mr. Rajbir Singh, Superintending Engineer

Mr. Sanjeev Kumar Choudhary, Assistant Engineer

Dr. D.D. Lal, Technical Officer

Mr. Jitender Ahlawat, Technical Officer – B

Mr. Arvind Singh Pundir, Technical Officer – B

Dr. Inderjeet Yadav, Veterinarian

Mr. Kedar Singh Bajetha, Computer Operator

Ms. Seepika,Computer Operator

Mr. Sachin Kumar, Computer Operator

Mr. Amit Kumar Gaurav, Computer Operator

Ms. Tarnnum Mansoori, Computer Operator

Mr. Sanjeev Bhardwaj, Computer Operator

Mr. Kanhaiya Lal Kumawat, Technician-C

Mr. Shankar Datt Joshi, Technician-C

Mr. Sumit Kumar Sinha Mahapatra, Technician-C

Mr. D. Narender, Technician-C

Mr. Sanjay Kumar, Technician-B

Mr. Mithlesh Kumar Singh, Technician-B

Mr. Ankit Sharma, Technician-B

Mr. Yunis Khan, Technician-B

Mr. Durga Lal Meena, Technician-B

Md. Irshad Alam, Technician-B

Mr. Manish Kumar, Technician-B

Mr. P. Manish, Technician-B

Mr. Dil Bahadur Karki, Technician-A

Mr. Rammehar, Technician-A

Mr. Hari Shankar, Technician-A

Mr. Mahendra Singh, Technician-A

Mr. Sanjay Kumar Singh, Technician-A

Administrative Staff

Mr. Tanmoy Bhattacharyya, Chief Administrative Officer

Mr. Santosh Kumar Choudhary, Deputy Finance Officer

Mrs. Pooja Gosain, Administrative Officer, (w.e.f. 14.06.2017)

Mr. Ravinder Pal, Stores & Purchase Officer

Mr. Suraj Bhan, Office Assistant

Mr. Rakesh Kumar Yadav, Office Assistant

Mr. Himanshu Mal, Office Assistant

Mr. Ajay Kumar Dehariya, Office Assistant

Mr. Parmander Singh Rawat, Office Assistant

Mr. Jitendra Kumar Meena, Office Assistant

Mr. Kailash Chandra Khuntia, Office Assistant (On Lien vacancy)

Mr. Bhupender Pal Sharma, Driver

Mr. Satish Kumar, Driver

Mr. Surender Kumar, Driver, (Upto 31.07.2017)

DIC Project

Mr. Sanjay kr. Gupta, Assistant Administrative Officer

Ms. Reema Saxena, Computer Operator

Ms. Sunita Yadav, Computer Operator

Mr. Amit Kumar, Computer Operator

Mr. R. Ganesh Gurumoorthy, Computer Operator

Contract Employees

Dr. Rema Velayudhan, Sr. Consultant

Mr. Suman Kumar, Consultant (Administration), (Upto 31.07.2017)

Dr. Tamanna Yadav, Resident Medical Officer, (w.e.f. 25.01.2018)

Dr. Karan Singh, Veterinarian at the level of application specialist

Ms. Nisha Devi, Nurse, (Upto 18.08.2017)

Mr. Hanish Kumar Sauda, Management Assistant (Admin.)

Mr. Mukesh Chauhan, Management Assistant (Acad.)

Ms. Sonam Saini, Management Assistant (A/cs), (Upto 13.03.2018)

Annual Financial Statements

Independent Auditor's Report

Re: The Members of National Brain Research Centre

A) We have audited the accompanying financial statements of M/s National Brain Research Centre (hereinafter referred to as "NBRC"), which comprises of the Balance- Sheet as at March 31, 2018, the Income & Expenditure Account and the Receipts & Payments Account for the year ending on that date read with significant accounting policies and notes to financial statements.

B) Management's Responsibility for the Standalone Financial Statements

The Management of the NBRC is responsible with respect to preparation of these financial statements that give a true and fair view of the financial position, financial performance and of the Receipts & Payments thereof in accordance with the Accounting Principles generally accepted in India including the Accounting Standards issued by the Institute of Chartered Accountants of India (ICAI). The responsibility also includes maintenance of adequate accounting records in accordance with the provisions of the Act for safeguarding the assets of the NBRC and for preventing and detecting 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 adequate internal financial controls, that were operating effectively for ensuring the accuracy and comp- leteness 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.

C) Auditor's Responsibility

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 ICAI. Those standards required 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. An audit involves performing procedures to obtain audit-evidence about the amounts and the 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 financial control relevant to the NBRC's preparation & fair presentation of the financial statements that give a true and fair view in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on whether the NBRC has in place an adequate internal financial controls system over financial reporting and the operating effectiveness of such controls. An audit also includes evaluating the appropriateness of the accounting policies used and the reasonableness of the accounting estimates made by the management, as well as evaluating the overall presentation of the financial statements. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion on these financial statements.

D) Opinion

Subject to clauses (4), (7), (9), (11), (12), (14), (15) & (21) of Notes to Accounts (Schedule-24) forming part of financial statements for current year & the observations in report on internal audit & in the report on audit by C&AG (both the audit reports along with action taken / compliance thereon, not having produced to us), the impact whereof on results of operations, receipts & payments for the year of NBRC and its state of affairs as at March 31, 2017 is not ascertainable due to its pending status, in our opinion and to the best of our information and according to the explanations given to us, the aforementioned financial statements gives a true and fair view in conformity with the accounting principles generally accepted in India:

(a) in case of the Balance Sheet, of the state of affairs of the Company as at March 31, 2018;

(b) in case of the Income and Expenditure Account, of the excess of income over expenditure for the year ended on that date;

(c) in case of the Receipts & Payment Account, of the receipts & payments during the year ended on that date.

E) Report on Other, Legal and Regulatory Requirements

a. Subject to our observations as referred to in para (D) above, 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 accounts have been kept by the NBRC so far as appears from our examination of those books;

c. The Balance Sheet, Income and Expenditure Account & the Receipts and Payment Account dealt with by this report are in agreement with the books of accounts;

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Date: 22.10.2018
New Delhi

Kapil Mittal
B.Com (H), F.C.A, D.I.S.A.(ICAI), A.I.I.I.S.L.A.
Partner
Membership No. 503378

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Balance Sheet As At March 31,2018

(Amount-Rs.)

CORPUS / CAPITAL FUND AND LIABILITIES	Schedule	Current Year	Previous Year
Corpus/Capital Fund	1	1,243,502,000.00	1,093,502,000.00
Reserve and Surplus	2	(114,354,308.02)	(215,139,232.61)
Earmarked/Endowment Funds	3	1,187,969,732.29	897,493,189.08
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	46,763,755.48	44,411,921.59
Total (Liabilities)		**2,363,881,179.75**	**1,820,267,878.06**
ASSETS			
Fixed Assets	8	1,228,875,012.89	1,284,242,640.97
Investments - From Earmarked/Endowment Funds	9	0.00	0.00
Investments-Others	10	31,526,119.18	19,537,816.00
Current Assets, Loans, Advances etc.	11	1,103,480,047.68	516,487,421.09
Miscellaneous Expenditure		0.00	0.00
(to the extent not written off or adjusted)			
Total (Assets)		**2,363,881,179.75**	**1,820,267,878.06**
Significant Accounting Policies	24		
Contingent Liabilites and Notes on Accounts	24		

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Income And Expenditure Account For The Year Ended March 31, 2018

(Amount-Rs.)

INCOME	**Schedule**	**Current Year**	**Previous Year**
Income from Sales/Services	**12**	0.00	0.00
Grants/ Subsidies (Revenue) from DBT	**13**	277,100,000.00	254,500,000.00
Fees/Subscriptions	**14**	2,045,382.78	1,353,863.50
Income from Investments (Income on Invest. From earmarked/endow. Funds transferred to funds)	**15**	2,950,807.80	2,134,622.00
Income from Royality, Publication etc.	**16**	0.00	0.00
Interest Earned	**17**	19,673,173.88	6,989,793.67
Other Income	**18**	2,153,676.84	1,398,613.00
Increase/(decrease) in stock of Finished goods and work-in-progress	**19**	0.00	0.00
Total Income (A)		**303,923,041.30**	**266,376,892.17**
EXPENDITURE			
Establishment Expenses	**20**	88,310,380.00	74,372,764.00
Other Administrative etc.	**21**	167,298,103.71	169,920,076.85
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)		33,002,815.00	33,044,815.00
Total Expenditure (B)		**288,611,298.71**	**277,337,655.85**
Balance being excess of Income over Expenditure (A-B)		15,311,742.59	(10,960,763.68)
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		**15,311,742.59**	**(10,960,763.68)**
Significant Accounting Policies	**24**		
Contingent Liabilites and Notes on Accounts	**24**		

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana

Receipts And Payments For The Year Ended March 31, 2018

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	160,755.00	164,213.00		i)	Establishment Expenses	8,891,249.00	8,825,278.00
	b)	Bank Balances				ii)	Administrative Expenses	3,533,097.21	2,767,593.88
		i) In Deposit Accounts	-	-	**II.**	**Payment Made Against Funds For Various Projects**			
		ii) Saving Accounts	494,595,608.23	150,227,029.30		i)	Recurring / Capital expenditure	29,284,337.05	590,601,262.53
		iii) CPF Investments	19,537,816.00	17,970,437.00		ii)	Capital Grant Refunded to DBT		-
II.	**Grants Received**					iii)	Refund to RCGB		-
	a)	From Government of India			**III.**	**Maintenance Cost**			
		Plan				**i)**	Lab Maintenance Expenses	40,613,374.66	30,311,351.38
	i)	Recurring Income	277,100,000.00	254,500,000.00		**ii)**	Office Maintenance	47,799,068.00	52,088,484.00
	ii)	Non-Recurring Income	150,000,000.00	25,000,000.00		iii)	Vehicle Running & Maintenance	638,975.00	631,069.00
		Plan (Recurring)			**IV.**	**Investment and Deposit Made**			
	b)	Fellowship Grant	1,085,280.00	1,506,706.50		i)	Out of Earkmarked/ Endowment funds	1,316,018.00	214,000.00
	c)	Delcon Projects (Including Interest)	765,764,625.00	883,910,787.00	**V.**	**Expenditure of Fixed Assets & Capital Work-in-progress**			
III.	**Receipt made against funds for various projects**					i)	Purchase of Fixed Assets	6,167,743.00	35,756,376.50
	i)	Recurring Receipt/ Capital Grant	262,855,562.00	7,881,075.34	**VI.**	**Training Expenses**		2,054,761.93	2,934,731.06
		(Including Interest)			**VII.**	**Other Payments(Specify)**			
IV.	**Interest Received**					i)	Advances to Supplier	6,310,579.14	7,367,793.24
	i)	On Bank Deposits	-	-		ii)	Advances to Staff	3,701,364.00	4,555,772.00
	ii)	Savings Account	19,295,909.00	5,386,124.00		iii)	Leave Encashment/ LTC/ Bonus	403,019.00	887,173.00
	iii)	On CPF Fund	1,278,245.59	1,567,379.00		iv)	Security Deposit Paid	527,296.00	337,909.00
	iv)	Other Interest	149,980.00	71,951.00		v)	EMD Refunded	3,673,353.00	4,960,128.00

Contd...

V.	Any Other Receipt					vi)	TDS Paid	62,288,998.00	8,717,917.00
	Indirect Income					vii)	Imprest	180,121.00	176,147.00
	i)	Advance to Supplier Received	12,307.00	32,340.00		viii)	Payment of Current Liabilities	673,391,300.33	165,417,767.32
	ii)	Advance to Staff Received	2,129,640.46	1,137,320.00		ix)	Prepaid Insurance	890,114.00	571,613.00
	iii)	Sale of Tender Documents	30,000.00	63,600.00	VIII.	Closing balances			
	iv)	Misc. Receipts.	793,583.00	369,528.00		a)	Cash in Hand	273,188.00	160,755.00
	v)	Earnest Money Deposit Received	4,944,980.00	5,206,704.00		b)	Bank Balance		
	vi)	Sale of Scrap	14,000.00	11,000.00		i)	In Deposit Accounts		
	vii)	Guest House Charges	248,400.00	200,250.00		ii)	Saving Accounts	1,083,725,273.34	494,595,608.23
	viii)	Hostel Deposit	510,000.00	386,000.00		iii)	CPF Investments	31,526,119.18	19,537,816.00
	ix)	CPF Fund Received	5,669,097.00	1,822,558.00					
	x)	Library Deposit	162,000.00	119,000.00					
	xi)	Current Liabilities Rec.	785,076.56	3,882,543.00					
	xii)	Other Receipts	66,484.00	-					
		TOTAL	2,007,189,348.84	1,431,416,545.14			TOTAL	2,007,189,348.84	1,431,416,545.14

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Schedule Forming Part Of Balance Sheet As At March 31, 2018

Schedule 1-Corpus/Capital Fund:					**(Amount-Rs.)**
		Current Year		**Previous Year**	
1	Grant-in-Aid - Balance as at the beginning of the year		1,093,502,000.00		1,068,502,000.00
	Add: Contribution towards Corpus/ Capital Fund	150,000,000.00		25,000,000.00	
	Add/(Deduct): Balance of net income/(expenditure) transferred from the Income and Expenditure Account		150,000,000.00		25,000,000.00
	Balance as at the year end		**1,243,502,000.00**		**1,093,502,000.00**

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Schedule Forming Part Of Balance Sheet As At March 31, 2018

Schedule 2 - Reserves And Surplus: **(Amount-Rs.)**

		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	(215,139,232.61)		(204,178,468.93)	
	Addition during the Year	85,473,182.00		-	
	Surplus during the yar (as per I&E A/c)	15,311,742.59		-	
	Less : Deductions during the year (deficit)	-	(114,354,308.02)	(10,960,763.68)	(215,139,232.61)
	Balance as at the year end		**(114,354,308.02)**		**(215,139,232.61)**

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Schedule Forming Part Of Balance Sheet As At March 31, 2018

Schedule 3 - Earmarked/Endowment Funds									**(Amount-Rs.)**
		Endowment Fund for Building		**Donation**		**Current Year**		**Previous Year**	
a)	Opening Balance of Project Fund		85,473,182.00		2,631,788.00		897,493,189.08		588,095,148.44
b)	Additions to the Funds:								
	i. Donations/grants/Additions to Fund	0.00		0.00		1,038,790,822.31		1,004,531,611.83	
	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	3,332,143.00	1,042,122,965.31	2,522,660.00	1,007,054,271.83
	Total (a+b)		85,473,182.00		2,631,788.00		1,939,616,154.39		1,595,149,420.27
c)	Utilisation/Expenditure towards objectives of funds								
	i. Capital Expenditure								
	Fixed Assets (net)	0.00		0.00		7,901,610.19		44,698,763.83	
	Others	0.00		0.00		0.00		0.00	
	Total		**0.00**		**0.00**		**7,901,610.19**		**44,698,763.83**
	ii. Revenue Expenditure								
	-Salaries, Wages and allowances etc	0.00		0.00		21,603,921.00		22,834,222.95	
	-Rent	0.00		0.00		0.00		0.00	
	-Others	85,473,182.00		0.00		662,357,019.91		561,026,483.41	
	-Depreciation	0.00		0.00		59,783,871.00		69,096,761.00	
	Total		**85,473,182.00**		**0.00**		**743,744,811.91**		**652,957,467.36**
	Total (C)		**85,473,182.00**		**0.00**		**751,646,422.10**		**697,656,231.19**
	Net Balance As At The Year-End (A+B-C)		**0.00**		**2,631,788.00**		**1,187,969,732.29**		**897,493,189.08**

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:
Schedule 5 - Unsecured Loans And Borrowings:
Schedule 6 - Deferred Credit Liabilities:

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

Contd.

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana

Schedule Forming Part Of Balance Sheet As At March 31, 2018

Schedule 3 - Earmarked/Endowment Funds (Amount-Rs.)

		Project Fund		Fixed Assets Fund (Project)		Contributory Provident Fund		DeLcon E-library Consortium	
a)	Opening Balance of Project Fund		35,782,823.69		393,198,394.41		13,748,696.00		366,658,304.98
b)	Additions to the Funds:								
	i. Donations/grants/Additions to Fund	261,187,505.12		7,901,610.19		6,077,907.00		763,623,800.00	
	ii. Income from investments made on account of funds	0.00		0.00		0.00		0.00	
	iii. Other additions (Interest Earned)	1,191,318.00	262,378,823.12	0.00	7,901,610.19	0.00	6,077,907.00	2,140,825.00	765,764,625.00
	Total (a+b)		**298,161,646.81**		**401,100,004.60**		**19,826,603.00**		**1,132,422,929.98**
c)	Utilisation/Expenditure towards objectives of funds								
	i. Capital Expenditure								
	Fixed Assets (net)	7,321,822.19		0.00		0.00		579,788.00	
	Others	0.00		0.00		0.00		0.00	
	Total		7,321,822.19		0.00		0.00		579,788.00
	ii. Revenue Expenditure								
	-Salaries, Wages and allowances etc	19,757,332.00		0.00		0.00		1,846,589.00	
	-Rent	0.00		0.00		0.00		0.00	
	-Others	33,179,323.42		0.00		1,316,018.00		542,388,496.49	
	-Depreciation	0.00		59,783,871.00		0.00		0.00	
	Total		52,936,655.42		59,783,871.00		1,316,018.00		544,235,085.49
	Total (C)		**60,258,477.61**		**59,783,871.00**		**1,316,018.00**		**544,814,873.49**
	Net Balance As At The Year-End (A+B-C)		**237,903,169.20**		**341,316,133.60**		**18,510,585.00**		**587,608,056.49**

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Schedule Forming Part Of Balance Sheet As At March 31, 2018

Schedule-7 Current Liabilities And Provisions					**(Amount-Rs.)**
		Current Year		**Previous Year**	
A.	Current Liabilities				
	1. Acceptances		0.00		0.00
	2. Sundry Creditors				
	-For Goods	0.00		0.00	
	- Others	753,403.00	753,403.00	2,753,910.25	2,753,910.25
	3. Advances Received		3,562,962.42		2,984,128.42
	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)	254,136.50		4,098.50	
			254,136.50		4,098.50
	6. Others current Liabilities		32,745,466.76		27,957,088.62
	Total (a)		**37,315,968.68**		**33,699,225.79**
B.	Provisions				
	1. For Taxation		0.00		0.00
	2. Gratuity		6,468,960.00		6,759,338.00
	3. Superannuation/Pension		0.00		0.00
	4. Accumulated Leave Encashment		2,978,826.80		3,953,357.80
	5. Trade Warranties/Claims		0.00		0.00
	6. Others (Specify)		0.00		0.00
	Total (b)		**9,447,786.80**		**10,712,695.80**
	Balance as at the year end (a+b)		**46,763,755.48**		**44,411,921.59**

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana

Schedule Forming Part Of Balance Sheet As At March 31, 2018

Schedule 8 - Fixed Assets/ Depreciaton

	DESCRIPTION	GROSS BLOCK					DEPRECIATION				NET BLOCK	
		Rate of Dep.	Cost /valuation As at beginning of the Year	Additions during the Year		Deductions during the Year	Cost /valuation As at end of the Year	As at the beginning of the Year	Depreciation for current year	On Deductions during the year	Total Depn. Upto 31.03.18	As at Current year-end	As at Previous year-end
				More than 6 Months	Less than								
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:						0.00				0.00	0.00	0.00
	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	0.00	0.00	0.00	71,887,574.00	28,379,263.67	4,350,831.00	0.00	32,730,094.67	39,157,479.33	43,508,310.33
	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
3	Plant Machinery & Equipment	15%	305,485,644.95	1,312,453.00	14,175,453.18	0.00	320,973,551.13	165,242,779.02	22,296,457.00	0.00	187,539,236.02	133,434,315.11	140,242,865.93
4	Vehicles	15%	2,086,342.00	0.00	0.00	0.00	2,086,342.00	1,510,685.80	86,348.00	0.00	1,597,033.80	489,308.20	575,656.20
5	Furniture, Fixtures	10%	39,550,753.00	150,662.00	477,537.00	0.00	40,178,952.00	20,015,897.84	1,992,429.00	0.00	22,008,326.84	18,170,625.16	19,534,855.16
6	Office Equipment	15%	32,932,585.40	515,302.00	12,015,623.55	0.00	45,463,510.95	18,797,200.65	3,098,775.00	0.00	21,895,975.65	23,567,535.30	14,135,384.75
7	Computer/Peripherals	40%	7,231,690.81	0.00	787,895.00	0.00	8,019,585.81	5,830,091.59	718,219.00	0.00	6,548,310.59	1,471,275.22	1,401,599.22
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		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
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%	5,100,392.00	82,522.00	0.00	0.00	5,182,914.00	3,343,890.75	459,756.00	0.00	3,803,646.75	1,379,267.25	1,756,501.25
	Total Of The Current Year		**464,274,982.16**	**2,060,939.00**	**27,456,508.73**	**0.00**	**493,792,429.89**	**243,119,809.32**	**33,002,815.00**	**0.00**	**276,122,624.32**	**217,669,805.57**	**221,155,172.84**
B	Capital Work In Progress (Building)		669,889,073.73	0.00	0.00	0.00	669,889,073.73	0.00	0.00	0.00	0.00	669,889,073.73	669,889,073.73
C	Project Equipments	15%	764,365,632.25	2,913,401.17	5,081,730.95	93,521.93	772,267,242.44	371,167,237.85	59,783,871.00	0.00	430,951,108.85	341,316,133.59	393,198,394.40
	Total (A+B+C)		**1,898,529,688.14**	**4,974,340.17**	**32,538,239.68**	**93,521.93**	**1,935,948,746.06**	**614,287,047.17**	**92,786,686.00**	**0.00**	**707,073,733.17**	**1,228,875,012.89**	**1,284,242,640.97**

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

Schedule 9 - Investment From Earmarked/Endowment Funds: NIL

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Schedule Forming Part Of Balance Sheet As At March 31, 2018

Schedule 10 - Investments-Others			**(Amount-Rs.)**
		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)	31,526,119.18	19,537,816.00
	Total	**31,526,119.18**	**19,537,816.00**

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Schedule Forming Part Of Balance Sheet As At March 31, 2018

Schedule 11 - Current Assets, Loans, Advances Etc.					**(Amount-Rs.)**
		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)		273,188.00		160,755.00
4	Bank Balances:				
a)	With Scheduled Banks:				
	-On Current Accounts	0.00		0.00	
	-On Deposit Accounts (includes margin money)	0.00		0.00	
	-On Savings Accounts	1,083,725,273.34		494,595,608.23	
			1,083,725,273.34		**494,595,608.23**
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)		**1,083,998,461.34**		**494,756,363.23**

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Schedule Forming Part Of Balance Sheet As At March 31, 2018

Schedule 11 - Current Assets, Loans, Advances Etc. (Contd.)					**(Amount-Rs.)**
		Current Year		**Previous Year**	
B.	**Loans, Advances And Other Assests**				
1	Loans:				
	a) Staff	5,737,970.00		6,686,226.06	
	b) Other Entities engaded in activities/ objectives similar to that	0.00		0.00	
	of the entity				
	c) Other (Imprest)	63,983.00		101,966.00	
			5,801,953.00		6,788,192.06
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)	890,114.00		571,613.00	
	C) Other - Advance to Parties	2,246,662.22		6,562,615.34	
	- Other Advances	5,762,502.45		2,184,039.20	
			8,899,278.67		9,318,267.54
3	Income Accured:				
	a) On Investments from Earmarked/ Endowment Funds	0.00		0.00	
	b) On Investments-Others	145,628.87		1,196,628.46	
	c) On Loans and Advances	0.00		0.00	
	d) Others (SB A/C)	89,156.00	234,784.87	0.00	1,196,628.46
b)	(includes income due unrealised- Rs.....)				
	-On Deposit Accounts	0.00		0.00	
	-On Savings Accounts	0.00	0.00	0.00	0.00
4	Claims Receivable (TDS Receivable)		4,545,569.80		4,427,969.80
	Total (B)		**19,481,586.34**		**21,731,057.86**
	Total (A+B)		**1,103,480,047.68**		**516,487,421.09**

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Schedule Forming Part Of Balance Sheet As At March 31, 2018

Schedule 12 - Income From Sales/Services		**(Amount-Rs.)**
	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	277,100,000.00	254,500,000.00
5 International Organisations	0.00	0.00
6 Others (Specify)	0.00	0.00
Total	**277,100,000.00**	**254,500,000.00**

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Schedule Forming Part Of Balance Sheet As At March 31, 2018

Schedule 14 - Fees/ Subscriptions			**(Amount-Rs.)**
		Current Year	**Previous Year**
1	Entrance Fees	790,917.78	211,821.00
2	Annual Fees/Subscriptions	491,000.00	387,150.00
3	Seminar/Program Fees	0.00	0.00
4	Consultancy Fees	0.00	0.00
5	Others (Fellowship Grants)	763,465.00	754,892.50
	Total	**2,045,382.78**	**1,353,863.50**

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Schedule Forming Part Of Balance Sheet As At March 31, 2018

(Amount-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	Inventories:				
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	348,941.00	410,286.00
4	Others (Project Receipts)	0.00	0.00	2,601,866.80	1,724,336.00
	b) Others	0.00	0.00	0.00	0.00
3	Cash balances in hand (including cheque/ drafts and imprest)		273,188.00		160,755.00
4	Bank Balances:				
	Total (B)	**0.00**	**0.00**	**2,950,807.80**	**2,134,622.00**
Transferred To Earmarked/Endowment Funds					

Schedule 16 -Income From Royality, Publication Etc. **NIL**

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Schedule Forming Part Of Income And Expenditure For The Year Ended March 31, 2018

Schedule 17 -Interest Earned			**(Amount-Rs.)**
		Current Year	**Previous Year**
1	On Term Deposits:		
	a) With Scheduled Banks	0.00	1,424,492.67
	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	19,460,697.88	5,386,124.00
	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	212,476.00	179,177.00
4	Interest on Debtors and Others Receivables	0.00	0.00
	Total	**19,673,173.88**	**6,989,793.67**

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Schedule Forming Part Of Income And Expenditure For The Year Ended March 31, 2018

Schedule 18 -Other Income			**(Amount-Rs.)**
		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	2,083,352.00	1,398,613.00
5	Prior Period Income	70,324.84	0.00
	Total	**2,153,676.84**	**1,398,613.00**

Note- Tax deducted at source to be indicated

Schedule 19 -Increase/(Decrease) In Stock Of Finished Goods & Work In Progress **NIL**

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Schedule Forming Part Of Income And Expenditure For The Year Ended March 31, 2018

Schedule 20 -Establishment Expenses		**(Amount-Rs.)**
	Current Year	**Previous Year**
a) Salaries and Wages	67,493,373.00	53,379,364.00
b) Allowances and Bonous	0.00	145,068.00
c) Contribution to Provident Fund	2,560,398.00	1,131,354.00
d) Contribution to Pension Scheme	0.00	0.00
e) Staff Welfare Expenses	114,330.00	154,578.00
f) Expenses on Employees Retirement and Terminal Benefits	0.00	0.00
g) Others - Children education reimbursement	427,450.00	1,098,000.00
- Leave encashment	390,035.00	2,065,359.00
- LTC expenses	318,216.00	1,085,194.00
- Medical reimbursement	1,060,163.00	969,818.00
- NPS(employer subscription)	3,921,146.00	2,732,074.00
- overtime allowance	7,194.00	18,317.00
- Skilled manpower	10,844,610.00	10,619,801.00
- Medical insurance (Staff)	665,245.00	765,505.00
- Office expenses	508,220.00	208,332.00
Total	**88,310,380.00**	**74,372,764.00**

Note- Tax deducted at source to be indicated

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana
Schedule Forming Part Of Income And Expenditure For The Year Ended March 31, 2018

Schedule 21 -Other Admiistrative Expenses			(Amount-Rs.)
		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	36,420,887.00	47,690,321.00
5	Water Charges	0.00	0.00
6	Insurance	503,007.00	568,098.00
7	Repairs and maintenance	28,125,094.16	23,738,493.45
8	Excise Duty	0.00	0.00
9	Rent (Lease Rent), Rates and Taxes	1,191,336.00	4,444,048.00
10	Vechicles Running and Maintenance	268,584.00	297,609.00
11	Postage, Telephone and Communication Charges	760,126.00	789,849.00
12	Printing and Stationary	1,761,738.00	1,147,369.00
13	Travelling and Conveyance Expenses	7,034,209.00	5,777,289.00
14	Expenses on Seminar/Workshops	852,433.00	1,140,051.00
15	Subscription Expenses	1,660,355.93	2,315,686.06
16	Expenses on Fees	0.00	0.00
17	Auditor Remuneraion	34,981.00	31,801.00
18	Hospitality Expenses	131,477.00	496,197.00
19	Professional Charges	929,795.00	645,632.00
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	1,106,638.00	506,117.00
26	Foreign Exchange Fluctuation Loss/Gain	79,368.56	0.00
27	Prior Period Expenses	6,454,048.00	6,834,783.00
28	Others - Bank charges	1,623.21	14,524.63
	- Misc. expenses	268,070.75	316,833.00
	- Books and Periodicals	183,000.00	79,294.00
	- Honorarium (others)	313,000.00	228,912.25
	- Petrol, Diesel & CNG etc.	587,388.00	599,703.00
	- Manpower	6,844,930.00	6,635,800.00
	- Horticulture	2,691,761.00	2,239,947.00
	- Training and networking expense	29,153,386.00	32,189,654.00
	- Laboratory & Animal Consumables	39,940,867.10	31,192,065.46
	Total	**167,298,103.71**	**169,920,076.85**

Note- Tax deducted at source to be indicated

SCHEDULE 22 -EXPENDITURE ON GRANTS, SUBSIDIES ETC. NIL
SCHEDULE 23 -INTEREST PAID NIL

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana

Significant Accounting Policies & Notes On Accounts Forming Part Of The Balance Sheet As At 31St March, 2018 And Income & Expenditure Account For The Year Ended 31Stmarch,2018

Schedule 24

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 The capital work-in-progress includes completed work/buildings under Phase-I as these works could not be transferred to 'Fixed Assets – Buildings' category for want of Building-wise information from the Project Management Consultant i.e. Directorate of Construction Services and Estate Management (DC&SEM) of Department of Atomic Energy.

3.5 NBRC has entered into a Memorandum of Understanding (MOU) with DC&SEM for construction of NBRC's Building at Manesar, Gurgaon. As per the MOU with the DC&SEM, NBRC is depositing funds with DC&SEM from time to time to be utilized by DC&SEM for construction. Total amount deposited with DC&SEM is Rs. 44,46,52,000.00 till 31st March 2018. Pending completion of construction, the payments made to DC&SEM are being shown as Deposit under the head Capital WIP in schedule-8 (i.e Fixed Assets / Depreciation). Final adjustment shall be done on submission of final account of the project by DC&SEM; Now the MOU with DC&SEM is discontinued. NBRC has again engaged Civil & Construction Wing (CCW) AIR, Prasar Bharti, as Project Management Consultant (PMC) for completing balance work and final bill is yet to be settled.

3.6 Fixed Assets have been created mainly out of grants received from the Department of Biotechnology, Ministry of Science and Technology, Government of India.

4. Depreciation:

4.1 From F.Y 2012-2013, depreciation is being charged as per Income Tax Act 1961 on W.D.V basis. As stated in F.Y 2012-13, in view of old information not being readily available, the retrospective calculation of depreciation as per Income Tax Act 1961 for adjustment of excess/short depreciation is vis-a-vis the old rates, as required under the Accounting Standard-6 issued by Institute of Chartered Accounts of India (ICAI), could not be made till date. The same shall be made in due course of the determination of the same.

4.2 Depreciation provided for current year on the fixed assets of Project for Rs. 5,97,83,871.00 (previous year Rs. 6,90,96,761.00) 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. 3,30,02,815.00 for current financial year (Rs. 3,30,44,815.00 for previous year) had been debited to Income & Expenditure Account.

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, which results in increase in profitability.

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 / subsidy 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 loans and current liabilities are converted at the exchange rate prevailing as at the year end and the resultant gain/loss is adjusted to cost of fixed assets, if the foreign currency liability related to fixed assets, and in other cases is considered to revenue.

7.3 The Centre had one FCRA Bank Account PNB Manesar related to the Grants. The submission of the returns of these accounts has been made up to Financial Year 31st March, 2009 under the FCR Act. The NBRC had received a notice for compliance from Govt. of India in FY 2016-17, which was also replied clarifying the position. There had been no further communication from either side about the same.

8. Lease:

The NBRC is located on the leasehold land at Manesar taken from Indian Vaccine Corporation Ltd. for Rs. 11, 91,336/- per annum lease rent with certain semi-built structure at a cost Rs. 45, 17,000/- towards such structures. The lease is for the period of 33 years, after which the land along with premises thereon are to be handed over to the lessor. 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 maximum number of employees joined New Pension Scheme (NPS) and as they had joined NBRC before 01st January, 2004.

9.2 The NBRC has not made any provision for gratuity and leave encashment during financial year 2017-2018 as against the requirement of AS-15 issued by ICAI. However, the amount of gratuity and leave encashment to the extent of Rs. 64,68,960.00 and Rs. 29,78,826.80 respectively already exists on 31st March, 2018, (Rs. 67,59,338.00 and Rs. 39,53,357.80 respectively as on 31st March, 2017) against provision made earlier.

10. Taxation:

In view of the tax exemption status of the Center, no provision for income tax has been considered necessary.

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:

Bank balance in Punjab National Bank, Manesar (FCRA) (i.e. A/c No. 4136000100008889) as on 31st March, 2018 of Rs. 10,98,981.54

(Previous Year Rs. 10,86,657.54) are subject to reconciliation.

13. Prior Period Items:

Accounting Standard-5 Issued by Institute of Chartered Accountants of India (ICAI), Prior Period items are income or expenses, which arises, in current period as a result of error or omission in the preparation of financial statement of one or more prior periods. In the current year, the Prior Period items recognized, related to expenditure i.e. Rs. 63,83,723.16 for the financial year 2017-18 (previous year 2016-17 Rs. 68,34,783.00) that was omitted in that year.

14. Fraud/Manipulation of funds encountered by NBRC:

As on 27th April, 2015, a cheque of Rs. 92,625.00 drawn on A/c No. 056010100453998 of NBRC with M/s Axis Bank was issued in favour of M/s Golden Feeds Pvt. Ltd., 894/8, Mehrauli, New Delhi-110030, against their invoice No. 2591 dtd. 09th March, 2015. The said cheque was dispatched via speed post (India Post Ref. No. EH643251489IN) to the said receipient. However, it was subsequently brought to notice of NBRC by said receipient that envelope received contained only payment advice. The cheque was found later to have been credited to some Mr. Bhagirath Chauhan's account, at Bank of India, Rajnagar Extn., Ghaziabad (Uttar Pradesh). The matter had been reported to police authorities, Haryana for further investigation and action which is pending since.

15. Outstanding Balances of Closed Projects:

As on 31st March, 2018, Fifty-Seven number of extramural projects had already been closed on account of their tenure expiring/ project execution, as applicable. Their respective balances (i.e. after meeting the project payments from project receipts) are included under the head "Earmarked/Endowment Funds" (schedule-3) in the balance sheet as on that date & are subject to reconciliation with the granting agencies.

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. 51,62,410.00 (Previous year Rs. 51,40,350.00) which is under representation before the concerned authorities. Further, TDS deducted and to be received as refund amounts to Rs. 45,45,569.80

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 (Previous year Rs. NIL).
- Raw Materials & Components (Including in transit) Rs. NIL (Previous year Rs. NIL).
- Capital Goods Rs. NIL (Previous year Rs. NIL).
- Stores, Spares and Consumables Rs. 1,18,66,195.17 (Previous year Rs. 4,75,54,906.70).

20.2 Expenditure in foreign currency:

a) Travel Rs. NIL (Previous year Rs. NIL).

b) Remittances and Interest payment to Financial Institutions/ Banks in Foreign Currency Rs. NIL (Previous year Rs. NIL).

c) Other expenditure

-Commission on Sales Rs. NIL (Previous year Rs. NIL).

-Legal and Professional Expenses Rs. NIL (Previous year Rs. NIL).

-Miscellaneous Expenses Rs. NIL (Previous year Rs. NIL).

20.3 Earnings:

Value of Exports of FOB basis Rs. NIL (Previous year Rs. NIL).

20. Remuneration to auditors:

- As Auditors Rs. 34,981.00 (Previous year Rs. 31,801.00).

Other remuneration payable to Auditor in respect of their services in respect of taxation matter (such as tax compliances, tax representation etc.) & other certification work done had not been provided for on account of non-receipt of their invoice so far.

21. Others

21.1 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. 7,53,403.00 (previous year Rs. 27,59,910.25).

21.2 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, 2018 and the Income and Expenditure Account for the year ended on that date.

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

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

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

National Brain Research Centre
NH-8, Nainwal More, Manesar, Gurugram, Haryana

Annexure Of Project Grants And Expenditure For The Year Ended 31.03.2018

S. No./ Annx. No.	NAME OF PROJECT	Opening Balance as on 01.04.2017	Grants received during the year 2017-18	Interest earned during the year 2017-18	Capital Exp. during the year 2017-18	Revenue Expenditure during the year 2017-18			Refund of Unspent Balance	Closing Balance as on 31.03.2018
						Manpower	Others	Total Expenditure		
1	Distributed Information Centre	243,198.33	3,220,000.00	0.00	0.00	2,916,258.00	503,988.00	3,420,246.00	0.00	42,952.33
2	Dementia Meeting	2,364,225.00	0.00	0.00	0.00	0.00	240,663.00	240,663.00	0.00	2,123,562.00
3	INDO-US & NIH RO1 - Dr. Pankaj Seth	142,087.58	0.00	0.00	0.00	0.00	12,680.00	12,680.00	0.00	129,407.58
4	Epilepsy Project of NBRC	1,561,757.30	19,152,000.00	189,801.00	1,021,584.00	6,500,904.00	6,672,466.00	13,173,370.00	0.00	6,708,604.30
5	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
7	Two Photon Microscope Facility Dr. Neeraj Jain	6,281,289.94	0.00	0.00	0.00	0.00	6,281,289.94	6,281,289.94	0.00	0.00
8	Neural Network Mechanism - Dr. Yoganarashimha	(1,538,855.61)	0.00	468,017.00	0.00	0.00	0.00	0.00	0.00	(1,070,838.61)
9	FICCI Millenum Alliance- DR. NANDINI C. SINGH	0.00	2,500,000.00	0.00	0.00	0.00	192,600.00	192,600.00	0.00	2,307,400.00
10	DBT ITPAR Grant-Dr.Nandini C. Singh	583,367.89	0.00	0.00	0.00	0.00	0.00	0.00	27,133.00	556,234.89
11	Neurobiology of Dyslexia Brain & Behavior-Dr.Nandini C.Singh	0.00	2,682,250.00	0.00	0.00	0.00	822,250.00	822,250.00		1,860,000.00
12	DBT Ramalingaswamy Fellowship - Dr.Saurav Banerjee	(12,393.12)	50,042.12	0.00	0.00	102,500.00	-64,851.00	37,649.00	0.00	(0.00)
13	Wellcom Trust/DBT Indian Alliance -Dr. Anindya Ghosh Roy	6,321,194.93	0.00	224,139.00	4,377,569.12	0.00	706,296.25	706,296.25	0.00	1,461,468.56
14	Neuro -Cognitive Networks Underlying Dr. Arpan Banerjee	457,375.00	1,406,000.00	0.00	0.00	0.00	1,627,171.00	1,627,171.00	0.00	236,204.00
15	Autism Behavior and Diffusion Tensor Imaging - Dr. Nandini C. Singh	267,024.00	0.00	0.00	0.00	0.00	126,668.00	126,668.00	0.00	140,356.00
16	Characterizing biomarkers of Alzheimer's disease Dr. Pravat Mandal	1,471,598.50	1,665,362.00	0.00	630,000.00	706,099.00	343,690.00	1,049,789.00	0.00	1,457,171.50
17	National Programme on Preception Engineering - Phase II- Dr. Pravat Kumar Mandal	306,959.60	2,170,000.00	0.00	10,999.00	690,750.00	209,108.00	899,858.00	0.00	1,566,102.60

18	National Programme on Preception Engineering - Prof. P.K. Roy	982,263.00	0.00	85,610.00	0.00	225,974.00	97,435.00	323,409.00	0.00	744,464.00
19	CSIR Japanese Enccephalities - Dr. Anirban Basu	(35,216.35)	0.00	0.00	0.00	0.00	(35,216)	(35,216)	0.00	0.00
20	Molecular Mechanism Of Microbial Activation - Dr. Anirban Basu	617,904.55	0.00	7,409.00	0.00	0.00	625,313.55	625,313.55	0.00	0.00
21	Multifaceted Kinase CDK5 - Dr. Aparna Dixit	368,783.07	0.00	0.00	(93,522)	370,772.00	445,848.93	816,620.93	0.00	(354,316)
22	Vision Guide Speech Percention- Dr. Arpan Banerjee	665,924.00	0.00	0.00	0.00	0.00	73,904.00	73,904.00	0.00	592,020.00
23	National Bioscience Award- Dr. Ellora Sen	46,052.09	500,000.00	3,012.00	0.00	0.00	116,208.00	116,208.00	0.00	432,856.09
24	Tata Innovation Fellowship- Dr. Nihar Ranjan Jana	193,433.91	895,334.00	4,815.00	0.00		581,674.00	581,674.00	0.00	511,908.91
25	Innovation In Science Pursuit For Inspired Research(INSPIRE)- Dr. Yogita	974,469.18	1,563,208.00	0.00	0.00	692,286.00	1,165,183.00	1,857,469.00	0.00	680,208.18
26	Mechanisms Of Adult Brain Reorganisation- Dr. Neeraj Jain	560,344.39	1,453,000.00	4,728.00	0.00	565,113.00	764,116.17	1,329,229.17	0.00	688,843.22
27	A critical assessment of the dual stream models of visual information processing- DST - Dr. Dipanjan Ray	231,436.00	0.00	0.00	0.00	0.00	231,216.00	231,216.00	0.00	220.00
28	Tata innovation fellowship award- Dr. Anirban Basu	43,638.81	892,292.00	10,544.00	0.00	0.00	831,029.00	831,029.00	0.00	115,445.81
29	Implications in tumor progression- Dr. Ellora Sen	480,788.19	1,642,000.00	58,510.00	0.00	771,344.00	518,747.00	1,290,091.00	0.00	891,207.19
30	Tata innovation fellowship Award - Dr. Pravat Mandal	116,797.00	894,499.00	8,828.00	0.00	0.00	881,264.00	881,264.00	0.00	138,860.00
31	Crspri System - Dr. Sourav Banarjee	105,534.56	2,374,624.00	0.00	27,838.00	464,833.00	777,558.08	1,242,391.08	0.00	1,209,929.48
32	DBT Mirna Meditate Control - Dr. Sourav Banarjee	(105,732)	2,017,294.00	0.00	93,955.00	300,000.00	1,292,459.29	1,592,459.29	0.00	225,147.97
33	A CROSS-CULTURE PERSPECTIVE(DBT-NETHERLANDS) -Dr. PRAVAT MANDAL	837,843.00	1,033,346.00	27,654.00	1,167,400.00	683,887.00	0.00	683,887.00	0.00	47,556.00
34	SPECIFIC BRAIN TEMPLATE DST Dr. PRAVAT K MANDAL	671,736.50	0.00	8,853.00	0.00	213,750.00	398,598.00	612,348.00	0.00	68,241.50
35	S&S LEARNING IN ZEBRA FINCHES Dr.SOUMYA IYENGAR	788,005.00	600,000.00	0.00	0.00	345,054.00	931,345.00	1,276,399.00	0.00	111,606.00
36	PDF-SERB(AKANSHA JALOTA)	512,035.00	487,555.00	0.00	0.00	605,000.00	240,782.00	845,782.00	0.00	153,808.00
37	**PDF-SERB(AMIT NASKAR)**	**456,581.00**	**639,726.00**	**11,209.00**	**0.00**	**651,129.00**	**110,415.00**	**761,544.00**	**0.00**	**345,972.00**

38	PDF-SERB(POONAM MEENA)	167,432.00	0.00	0.00	0.00	178,000.00	138,790.00	316,790.00	0.00	(149,358.00)
39	PDF-SERB(SUVADIP MALLICK)	534,786.00	559,246.00	0.00	0.00	760,178.00	261,671.00	1,021,849.00	0.00	72,183.00
40	J.C.Bose Fellowship(PROF. SUBRTA SINHA	451,786.00	1,500,000.00	42,899.00	0.00	247,581.00	1,645,383.42	1,892,964.42	0.00	101,720.58
41	PDF-SERB(Ashok Datusalia)	0.00	960,000.00	0.00	0.00	602,559.00	114,017.00	716,576.00	0.00	243,424.00
42	PDF-SERB(Soibam Shyamchand)	0.00	976,129.00	0.00	0.00	347,742.00	271,150.00	618,892.00	0.00	357,237.00
43	DST- Inspired Fellow (Sriparna Mukherjee)	0.00	384,000.00	0.00	0.00	300,000.00	14,096.00	314,096.00	0.00	69,904.00
44	TWAS-DBT (Saliu Ibrahim)	0.00	436,472.00	0.00	0.00	164,167.00	15,043.00	179,210.00	0.00	257,262.00
45	C V Raman Interest Income Fellow(Dr. Rolland Kipre)	0.00	285,000.00	0.00	0.00	60,645.00	0.00	60,645.00	0.00	224,355.00
46	Dementia Science Programme	0.00	92,835,000.00	0.00	0.00	0.00	0.00	0.00	0.00	92,835,000.00
47	DST-CSRI (Dr. Prem Chand)	0.00	880,000.00	0.00	0.00	290,807.00	20,000.00	310,807.00	0.00	569,193.00
48	MicroRNA mediated Reg. of Neural stem(Dr. Anirban Basu)	0.00	4,467,000.00	0.00	0.00	0.00	265,011.00	265,011.00	0.00	4,201,989.00
49	Therapeutic Role DBT(Dr. Anirban Basu)	0.00	850,000.00	0.00	0.00	0.00	35,216.35	35,216.35	0.00	814,783.65
50	Oscillatory network dynamics DST(Dr. Depanjan Roy)	0.00	3,453,722.00	0.00	85,999.00	0.00	83,981.00	83,981.00	0.00	3,283,742.00
51	BRICS Research Project(Dr. Nihar Ranjan Jana)	0.00	1,385,000.00	0.00	0.00	0.00	0.00	0.00	0.00	1,385,000.00
52	Dyslexia Linked RNA(Dr. Pankaj Seth)	0.00	2,854,800.00	35,290.00	0.00	0.00	395,047.54	395,047.54	0.00	2,495,042.46
53	Fetal neural stem cells to oligodendrocytes (Dr. Pankaj seth)	0.00	1,004,000.00	0.00	0.00	0.00	0.00	0.00	0.00	1,004,000.00
54	Novel Imaging Dignostics Indo-Aus grant(Dr. Pravat Kumar Mandal)	0.00	7,278,000.00	0.00	0.00	0.00	0.00	0.00	0.00	7,278,000.00
55	Dementia Tissue MRI studies(Dr. Dipanjan Roy)	0.00	1,709,000.00	0.00	0.00	0.00	0.00	0.00	0.00	1,709,000.00
56	Dementia Basic Biology(Dr. Shiv Kumar Sharma)	0.00	5,108,000.00	0.00	0.00	0.00	0.00	0.00	0.00	5,108,000.00
57	Dementia Imaging studies(Dr. Pravat Kumar Mandal)	0.00	1,709,000.00	0.00	0.00	0.00	0.00	0.00	0.00	1,709,000.00
58	Centre for Excellence for Epilepsy(Phase-II)	0.00	82,197,000.00	0.00	0.00	0.00	0.00	0.00	0.00	82,197,000.00
59	Workshop & Conference(NBRC)	-1,012,934.78	2,542,992.00	0.00	0.00		2,179,678.00	2,179,678.00	0.00	(649,620.78)
60	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
61	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)
62	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)

63	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)
64	Material Malnutrition - Dr. Shyamala	-579,048.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	(579,048.00)
65	M.Sc. Neuroscience (Dr.Aditya-DBT)	5,073.00	0.00	0.00	0.00	0.00	5,073.00	5,073.00	0.00	-
66	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)
67	Stochastic Resonance - Prof. P.K. Roy	-471.00	0.00	0.00	0.00	0.00	-471.00	-471.00	0.00	-
68	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)
69	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)
70	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)
71	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
72	BBNSC - Dr. Dhingra	144.00	0.00	0.00	0.00	0.00	144.00	144.00	0.00	-
73	BBNSC - Dr. Shyamala	-392,947.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	(392,947.00)
74	BBNSC - Dr. Neeraj	296,937.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	296,937.00
75	BBNSC - Dr. Ellora	-403,419.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	(403,419.00)
76	BBNSC - Dr. Soumya	1,246.00	0.00	0.00	0.00	0.00	1,246.00	1,246.00	0.00	-
77	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)
78	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
79	Japanese Enceph. Virus - Dr. Anirban Basu	451.00	0.00	0.00	0.00	0.00	451.00	451.00	0.00	-
80	Functional Role of E6-AP - Dr. Nihar Rnajan Jana	168.00	0.00	0.00	0.00	0.00	168.00	168.00	0.00	-
81	Charac. of Molecular Interac. - Dr. Pravat Kumar Mandal	2,106.00	0.00	0.00	0.00	0.00	2,106.00	2,106.00	0.00	-
82	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)
83	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)
84	Multilingualism - Dr. Nandini C Singh	823.00	0.00	0.00	0.00	0.00	823.00	823.00	0.00	-
85	DBT Grant - Dr. Kallol Dutta	7,920.00	0.00	0.00	0.00	0.00	7,920.00	7,920.00	0.00	-
86	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
87	Perception Engineering Project of DIT - Dr. Neeraj Jain	-1.31	0.00	0.00	0.00	0.00	-1.31	-1.31	0.00	0.00

88	Functional Imaging Study of Dyslexia - Dr. Nandini C. Singh	-0.23	0.00	0.00	0.00	0.00	-0.23	-0.23	0.00	-
89	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
90	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)
91	Understanding the Psychological Function of Malin - Dr. Nihar Ranjan Jana	350.11	0.00	0.00	0.00	0.00	350.11	350.11	0.00	-
92	Circadian System Linkage (DST) - Dr. Soumya Iyengar	0.39	0.00	0.00	0.00	0.00	0.39	0.39	0.00	0.00
93	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)
94	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)
95	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
96	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)
97	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)
98	Role of Human Umbilical Cord Blood Stem (AIIMS) - Dr. Pankaj Seth	55.44	0.00	0.00	0.00	0.00	55.44	55.44	0.00	-
99	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
100	DBT 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)
101	DBT EDUCATIONAL NEUROSCIENCE MEETING-Dr. NANDINI C SINGH	476.00	0.00	0.00	0.00	0.00	476.00	476.00	0.00	-
102	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
103	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
104	DST PDF Project Under CSI - Dr.D Subhashree	-21,941.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	(21,941.00)
105	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)
106	DBT Tata Innovation Fellowship -Dr P.K.Roy	-207,575.40	0.00	0.00	0.00	0.00	0.00	0.00	0.00	(207,575.40)
107	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

108	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)
109	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)
110	Chromatin Remodelers in regulating associated - Dr. Ellora sen	-2,562.16	0.00	0.00	0.00	0.00	0.00	0.00	0.00	(2,562.16)
111	Deregulation of micro RNA in cell and animal models of Huntington's disease Dr. Nihar Ranjan Jana	-2,999.59						0.00	0.00	(2,999.59)
112	Non-invasive Imaging based detection and of brain oxidative (U.S. Airfore) - Dr. Pravat Kumar Mandal	-0.15	0.00				-0.15	-0.15	0.00	(0.00)
113	Influence of social cues omapatial cognition - Dr. Chetan Yadav	-4,873.00	1,745.00	0.00	0.00	0.00	0.00	0.00	0.00	(3,128.00)
114	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)
115	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
116	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
	Total (A)	**35,782,823.69**	**261,214,638.12**	**1,191,318.00**	**7,321,822.19**	**19,757,332.00**	**33,179,323.42**	**52,936,655.42**	**27,133.00**	**237,903,169.20**
6	DELCON E-LIBRARY CONSORTIUM (B)*	366,658,304.98	763,623,800.00	2,140,825.00	579,788.00	1,846,589.00	542,388,496.49	544,235,085.49	0.00	587,608,056.49
	Grand Total (A+B)	**402,441,128.67**	**1,024,838,438.12**	**3,332,143.00**	**7,901,610.19**	**21,603,921.00**	**575,567,819.91**	**597,171,740.91**	**27,133.00**	**825,511,225.69**
	Note:- Projects from Sl. No 60 to 116 are closed and non operational.									

Santosh Kumar Choudhary
Dy. Finance Officer & Offg. F&Ao

Prof. Neeraj Jain
Director

As Per Our Separate Report Of Even Date Attached

For N.C. Mittal & Co.
Chartered Accountants
(Frn-000237N)

Kapil Mittal
Partner
Membership No. 503378
Date: 22.10.2018
New Delhi

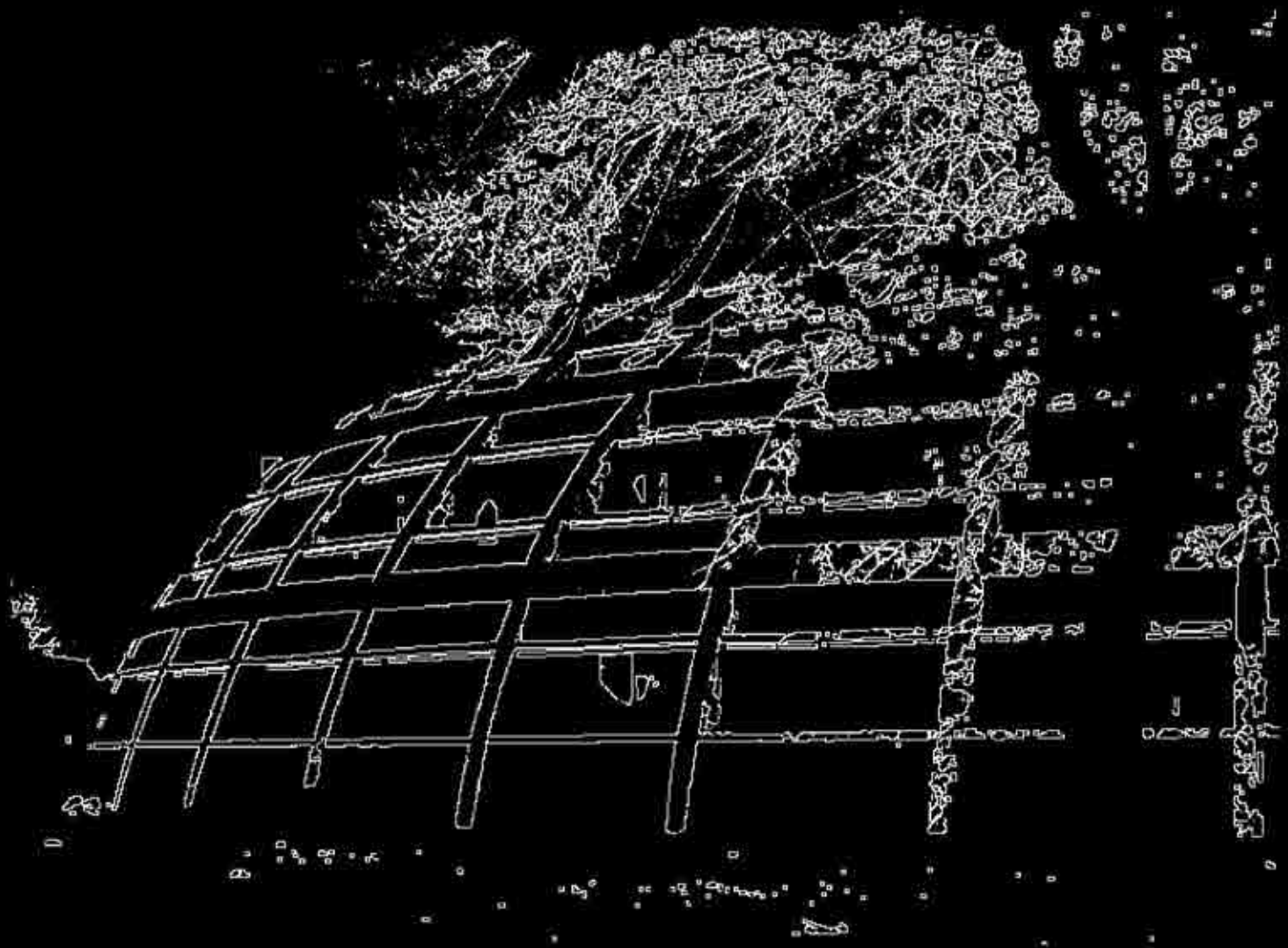
Compiled and Edited by V. Rema and Kedar Sing Bajetha.

Front cover: Mouse barrel cortex with pyramidal neurons expressing enhanced green fluorescent protein (EGFP) and inhibitory parvalbamin neurons labeled with genetically expressed Td-Tomato.

Image courtesy Arti Kumari.

Back cover: NBRC

Photograph and Stylization: Neeraj Jain



National Brain Research Centre

NBRC

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