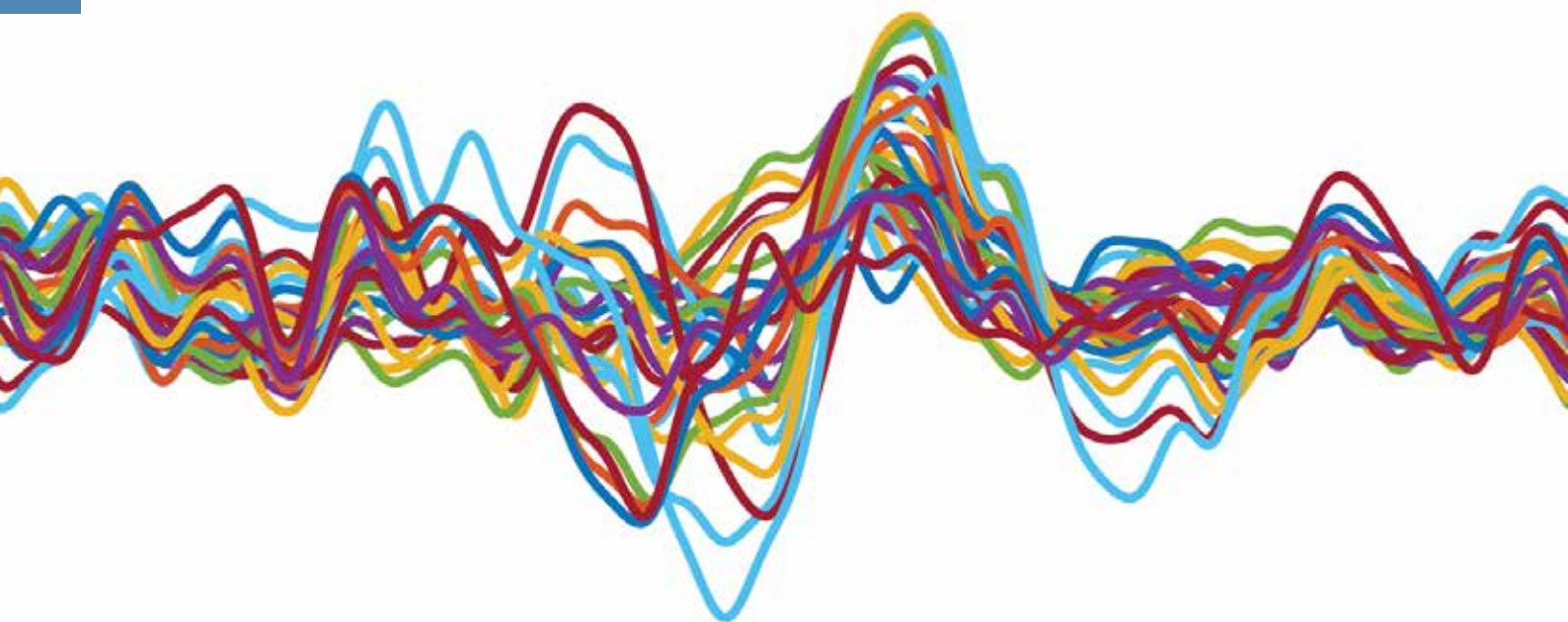


National Brain Research Centre



ANNUAL REPORT

2016-2017



NATIONAL BRAIN RESEARCH CENTRE

ANNUAL REPORT

2016-17

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Mandate & Objective

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

Globally, it is time to think about the 'purpose and relevance' of science. Knowledge for the betterment of humanity or knowledge for the sake of knowledge! Are the two not really different? At NBRC we are acutely conscious of the society that supports us, and also gives us the opportunity of being at the crest of the wave of scientific endeavour. In our attempt to blend the adventure of discovery with the concrete betterment of our fellow citizens we see no boundaries – just the realization that with creativity, imagination and drive we are moving to justify the faith reposed in us.

Dr Anirban Basu has been able to successfully combine basic and applied research in the field of Neurovirology. After the publication of a field trial regarding the use of minocycline in patients of Japanese Encephalitis, efforts are ongoing to enhance its use in appropriate patients. At a basic science level, Dr Anirban Basu's results which show that the host microRNA miR-301a blocks the IRF1-mediated neuronal innate immune response to Japanese encephalitis virus (JEV) infection. The neutralization of miR-301a reinforces host innate immunity by restoring IFN- β expression, thereby restricting viral propagation in neurons. They have also shown that JEV induces human neural stem/progenitor cell death by elevating endoplasmic reticulum

(ER) resident chaperone GRP78, mitochondrial protein Prohibitin (PHB) and heterogeneous nuclear ribonucleoprotein hnRNPC through stress. This unravels a novel mechanism underlying stem/progenitor cell death following viral infection.

Despite global efforts, HIV/AIDS remains one of the major cause of death and disability in several countries around the world. The neuroAIDS laboratory at NBRC headed by Dr Pankaj Seth is actively engaged in unravelling cellular and molecular mechanisms for HIV-1 induced damage to brain cells in AIDS patients. The laboratory uses a unique model of primary cultures of human neural stem cells derived from aborted fetal brain samples, as well as autopsy brain sections from HIV/AIDS patients for studying HIV related brain dysfunctions. The laboratory is currently investigating role of HIV-1 transactivator of transcription (HIV-1 Tat) protein in alterations of glia-neuronal interactions, leading to neuronal damage and compromise in cognitive and motor functions in AIDS patients. Recently, Dr Seth's laboratory has gained novel insights into astrocyte mediated neuronal damage following exposure to HIV-1 Tat protein and discovered that the increased ATP levels from astrocytes are via voltage dependent anion channel-1 (VDAC-1) that was regulated by miR320a, as blocking of VDAC-



1 attenuated the glia mediated neuronal damage. The laboratory has also successfully established protocols for human inducible pluripotent cells (Human iPSCs) from peripheral blood cells and is now deriving neurons from them. This will serve as human neural stem cell platform for various laboratories within NBRC as well as other neuroscientists in India.

Dr Nandini Singh and her group at NBRC have been working of the mechanisms by which the brain is able to read, and the aberrations that lead to specific learning disabilities, especially dyslexia. A tool in Indian languages for the screening, assessment and remediation for students for dyslexia is being operationalised. She partnered with UNESCO MGIEP, and Saajha, to organize a 4-week summer reading camp for 6-10 years old students of MCD schools in New Delhi. Six camps were in different parts of Delhi and nearly 150 students were trained weekly on identifying akshara, matra and introduced to shabd. Pre-assessment and post-assessment tests from Dyslexia Assessment for Languages of India (DALI) toolkit which had been adapted

for the reading camp were used to identify children who might be at risk for learning disabilities, and to understand the scope for improvement through effective intervention.

Significant strides have been made by scientists at NBRC working on various kinds of brain tumours. In addition to highlighting the previously unknown role of telomerase in the regulation of pentose phosphate pathway, Dr Ellora Sen's lab has indicated the involvement of Nrf2-TERT loop in maintaining oxidative defence responses in glioma. Her lab is also investigating the importance of dysregulated metabolism in immune surveillance has highlighted the importance of Protein arginine methyltransferase 1 (PRMT1 - the predominant arginine methyltransferase) in modulating chromatin landscape crucial for facilitating HLAB gene expression in glioma. Dr Subrata Sinha's lab is devising strategies to tackle the resistance induced by low oxygen tension (hypoxia), especially the use of already approved drugs in combination.

Dr Ranjit Giri's group has been working on Brain expressed X-linked (Bex) genes, a newer group of tumor suppressor genes which are silenced in different varieties of cancers. For the first time, his group has investigated the induction of all Bex genes and associated mechanisms by curcumin in an aggressive neuroblastoma cell line (N2a).

Curcumin induced all endogenous Bex genes in N2a cells in a dose- and time-dependent manner and also activated p53 prior to Bex genes induction. Most importantly, inhibition of curcumin-mediated induction of Bex genes by pifithrin- α (p53 inhibitor) and siRNA for Bex mRNAs also inhibited N2a cells apoptosis suggesting, a direct role of Bex genes in N2a cells apoptosis and the involvement of p53 in the induction of Bex genes. These results suggest that re-expression of Bex genes by curcumin act as tumour suppressors and may provide a new strategy to treat neuroblastomas.

In collaboration with Dr Nandini Singh and Dr Pankaj Seth, Dr Subrata Sinha's laboratory, in its study of familial dyslexia in endogenous groups has shown that there are distinct patterns of inheritance in the affected families. This work has also shown that an autosomal recessive dinucleotide insertion associate with dyslexia maps to an as yet uncharacterized long non coding RNA that is critical for neuronal differentiation of human neural progenitor cells.

Scientists at NBRC have also made substantial contributions to address questions in basic research in the past year. Dr Neeraj Jain has been investigating how information is processed in the somatosensory and motor systems of different mammalian species. His work has demonstrated subtle but important differences in the organisation of the movement systems in two

closely related rodent species - mice and rats. Interestingly, mice have more of a mosaic pattern of the movement representation in the cortex as compared to rats. Such differences optimise the survival of these species in their individual niche.

Dr Anindya Ghosh Roy's group has used peripheral neurons of *C. elegans* to study axonal regeneration. They found that let-7 microRNA inhibits functional regeneration by regulating the expression of ced-7 coding for a homotypic cell adhesion protein. Further, the loss of this microRNA promotes repair process by increasing axon fusion events during regeneration.

Dr. Nihar Ranjan Jana's group have found that the nanoparticle form of some of the sugar molecules can significantly enhance their chaperone performance in inhibiting protein aggregation and in lowering of amyloidogenic cytotoxicity in collaboration with scientists from IACS, Kolkata.

Dr Yoganarasimha Doreswamy's research group has been working on questions relating to the neural basis of learning, memory and spatial navigation. Specifically, he uses electrophysiology to study the subiculum, a part of the hippocampus which is involved in these functions. His group has recently shown that the heading dynamics during exploration acts as a self-organized critical system. Further, it plays a crucial role in information gathering

and comparison with previously acquired information to make logical decisions about excursions in sequence.

Dr Soumya Iyengar's group has been working on songbirds (zebra finches) as a model system to understand the neural basis of vocal learning. They have recently shown that a component of the endogenous opioid system (delta opioid receptors) are important for vocal learning since blocking these receptors in young male birds for a short period prevents them from producing a normal song in adulthood. Further, blocking delta opioid receptors in young birds leads to changes in the number of dopaminergic neurons in the avian basal ganglia, suggesting that the opioid system may be involved in the proliferation and/or differentiation of this cell type in the brain.

A number of interesting discoveries have also been made by the Computational and Neuroimaging Division at NBRC. Dr Prasun K Roy's group has developed an accurate procedure to map out information flow and cause-effect based connectivity in the brain from functional magnetic resonance imaging (fMRI) studies and also adapted this as a screening test to differentiate Attention Deficit Hyperactivity Disorder in children with high sensitivity and specificity. The improved method identifies a number of extra connectivity paths in these children. Further, using MRI Tractographic studies,

his team has also elucidated the generative action that the white matter compartment exerts on the grey matter compartment. The lab has shown that the number of connected networks per anatomical node regions maximizes at the age of 50 as a coping mechanism to compensate for age-related neurodegenerative processes. Gender differences are caused by comparatively less myelination intensity in women due to hormonal transition during the menopausal process. The techniques developed can have important applications in neurosurgical or radiotherapeutic planning in different disorders, by identifying the development of new functional networks.

From the same division, Dr Pravat Mandal and his group have developed a comprehensive brain signal processing toolbox called "KALPANA" for brain metabolic profiles and quantitation, which has a direct application in clinical settings. This entire protocol for signal processing has been submitted for an International (USA) patent funded by the Ministry of Information Technology, Govt of India.

In addition to important scientific discoveries, NBRC has also hosted a series of events related to promoting science by inviting renowned speakers to give talks and lectures at the institute. The Ramamurthi Memorial Lecture is organized annually at NBRC to commemorate the

birth anniversary of the eminent neurosurgeon, Prof B Ramamurthi. On this occasion, Dr S Swaminathan, Director General, Indian Council of Medical Research (ICMR) delivered a lecture entitled "Recent Advances in TB Diagnosis and Management", wherein she stressed the need for early diagnosis and treatment to prevent the spread of multi-drug resistant tuberculosis in India. This highly informative lecture was followed by an interactive session with students and faculty of NBRC.

A two-day national conference on Advances in Neuroimaging and Applications in Cognitive Disorders (ANACoD) organized by Dr Pravat Mandal (sponsored by Department of Science and Technology and Philips India) was held at NBRC on 3rd and 4th May, 2016 and was attended by experts in the fields of neurology, radiology, cognitive and developmental neurosciences, biostatistics and electrical engineering as well as by students from diverse disciplines related to neuroscience. Talks and discussions during the conference focused on the advancements and clinical and research-oriented applications of neuroimaging in cognitive disorders, especially Parkinson's disease, Alzheimer's disease and autism spectrum disorders. Students attending the conference participated in a poster session to get inputs regarding their research from experts in the field. One of the highlights of this event was a violin recital by the esteemed violinist Ms Sunita Bhuyan, who is a recipient of the

Indira Gandhi Priyadarshini Award.

One of the major events that was held at NBRC was the 34th Annual Meeting of Indian Academy of Neurosciences, October 19th – 21st, 2016, which was organized by Dr Pankaj Seth and Dr Anirban Basu, which brought together neuroscientists from within India and abroad to discuss and exchange ideas and their findings. This year's conference was particularly important because it was themed 'Molecules to Mind' and covered emerging trends and technologies in neurosciences including fundamentals of neuroscience and its state-of-the-art application in basic and clinical research. The conference was preceded by a workshop on 'Scientific Communication and Career' for students to gain insights into scientific writing. The highlight of the meeting were 5 plenary talks, 11 invited talks, 11 symposia, platform presentations, short talks and special evening lectures. The conference also included more than 150 poster presentations wherein budding researchers in different fields of neuroscience including neuroinflammation and neurotoxicity, human cognition and behavior, computational neuroscience, circuits and behavior, animal cognition and behavior and brain diseases and therapy. Besides the scientific talks, an important Expert Group Meeting was held during the meeting for Advocacy in Neuroscience to augment funding in the area of Brain Research by governmental

agencies and to sensitize non-governmental agencies and the general public to the importance of neuroscience research in India. Another important event at the conference which was sponsored by the National Academy of Sciences India was a talk about the basic functions of the human brain and brain diseases by Prof Nihar Ranjan Jana, NBRC which was attended by 120 students from schools in and around Manesar. Overall, the IAN 2016 meeting at NBRC served as a catalyst for neuroscientists to disseminate their research and also to get important insights through discussions with other researchers.

NBRC's 13th Foundation Day (16th December, 2016) was held with customary fervour with an open day for students of local schools who were invited to attend a lecture on brain functions by Prof Shiv K Sharma. Students, post-doctoral fellows and project assistants of NBRC organized poster presentations, demonstrations and a quiz for the school students. The festivities concluded with a public lecture presented by Prof Vikram Patel (FMedSci, DSc; Co-Founder and former Director, Professor of International Mental Health and Wellcome Trust Principal Research Fellow, Centre for Global Mental Health, London School of Hygiene and Tropical Medicine, London, UK; Co-Director, Centre for Control of Chronic Conditions, Public Health Foundation of India, Gurugram, India) entitled 'Translating Neuroscience to serve India's

public health needs: from hype to substance'. During the course of the lecture, he stressed the role of nutrition for normal brain development especially in children and adolescents.

NBRC has been awarded Deemed University status since 2002 and one of its mandates is to generate highly trained manpower in the field of neuroscience. In this capacity, NBRC awarded the degree of Doctor of Philosophy (PhD) in Neuroscience to 9 students who successfully defended their doctoral research. Of these students, five were from NBRC's dual degree (Integrated MSc-PhD) programme and also received their Master's degree. A second batch of Master's students who joined NBRC's two-year Master's in Neuroscience programme have successfully completed their course-work requirements and have joined various laboratories for their dissertation research. We have also continued to provide hands-on training to students under the summer training programme which is conducted by the Indian Academy of Science, Bangalore, Indian National Science Academy, New Delhi and National Academy of Sciences, Allahabad. Summer trainees are provided hostel accommodation on campus and are encouraged to join all activities of the lab they are hosted by as well as the NBRC journal club during their two-month tenure at NBRC.

Besides academic activities,

students at NBRC also organize the annual student festival Tantrika, which blends science with cultural events. For Tantrika 2016, NBRC students had invited Dr Alok Sarin, Consultant Psychiatrist, Sitaram Bhartia Institute of Science and Research, New Delhi to present a talk on 'The Nature of Choice: Addressing the complexities of choice in severe mental illness',

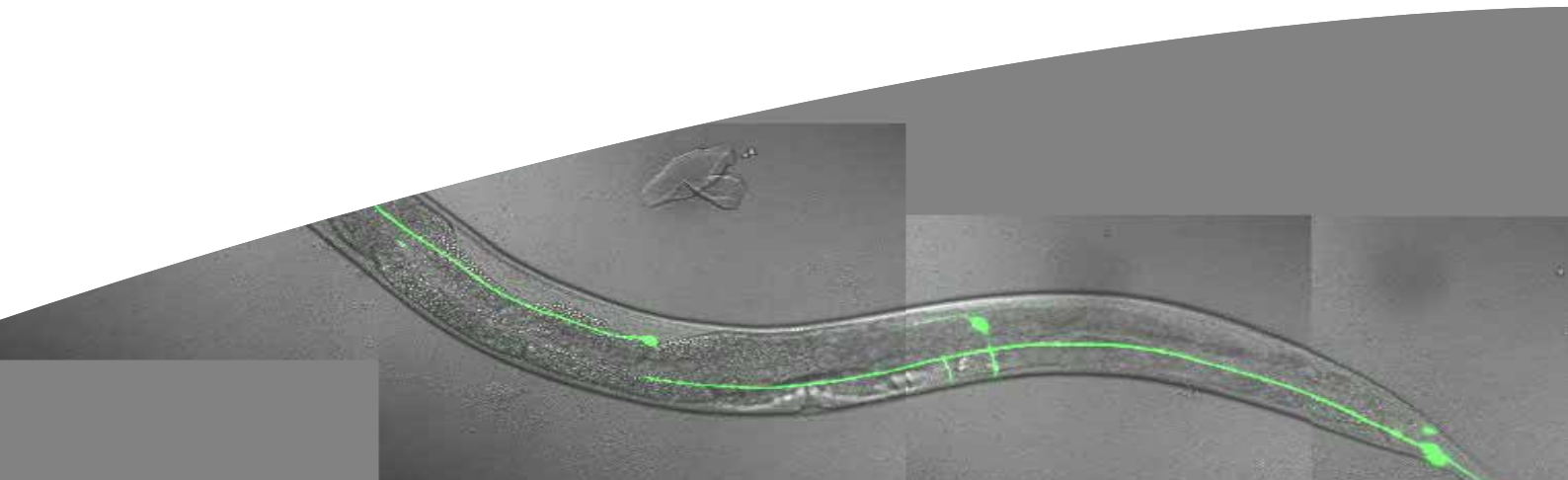
followed by high tea and interaction with NBRC students and faculty. The cultural program on the following day included a medley of music and dance, including a dance drama choreographed by the students, once more showcasing the amazing talent in the budding scientists.

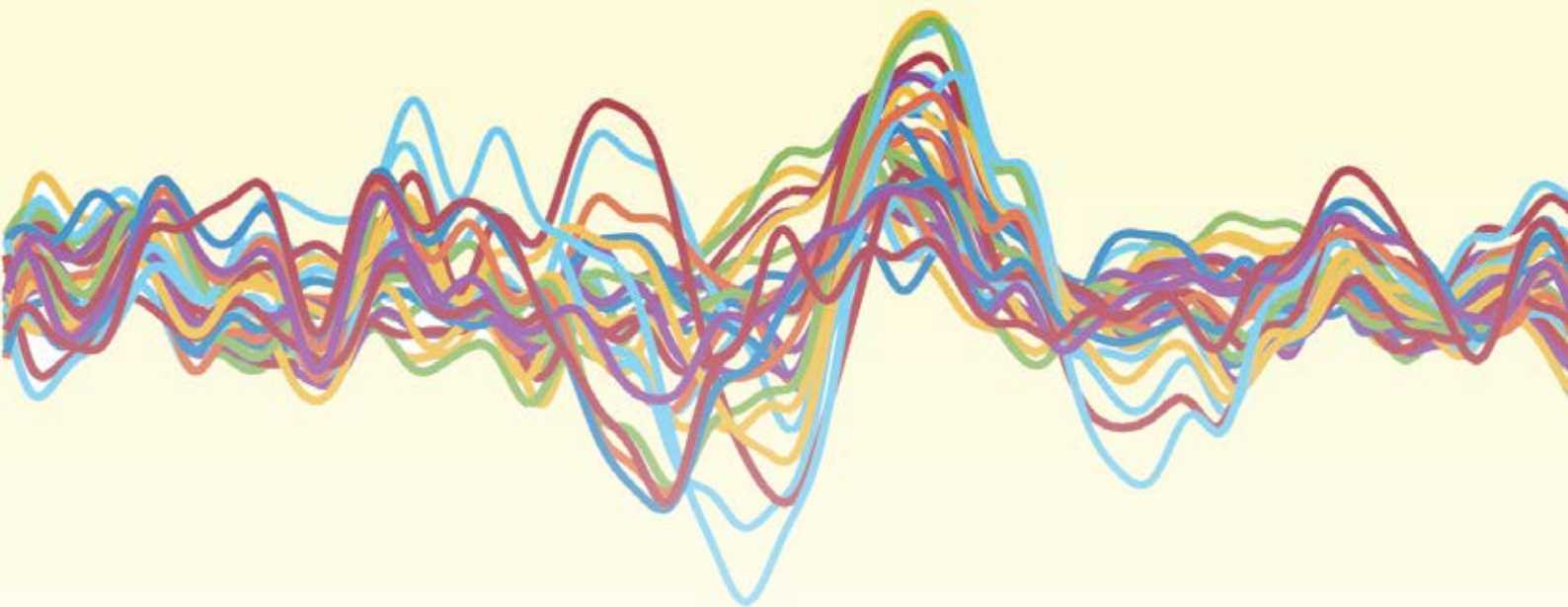
At NBRC, our evolution into an institution of this millennium,

seamlessly integrating the advances of science, creating new knowledge and generating novel insights continues. Our scientists and staff move forward hand in hand in this journey. Our students are now our ambassadors to the rest of the world. We are confident that we are leaving an imprint that will be positive and forward looking.

Subrata Sinha,
Director, NBRC

Molecular and Cellular Neuroscience Division





Non-canonical mechanisms of synapse formation and synaptic plasticity

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All cognitive outputs rely on the precise connectivity between neurons. How neurons communicate with each other is the fundamental determinant of all behaviors, ranging from simple reflexes to complex multifaceted behaviors. A high degree of spatial and temporal regulation is required at all the stages of formation of a complete neuronal circuitry; right from neuronal differentiation and development to synapse formation. Synapses are extremely dynamic and their modification is activity dependent. This activity dependent restructuring of synaptic connections is known as synaptic plasticity, and as such this phenomenon is brought about by a myriad number of factors. Identifying all processes that regulate synapse formation and plasticity will be essential towards understanding mechanisms of various cognitive functions including learning and memory

as well as provide valuable insight into various aberrations of cognitive functions, such as Autism Spectrum Disorders and Schizophrenia.

Our focus has been to identify the following aspects of neuronal circuitry development and its function:

1. Regulatory mechanism of activity regulated synapse maturation by non-proteolytic function of ubiquitination.
2. Localized regulatory mechanism of synaptic plasticity by activity dependent miRNA turnover at the synapse.

REGULATORY MECHANISM OF ACTIVITY REGULATED SYNAPSE MATURATION BY NON-PROTEOLYTIC FUNCTION OF UBIQUITINATION

Synapse formation in vertebrates occurs in early development,

during the establishment of neuronal circuitry, and in the adult brain, during learning and memory formation. Development of a synapse begins with contact between an axon and a dendrite followed by a cascade of events that includes formation of functional pre- and post-synaptic compartments for initial neurotransmission. Nascent synapses then undergo a process of refinement for further stabilization and maturation. Most of our current understanding of regulatory mechanisms of synapse formation is primarily focused on transcriptional control or protein-protein interactions between pre- and post-synaptic surface. Recently, modulation of various signaling mechanisms by post-translational modification emerged as a key regulatory control point for synapse formation, particularly at the synapse maturation step. Among various post-translational modifications, we have focused on protein ubiquitination because it can reversibly regulate nervous system development and function. Ubiquitination involves the conjugation of the 76 amino acid ubiquitin moiety to a lysine residue of the substrate protein. The conjugation of ubiquitin to specific set of proteins is facilitated through three sequential enzymatic reactions involving an E1 ubiquitin activating enzyme, an E2 ubiquitin conjugating enzyme and an E3 ubiquitin ligase that work in tandem. Among these, the E3 ubiquitin ligase is a crucial regulator of ubiquitination as it can selectively recruit a subset of target proteins and bind them

to the substrate directly. Recent reports have clearly demonstrated that apart from regulating conventional protein degradation, ubiquitination can also modulate signaling mechanisms *via* non-degradative function. These non-canonical mechanisms potentially include assembly of protein complexes, protein sorting, protein transport and modulation of activity of signaling molecules.

To investigate non-canonical role of ubiquitination in modulation of functional synapse development, we focused onto following questions. These include: (i) Are these E3 ligases differentially expressed in response to neuronal activity during synapse formation? (ii) Are activity regulated E3 ligases can specifically modulate excitatory or inhibitory synapse formation? (v) How do they modulate the synaptogenic program with spatio-temporal precision?

Using cultured hippocampal neurons as a model system, we have identified specific set of candidate E3 ligases those are differentially expressed in response to neuronal activity during temporal window of synaptic maturation step of functional synapse development. Among these differentially expressed E3 ligases, we focused on an RING domain containing E3 ligase, RNF2 primarily because of two reasons: (i) our *in situ* hybridization data suggested its restricted expression in hippocampus as well as in cerebellum (ii) expression of RNF2 is regulated at post-transcriptional level via NMDA receptor activation and subsequent influx of calcium – a critical step for activity induced

synapse maturation.

RNF2 is a component of Polycomb group (PcG) transcription repressor complex regulating various developmental programme. RNF2 has been shown to function as master E3 ligase-modulating function of several downstream E3 ligases implicated in developmental decisions. More recently, RNF2 has shown to be ubiquitinated by UBE3A, another master E3 ligase implicated in Angelman Syndrome – a neurodevelopmental disorder, and subsequently degraded. In contrary, RNF2 is also self-ubiquitinated that protects the protein from its degradation. Interestingly, self-polyubiquitination of RNF2 or by UBE3A occurs at same lysine residue. However, branching pattern of polyubiquitin chain trigger its stabilization through self-ubiquitination or degradation through UBE-3A –mediated polyubiquitination. Prompted by these observations, we hypothesized that neuronal activity can potentially modulate RNF2 stability through patterns of ubiquitination and thereby regulates functional synapse development.

To test this hypothesis, we stimulated primary hippocampal neuronal culture derived from UBE3A mutant mice as well as wild type mice, stimulated these neurons, immunoprecipitated RNF2 and assessed its polyubiquitination by western blot analysis using antibody that specifically recognize polyubiquitin chain. We observed high molecular weight polyubiquitin conjugates of Rnf2 in response to neuronal activity and these high

molecular weight polyubiquitin conjugated forms of Rnf2 is enhanced in hippocampal neurons obtained from Ube3A deficient mice (Figure 1A). Furthermore, we observed total

Rnf2 level was increased in stimulated hippocampal neurons obtained from Ube3A deficient mice as compared to wild type mice (Figure 1 B-C). These observations demonstrate that the neuronal

activity function as pivotal switch to trigger self-polyubiquitination of Rnf2 and subsequently stabilizes Rnf2 rather than its degradation *via* conventional function of polyubiquitination.

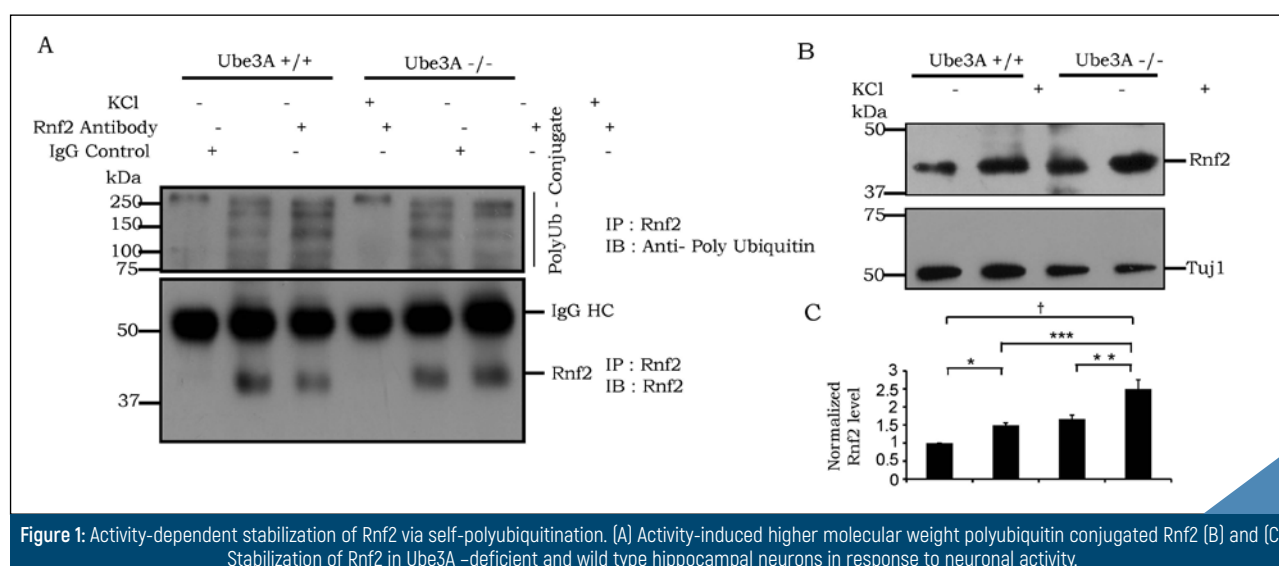


Figure 1: Activity-dependent stabilization of Rnf2 via self-polyubiquitination. (A) Activity-induced higher molecular weight polyubiquitin conjugated Rnf2 (B) and (C) Stabilization of Rnf2 in Ube3A -deficient and wild type hippocampal neurons in response to neuronal activity.

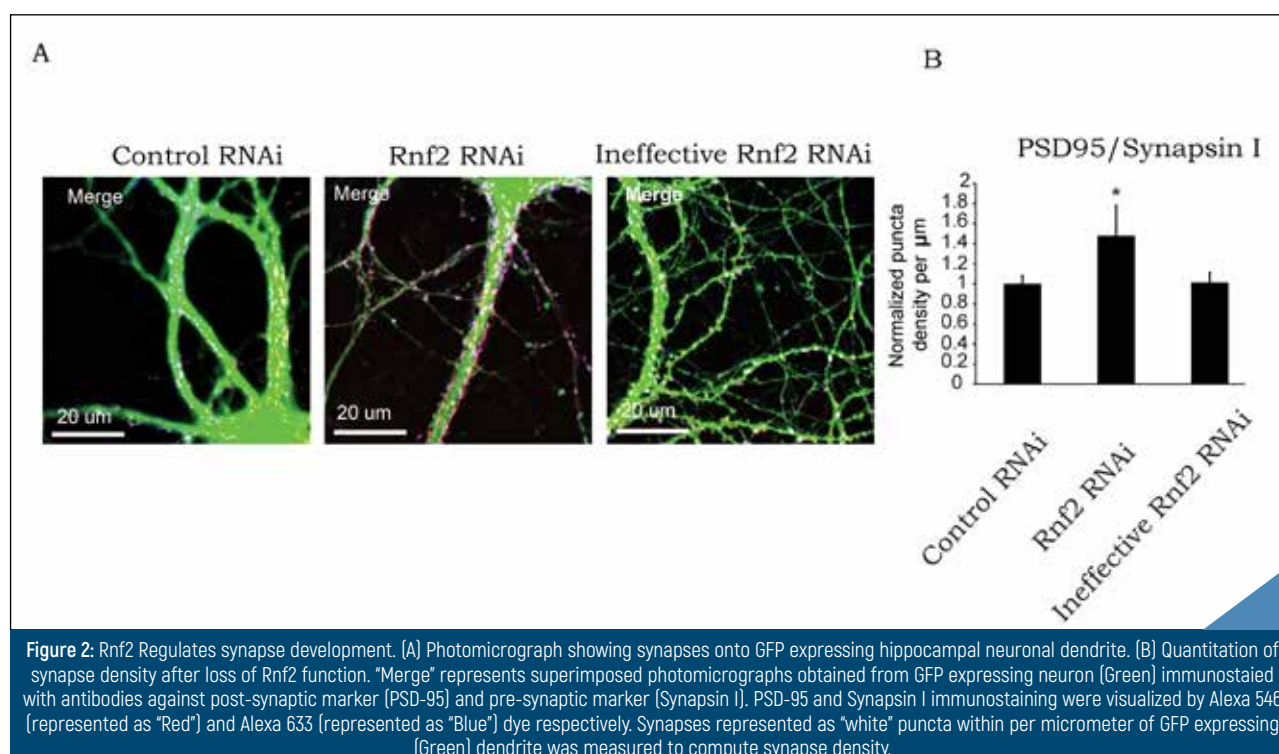


Figure 2: Rnf2 Regulates synapse development. (A) Photomicrograph showing synapses onto GFP expressing hippocampal neuronal dendrite. (B) Quantitation of synapse density after loss of Rnf2 function. "Merge" represents superimposed photomicrographs obtained from GFP expressing neuron (Green) immunostained with antibodies against post-synaptic marker (PSD-95) and pre-synaptic marker (Synapsin I). PSD-95 and Synapsin I immunostaining were visualized by Alexa 546 (represented as "Red") and Alexa 633 (represented as "Blue") dye respectively. Synapses represented as "white" puncta within per micrometer of GFP expressing (Green) dendrite was measured to compute synapse density.

Since, this non-canonical control of Rnf2 stability by self-polyubiquitination is regulated during the window of activity regulated synapse refinement, we evaluated functional implication of this activity-regulated process in modulation of synapse maturation. We inhibited RNF2 function by lentivirus -mediated RNA interference (RNAi) method and then measured synapse density after staining these neurons with pre- and post-synaptic markers of excitatory synapses. Synapse density was measured from confocal images using custom written algorithm.

We observed that the loss of RNF2 function (Rnf2 RNAi) leads to an increase of synapse density. We also observed that short hairpin RNA targeting Rnf2 without any effective knockdown did not increase synapse density. This

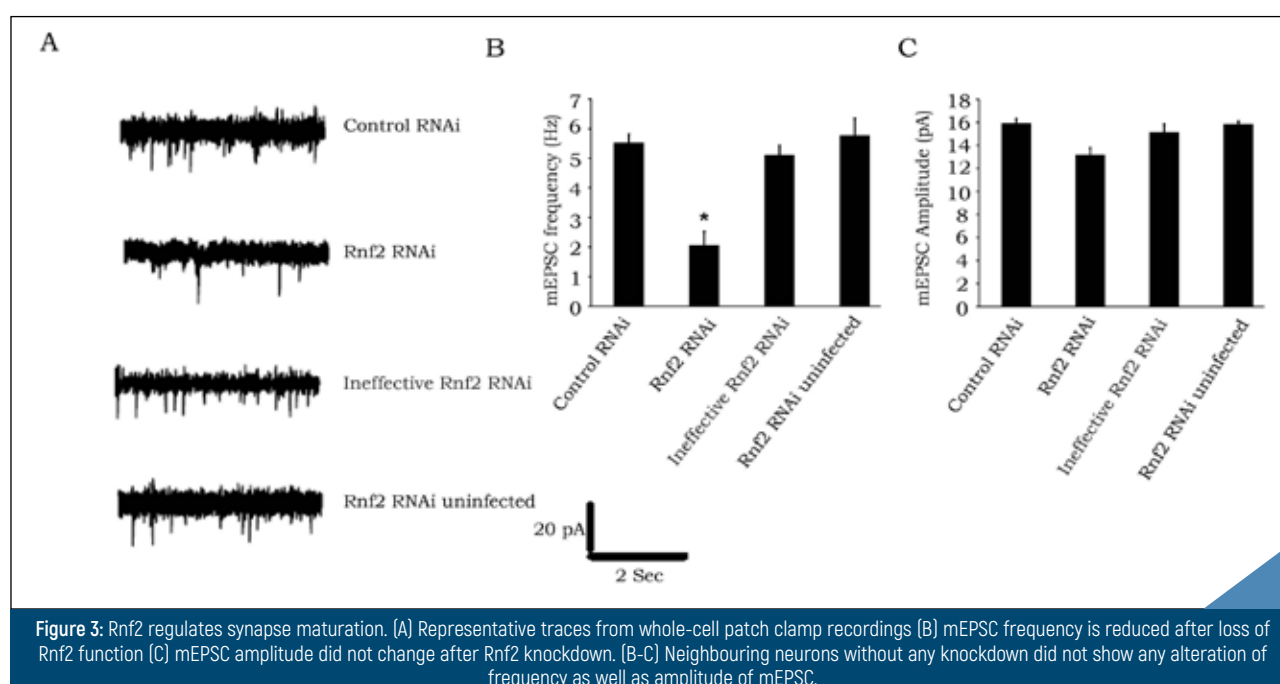
observation rules out the possibility of off-target effect of RNAi - a common factor that confounds phenotypic evaluation after RNAi (Figure 2).

To assess whether these synapses are functional, we have measured amplitude as well as frequency of miniature Excitatory Post-Synaptic Current (mEPSC) using whole cell patch clamp recording. Surprisingly, we observed significant reduction of frequency of synaptic events after loss of RNF2 function, suggesting that these synapse are 'silent'. We reasoned that the loss of Rnf2 function can potentially modulate global network activity leading to overall decrease in frequency of mEPSC. To delineate this possibility, we have sparsely

Infected hippocampal neuron and measured mEPSC from both lentivirus infected neurons

expressing shRNA against Rnf2 for effective knockdown as well as neighbouring uninfected neurons. We observed that neighbouring uninfected neuron did not show any decrease in frequency and amplitude of mEPSC as compared to neurons lacking Rnf2. This observation indicates that Rnf2 RNAi affects post-synaptic function rather than influencing global network activity.

We hypothesize that these silent synapses may lack AMPA receptors at the synaptic surface, as these receptors are key determinant for synaptic maturation. To address this possibility, we have measured surface expression of AMPA receptor after loss of RNF2 function. We have live-labeled subunit of AMPA receptor, such as GluA1 and GluA2 in hippocampal neuron and measured density of these receptor subunits



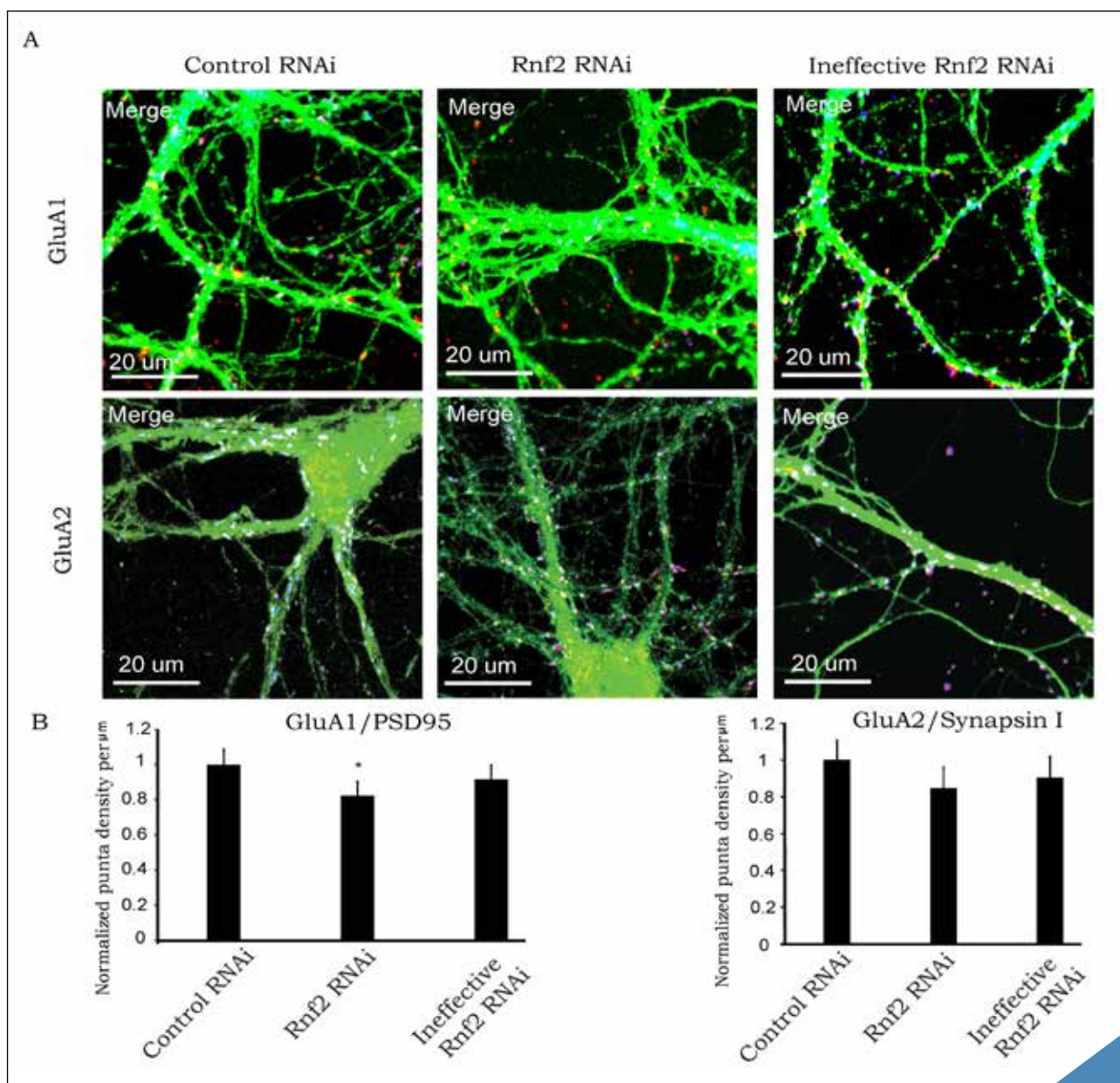


Figure 4: Rnf2 regulates synapse maturation by AMPA receptor insertion at the synapse. (A) Photomicrograph showing surface expression of GluA1 and GluA2 subunit of AMPA receptor after loss of Rnf2 function (B) Quantitation of GluA1 and GluA2 surface expression after loss of Rnf2 function. "Merge" represents superimposed photomicrographs obtained from GFP expressing neuron (Green) immunostained with antibodies against post-synaptic marker (PSD-95) or pre-synaptic marker (Synapsin I) and AMPA receptor subunit, GluA1 or GluA2. PSD-95 or Synapsin I immunostaining were visualized by Alexa 633 (represented as "Blue") and GluA1 or GluA2 was visualized by Alexa 546 (represented as "Red") dye. GluA1 or GluA2 AMPA subunit expression represented as "white" puncta within per micrometer of GFP expressing [Green] dendrite was measured to compute expression of GluA1 or GluA2 at the synaptic surface.

expressed on synaptic surface. Our observation demonstrates that reduced expression of surface AMPA receptor containing GluA1 contributes to immature or silent

synapse development upon loss of RNF2 function (Figure 4). In conclusion, our data point toward activity dependent regulation of a novel non-proteolytic function

of protein ubiquitination and its importance in functional synapse development (Figure 5).

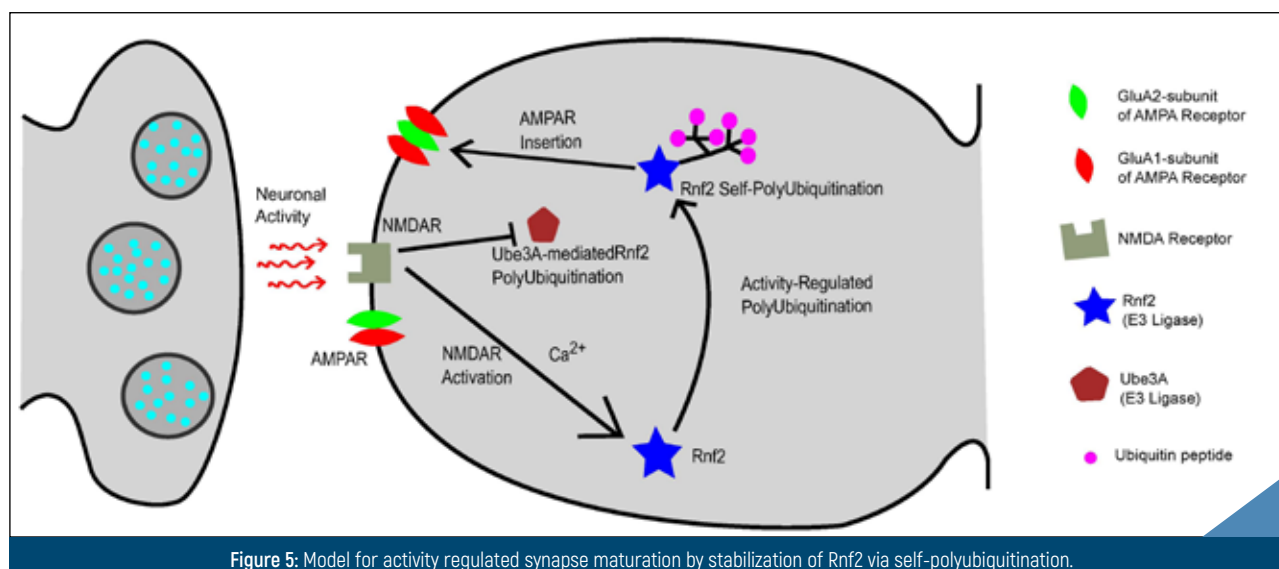


Figure 5: Model for activity regulated synapse maturation by stabilization of Rnf2 via self-polyubiquitination.

Taken together, this study will not only address novel mechanisms of synapse formation through non-canonical functions of ubiquitination but also will provide clue to our understanding of impaired synaptogenic programme that leads to onset of neurodevelopment disorders, such as Angelman Syndrome.

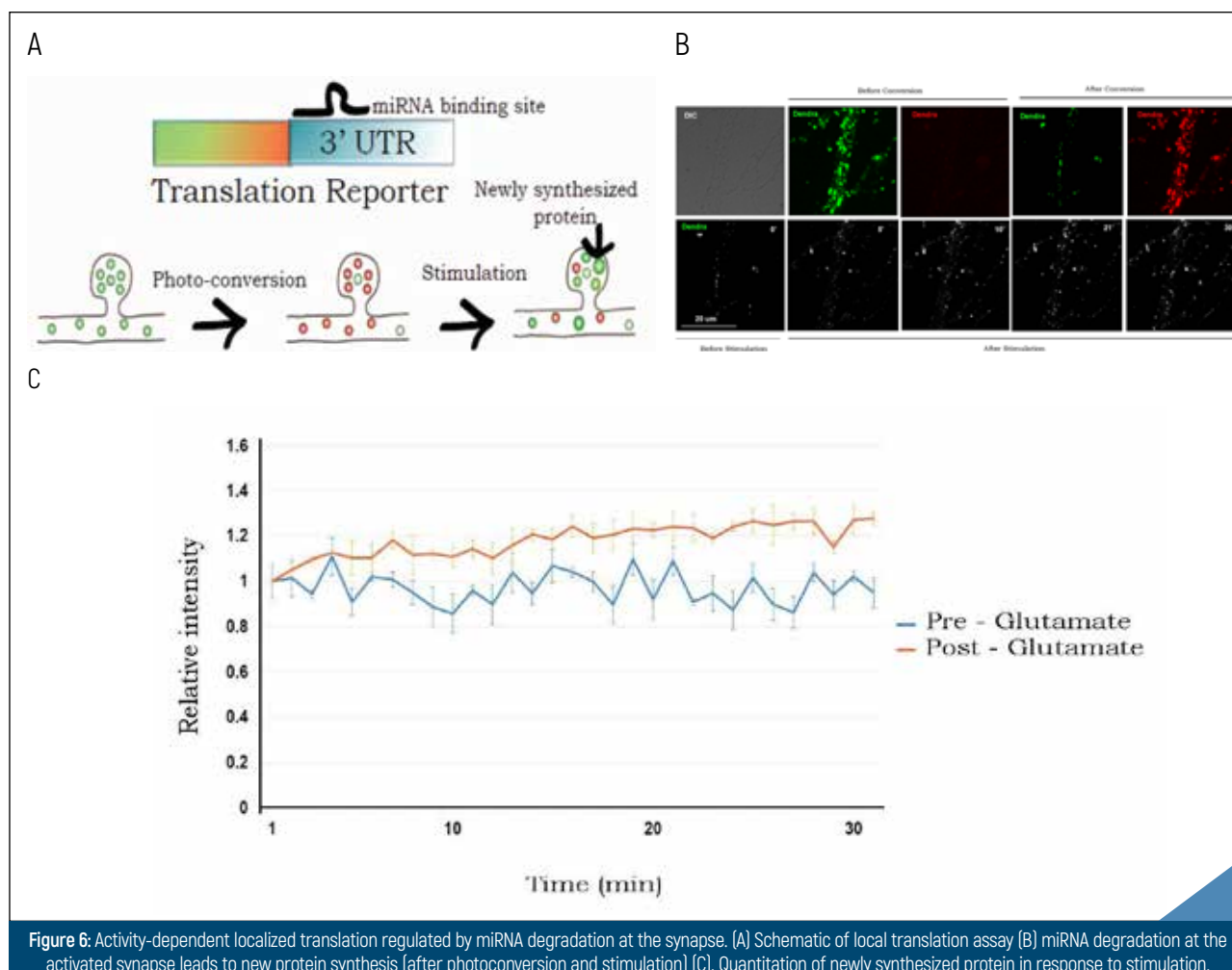
LOCALIZED REGULATORY MECHANISM OF SYNAPTIC PLASTICITY BY ACTIVITY DEPENDENT MIRNA TURNOVER AT THE SYNAPSE.

Spatio-temporal regulation of dendritic protein synthesis has emerged as a key modulator of synaptic plasticity. Neuronal activity can induce new protein synthesis at discrete locations along the dendrite that results in persistent structural, physiological, and biochemical changes in dendritic spines. The reversibility of microRNA (miRNA)-mediated regulation of their targets makes them perfect candidates for activity-dependent translational control of neuronal

plasticity. miRNAs guide a multi-protein complex, known as the RNA-induced silencing complex (RISC), to specific sites on mRNAs targeted for translational silencing or transcript degradation. Although emerging studies have demonstrated mechanisms involved in RISC-mediated control of dendritic protein synthesis, some intriguing questions are yet to be addressed. These include: (i) Which miRNAs are enriched at the synaptic compartment? (ii) How miRNA activity itself is regulated at the synapse? (iii) How miRNAs selectively regulates gene expression at the synapse? (iv) What is the implication of miRNA-mediated local control of gene expression in synaptic plasticity?

To gain a mechanistic insight into miRNA-mediated control of synaptic plasticity, we have identified miRNAs that are enriched at the synaptic compartment and assessed how these miRNAs regulated at the synapse in response to neuronal activity.

Our genome wide sequencing data revealed that a select group of miRNAs is enriched at the synapse. We then evaluated how this set of synapse-enriched miRNAs is regulated by neuronal activity. We have isolated synaptic fraction (synaptoneurosomes) by biochemical fractionation method and stimulated this synaptoneurosomal fraction by glutamate, an endogenous neurotransmitter. We measured the amount of miRNAs post-stimulation by quantitative PCR. We observed that among these synapse-enriched miRNAs, selective miRNAs are rapidly degraded and whereas another set of miRNAs are selectively matured locally at the synapse. To obtain precise temporal resolution of miRNA degradation at the synapse, we have designed miRNAs sensors by fusing complementary miRNA binding site with photo-convertible translation reporter. We observed that specific miRNAs are degraded at the synapse upon synaptic activation and their rapid



degradation occurs within minute time scale. The time scale of rapid turnover of selective miRNAs suggests that degradative control of miRNA activity could play a role in modulating protein synthesis dependent form of long lasting synaptic plasticity.

Furthermore, to investigate mechanistic details of miRNA turnover -mediated control of synaptic plasticity, we have identified factors that can potentially modulate rapid miRNA turnover and subsequently release translational suppression

of specific subset of transcripts localized at the synapse. We have identified target of a specific miRNA that is rapidly degraded at the synapse. Experiments are in progress to address how miRNA turnover -mediated control of protein synthesis at the synapse can make long lasting modification of the activated synapses and how these localized modification can fine tune neural circuitry to regulate long-term memory formation. Taken together our study will enumerate novel mechanisms of miRNA-mediated

protein synthesis dependent form of long lasting plasticity and its implication in long-term memory formation.

PRESENTATIONS

- ❖ Pushpa Kumari, Balakumar Srinivasan and **Sourav Banerjee** "A novel non-canonical function of E3 ubiquitin ligase in synapse formation" Janelia Farm / HHMI meeting on Molecular mechanisms at the synapse : Experiments and Modelling, USA, May, 2016.

❖ Balakumar Srinivasan and **Sourav Banerjee** "Burn your fat: Glial control of high fat diet induced modulation of feeding circuitry" Asia Pacific Society for Neurochemistry Annual Meeting, Kuala Lumpur, Malayasia, August 2016.

❖ Sarbani Samaddar and **Sourav Banerjee** "Creative Destruction: Regulation of synaptic plasticity by selective degradation of miRNAs at the synapse" WE-Heraeus-Seminar on Neuronal Mechanics, Physikzentrum Bad Honnef, Germany, August 2016.

❖ Pushpa Kumari, **Balakumar Srinivasan** and **Sourav Banerjee** "A novel non-canonical function of E3 ubiquitin ligase in synapse formation" Bangalore Microscopy Course, Bangalore, September 2016.

FUNDING

Ramalingaswami Fellowship, DBT

RNAi grant, DBT

Genome Engineering Grant, DBT

NBRC core fund

COLLABORATOR

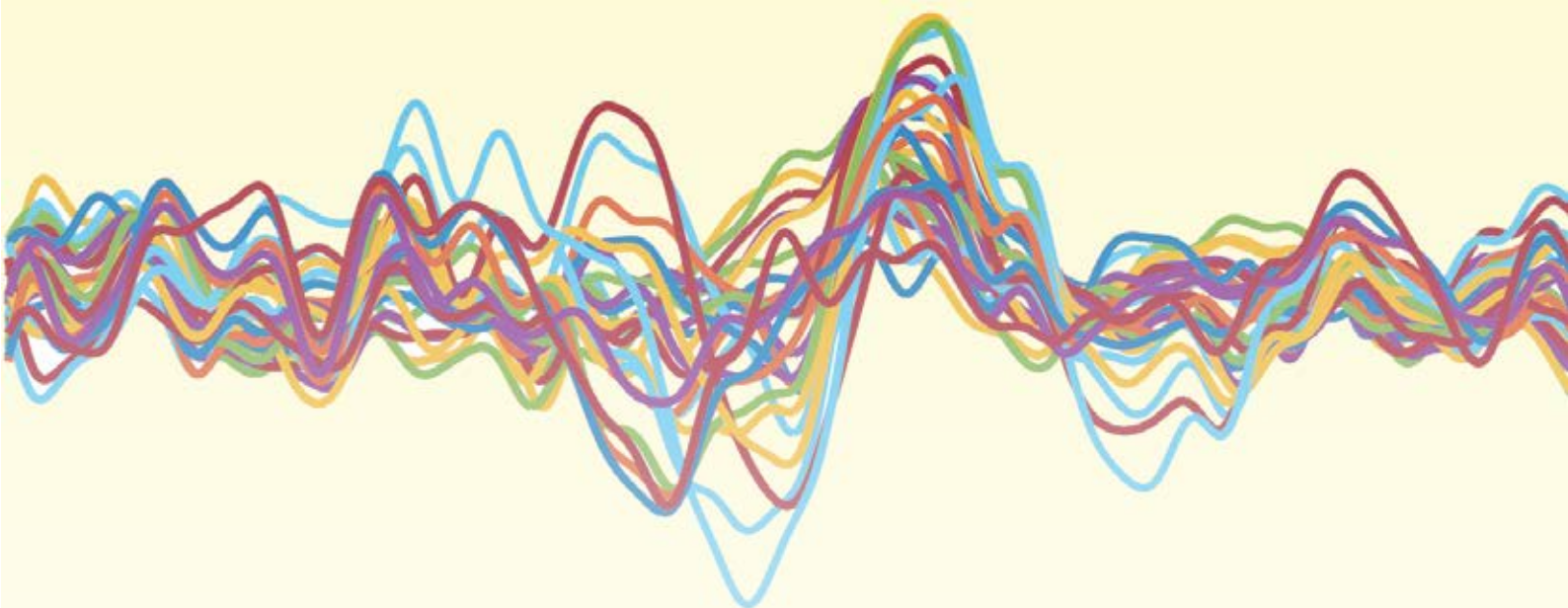
Dr. Dasaradhi Palakodeti, inSTEM, Bangalore

Dr. Sharba Bandyopadhyay, IIT, Kharagpur

Dr. Nihar Ranjan Jana, NBRC, Manesar.

Dr. Dan Ohtan Wang, iCeMS, Kyoto University, Japan

Prof. Ted Abel, University of Pennsylvania, USA



Molecular approaches to understand the pathophysiology and pharmacology of infection and inflammatory disorders of central nervous system

PRINCIPAL INVESTIGATOR

Anirban Basu

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LAB ATTENDANT

Manish Dogra

The neuro-immune response is modulated through multi directional cross talks among the nervous, endocrine, and the immune systems. Spatial and temporal information about inflammatory processes is conveyed to the central nervous system (CNS) where neuroimmune modulation control the extent and intensity of the inflammation. Over the past two decades, tremendous amount of research has revealed various routes by which the nervous system and the immune system communicate with each other. The CNS regulates the immune system via hormonal and neuronal pathways, including the sympathetic and parasympathetic nerves. The immune system signals the CNS through cytokines that act both centrally and peripherally.

The research questions in our laboratory hovers around the concept of neuro-immune interaction and consider its potential clinical application, in an attempt to broaden the awareness of this rapidly evolving as well as emerging area. We are also exploring new avenues that may be helpful in the treatment of brain disorders, in particular, the diseases, which has conspicuous inflammatory compartment. We use several models of viral infection to understand this area. We also use pro-inflammatory cytokine like IL-1 β , to better understand the signaling cascades in the inflammatory micro-environment.

Effective recognition of viral components and subsequent triggering of type-I interferons (IFNs) is crucial for induction

of host antiviral innate immunity. Failure of host to produce type-I IFNs efficiently against the Japanese encephalitis virus (JEV) has been linked with an increased probability of the disease to turn lethal. We have recently showed that JEV-induced miR-301a, inhibits type-I interferon pathway by targeting IRF1 and SOCS5. Neutralization of miR-301a reinforces host innate immunity by restoring IFN- β expression, thereby restricting viral propagation in neuron. Furthermore we have showed that NF- κ B activation is detected as key mechanism to induce miR-301a transcription upon JEV infection. *In vivo* validation by deactivation of miR-301a in mouse brain rescues IRF1 and SOCS5, increases IFN- β response, reduces JEV load and improves survival. Overall, we have suggested that JEV-induced miR-301a assists viral pathogenesis by suppressing IFN and provide new insights to develop effective antiviral strategy.

We have earlier showed that JEV infects neural stem/progenitor cells and decreases their proliferation capacity. We have performed a 2-DE based proteomic study of the human neural stem cells (hNS1 cell line) post JEV infection and found that 13 proteins were differentially expressed. The altered proteome profile of hNS1 cell line revealed sustained endoplasmic reticulum (ER) stress which deteriorated normal cellular activities leading to cell apoptosis. The proteomic changes found in hNS1 cell line were validated *in vivo* in the subventricular zone of JE infected BALB/c mice. Congruent alterations were also witnessed in multipotent neural precursor cells isolated from human foetus and in autopsy samples of human

brain clinically diagnosed as cases of JE patients. We have shown that ER resident chaperone GRP78, mitochondrial protein Prohibitin (PHB) and heterogeneous nuclear ribonucleoprotein hnRNP C (C1/C2) interact with viral RNA. Hence, we have proposed that these are the principle candidates governing ER stress induced apoptosis in JEV infection.

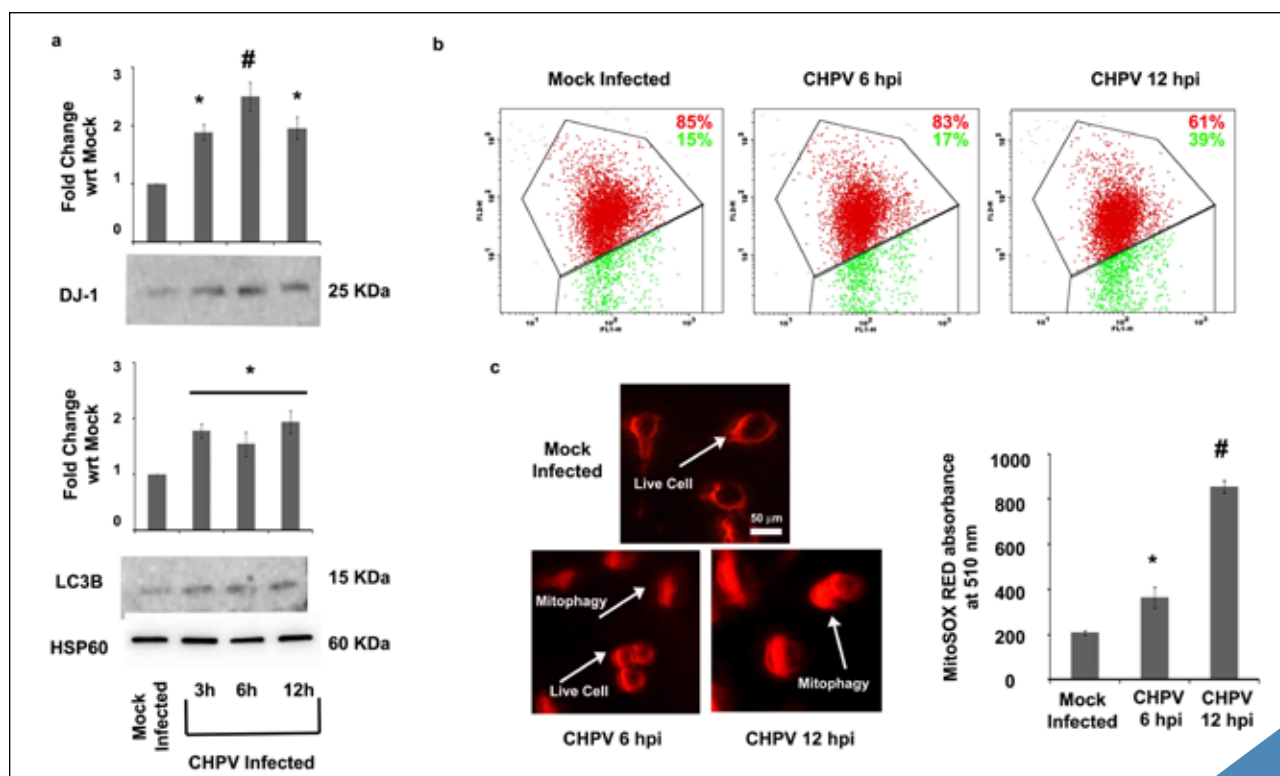
In another work, we have shown that Protein deglycase or DJ-1 plays a critical role in pathogenesis of both Chandipura virus (CHPV) and JEV infection in neurons. Viral replication in neurons triggers ROS activity in response to which DJ-1 over-expresses in the initial phase of infection to prevent inflammation. Thus, DJ-1 has a neuroprotective role attributed to its anti-oxidant property. In the initial phase of infection, DJ-1 induces mitophagy in response to viral infection. Prolonged infection causes uncontrolled release of ROS in response to which DJ-1 activity also increases. DJ-1 triggers the transcription of Low density Lipoprotein receptor (LDLR). As previously reported by us, enhanced expression of LDLR increases the import of excess cholesterol in neurons from astrocytes that is utilized by CHPV for its envelope formation. Another very important aspect that evolved from our work is that both JEV and CHPV adapt a similar mechanistic approach in neuronal infection. (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-1 β , 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-1 β 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-1 β induced inflammation in microglia. For this purpose, we carried out the proteomic profiling of the N9 microglial cells in response to IL-1 β treatment to identify the comprehensive profile of the proteins, which play critical role in microglial activation. Our studies showed the altered expression of various stress proteins. Among these proteins, we have focussed our study on HSP60, a molecular chaperone, which is highly upregulated in IL-1 β treated microglia and is known to be involved in neuron-glia crosstalk. Our results suggested that HSP60 plays a regulatory role in IL-1 β induced inflammation in microglia by stimulating TLR4-MEK3/6-p38 axis. We have also showed that how HSP60 affects the expression of IL-1 β itself, thus completing the inflammatory loop. Our study thus adds to the existing knowledge of microglial activation pathways and it will help us to develop novel approaches for therapeutic applications in inflammatory brain disorders.

PUBLICATIONS

- ❖ M Nain, S Mukherjee, S Karmakar, A Paton, J Paton, M Abdin, **A Basu**, M Kalia, and S Vрати (2017) GRP78 is an important host-factor for Japanese encephalitis



(Figure 1): Immunoblot image shows the expression of DJ-1 and LC3B in mitochondria from a time-dependent study of CHPV infection of Neuro2A (A). HSP60 was used as loading control. JC-1 staining indicates the mitochondrial membrane potential. Representative figures show JC-1 staining with the help of flow cytometric analysis from a time-dependent analysis of CHPV infection of Neuro2A cells (C). The representative plots were a result of gating: Mock Infected= 6075 events, CHPV 6hpi= 5976 events and CHPV 12hpi= 5903 events out of total 10000 events. The percentages mentioned in the panels (percentage of the gated events mentioned previously) quantify the number of cells having majority of mitochondria in polarized state (red) and in depolarized state (green) simply interpreting the oxidative stress condition of the cells. MitoSOX Red staining determines the mitochondrial superoxide production which is hallmark of mitophagy. The representative image panels show MitoSOX Red staining from a time-dependent analysis of CHPV infection of Neuro2A cells. Scale= 50µm. Corresponding graph indicates the absorbance of MitoSOX Red staining at 510 nm for various time-dependent analysis of CHPV infection of Neuro2A cells. * represents $p < 0.05$ and # represents $p < 0.01$. (n=3)

virus entry and replication in mammalian cells. *Journ of Virology* Feb 28; 91(6). pii: e02274-16.

- ❖ B Hazra, K L Kumawat, **A Basu**, [2017] The host microRNA miR-301a blocks the IRF1- mediated neuronal innate immune response to Japanese encephalitis virus infection. *Science Signaling* 10(466):eaaf5185. [Cover page article].
- ❖ S Mukherjee, N Singh, N Sengupta, M Fatima, P Seth, A Mahadevan, S K Shankar, A Bhattacharyya, **A Basu**

[2017] Japanese encephalitis virus induces human neural stem/progenitor cell death by elevating GRP78, PHB and hnRNPC through ER stress. *Cell Death & Disease*; 8(1):e2556.

- ❖ P Mall, A Verma, **A Basu**, Chandrakanta, S F Khan, A Jain, P Tripathi, S Jain, A Parihar, R Kumar [2016] Clinical and magnetic resonance imaging features in survivors of acute encephalitis syndrome in Uttar Pradesh, India. *Curr Pediatr Res* 2016; 20 (1&2): 245-249.
- ❖ S Ghosh, S Mukherjee, N Sengupta, A Roy, D Dey, S

Chakraborty, D J Chattopadhyay, A Banerjee, and **A Basu** [2016] Network analysis reveals common host protein/s modulating pathogenesis of neurotropic viruses. *Scientific Reports* 1; 6:32593.

- ❖ N Sharma, K Kumawat, M Rastogi, **A Basu**, and S Singh [2016] Japanese Encephalitis Virus exploits the microRNA-432 to regulate the expression of Suppressor of Cytokine Signaling (SOCS) 5. *Scientific Reports*; 6:27685.

REVIEW

- ❖ **A Basu**, and K Dutta [2017]

Recent advances in Japanese encephalitis. *F1000Res*. 2017 Mar 13;6:259.

COMMENTARY

- ❖ S Ghosh, and **A Basu** [2016] Acute Encephalitis Syndrome in India: The changing scenario. *Ann Neurosci* 2016; 23:131-133.

PRESENTATION

- ❖ **A Basu** [2017] Neural stem/progenitor cell response to Japanese encephalitis virus infection. Microbial Pathogenesis, UGC-SAP, Dept. of Microbiology, DU South Campus. 23rd January, 2017.
- ❖ **A Basu** [2016] Insights into the neural stem/progenitor cell response to Japanese encephalitis virus infection. INDO-US Symposium on CNS Viral infection, 14-17th Nov, 2016, Sinclairs Retreat Dooars, Chalsa, West Bengal.
- ❖ **A Basu** [2016] Host pathogen interaction in Japanese Encephalitis Virus infection: from bench to bedside. 4th International Conference of Drug Discovery India 2016; Le Meridian Hotel, Bengaluru, 29-30th September, 2016.
- ❖ **A Basu** [2016] HSP60 Plays a Regulatory Role in IL-1 β Induced Microglial Inflammation via TLR4-p38 MAPK Axis. July 17-21st, IUBMB 2016, Vancouver, BC.

- ❖ **A Basu** [2016] Deciphering Mechanism of Neuronal Death in Chandipura Virus (CHPV) Infection: From Molecules to Network. Biology and Pathogenesis of Virus; Microbiology and Cell Biology Department, IISC, Bengaluru, 20-21st June, 2016.

FUNDING

- ❖ microRNAs as a potential therapeutic target in Neurotropic Viral infection [Tata Innovation Fellowship from the Department of Biotechnology [BT/HRD/35/01/02/2014]] [2015-2018].
- ❖ Identification and characterization of brain cellular membrane components acting as receptors for Japanese Encephalitis virus. [CSIR, 27(0307)/14/EMR-II] [2015-2017].
- ❖ To study the molecular mechanism of microglial activation and identify the therapeutics targets critical for IL-1 β signaling in brain following inflammation. [Department of Science and Technology, No SB/SO/HS-070/2013] [2014-2017].
- ❖ Implementing proteomic approach to understand the etiology of Neuropathogenesis induces Chandipura Virus infection [Department of

Biotechnology [BT/PR7907/MED/29/702/2013]] [2013-2016]

AWARD

Elected as a Fellow of the Indian National Science Academy (INSA).

STUDENT'S AWARD

Abhishek Verma, an Integrated PhD student received the best poster presentation award in INDO-US Symposium on CNS Viral infection, 14-17th November, 2016, Sinclairs Retreat Dooars, Chalsa, West Bengal.

PHD DEGREE AWARDED

Sourish Ghosh

COLLABORATORS

Arpan Banerjee and Pankaj Seth
NBRC

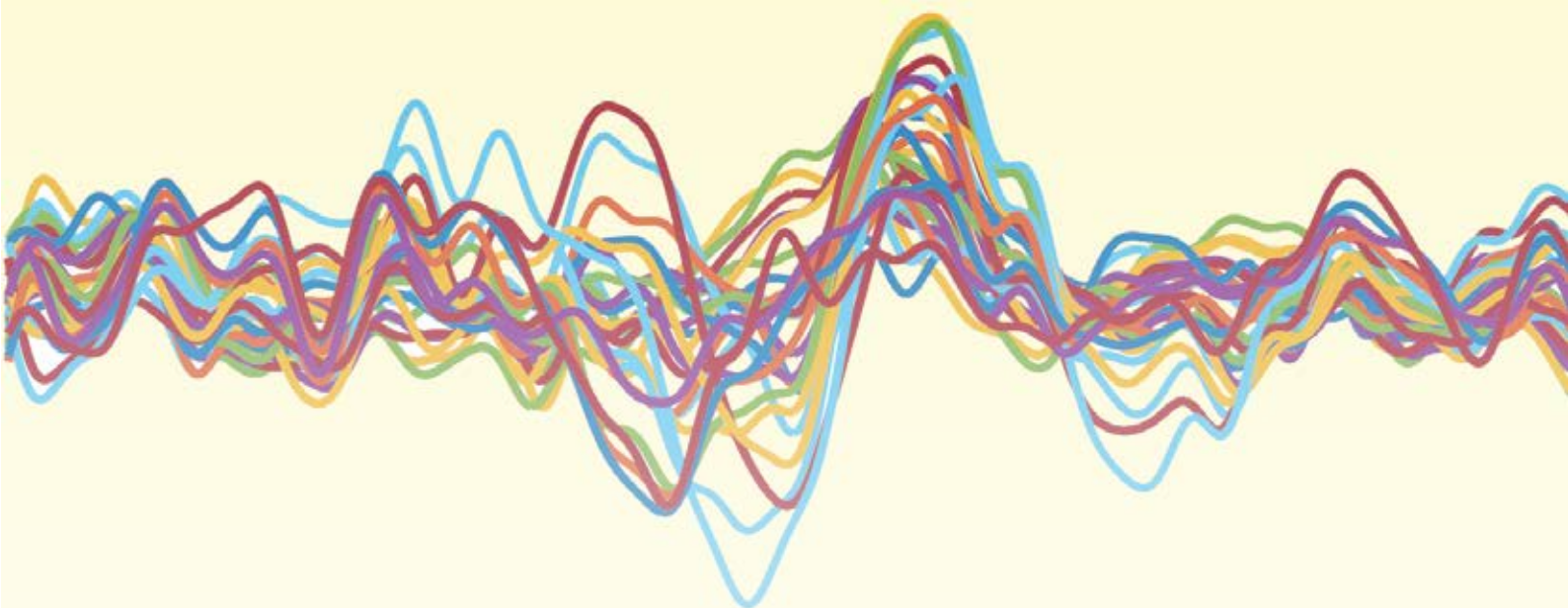
Rashmi Kumar
Dept of Pediatrics, CSM Medical University, Lucknow

SK Shankar, and Anita Mahadevan
NIMHANS, Bangalore

Sunit Singh
BHU, Varanasi.

Sudhanshu Vrat, Arup Banerjee, Manjula Kalin
RCB, and THSTI, NCR Biotech Cluster, Faridabad

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Institute of Life Sciences, Bhubneswar



Harnessing the anti-cancer function of Bex genes by curcumin treatment in neuroblastoma cells, which are novel targets of p53 tumor suppressor protein

PRINCIPAL INVESTIGATOR

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RESEARCH FELLOW

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Lalit Bidla

Brain expressed X-linked (*Bex*) genes are newer group of tumor suppressor genes. The *Bex* genes belong to a small family of genes including *Bex1*, *Bex2*, *Bex3*, *Bex4* and *Bex6* in mouse while *Bex5* instead of *Bex6* in humans. All these genes are located on X-chromosome except *Bex6*, which is located on chromosome 16 in the mouse genome. *Bex1* and *Bex2* genes are silenced in malignant glioblastoma and act as tumor suppressor genes in various cancers. Re-expression of *Bex1* and *Bex2* genes by gene transfection reduces glioblastoma cells growth and sensitizes the glioma cells to anti-cancer drugs. Similarly, overexpression of *Bex3* inhibited breast cancer xenografts in

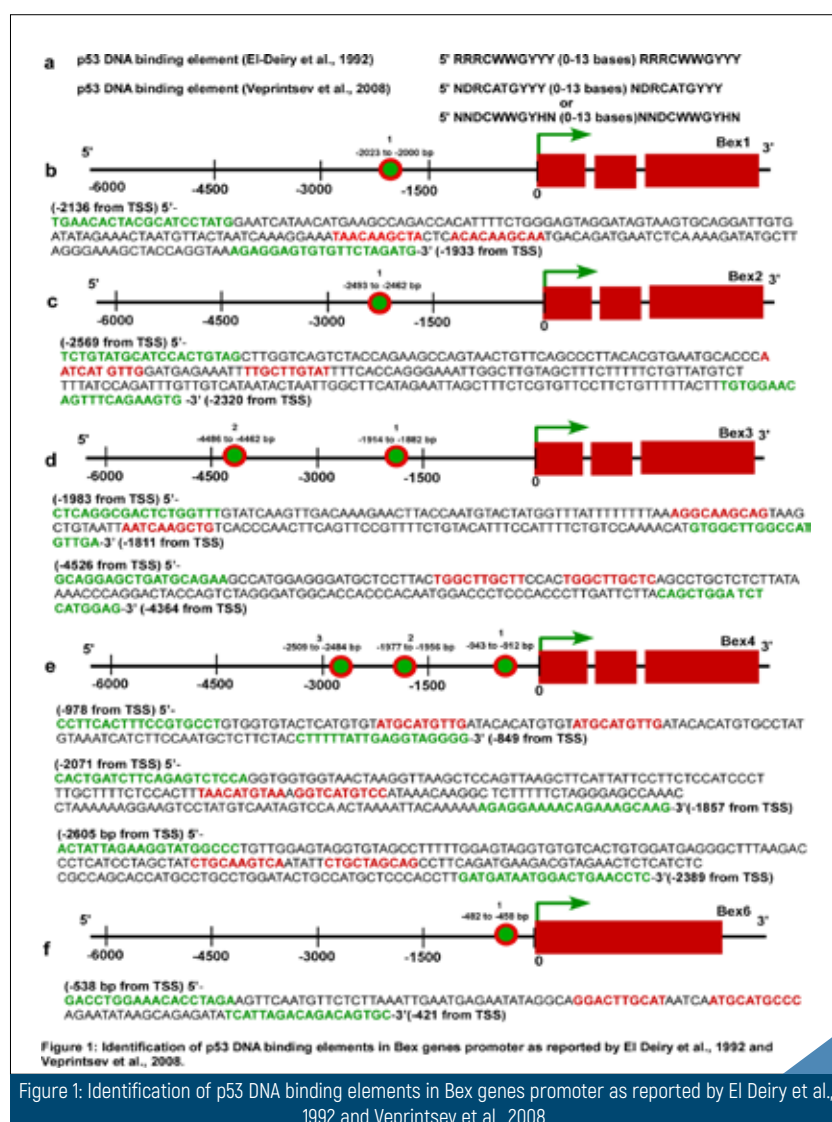
mouse models. The role of *Bex4* and *Bex6* in cancer formation and treatment was not known. Furthermore, there was no report on any chemical that can induce all the endogenous *Bex* gene/s to harness their anti-cancer properties. Here, we investigated the induction of all endogenous *Bex* genes by curcumin using a murine neuroblastoma neuro 2a cell line. Our results show, curcumin induced *Bex* genes in dose and time dependent manner and are tightly associated with neuroblastoma cell deaths by activating intrinsic apoptotic pathway, using various types of assays, such as MTT, LIVE-DEAD, DNA fragmentation, TUNEL, Semi-quantitative RT-PCR, western

blot, immunofluorocytochemistry, cell signaling and SiRNA (small Inhibitory RNA) against *Bex* mRNAs. It is also evident from cell signaling experiments that p53 might be playing a role in curcumin-mediated induction of *Bex* genes. In order to establish a direct interaction of p53 to the promoter region of *Bex* genes, we employed chromatin immunoprecipitation (ChIP) using an antibody specific for an activated form of p53. Bioinformatics analysis of promoter region of *Bex* genes shows the presence of p53 cis-acting elements as reported earlier (Figure 1). Moreover, our results from ChIP assay clearly demonstrated p53 binding to *Bex* genes, upstream to transcription start site (Figure 2) suggesting, curcumin engages p53 to activate *Bex* genes, which are generally silenced in cancerous cells. Collectively, our work demonstrates two new things. First, curcumin, the active principle of turmeric (a commonly used spice) can be used to activate all endogenous *Bex* genes to kill neuroblastoma cells in culture. Second, *Bex* genes are new downstream targets of p53 protein. Therefore, our finding highlights a new way to treat neuroblastoma and possibly other cancers with silenced *Bex* genes (Sidhar et al., 2017).

(a) Western blot analysis of p53 phosphorylation at ser15 in curcumin (25 μ M)-treated N2a cells at indicated time points using anti-phospho-p53-ser15, anti-p53 or anti-GAPDH antibodies. (b) Fold change of p53 and phospho-

p53-ser15 level after normalizing with GAPDH level was calculated and plotted as histograms of mean $\pm$ standard deviation from three independent experiments. Immunofluorocytochemical analysis of phospho-p53-ser15 (c) and p53 (d) level at 30 minutes of curcumin treated or untreated N2a cells. (e) Percent phospho-p53-ser15 and p53 positive cells were calculated in both the groups and plotted as histograms. (f) Interaction of

activated p53 to the promoters of *Bex* genes by chromatin immunoprecipitation (ChIP) assay. N2a cells were treated with curcumin (25 μ M) for 30 minutes followed by ChIP using anti-phospho-p53-ser15 antibody. PCR amplification and densitometric analysis of p53 binding elements of *Bex1* (f), *Bex2* (g), *Bex3* (h), *Bex4* (i) and *Bex6* (j) genes to phospho-p53-ser15 show at least one p53 binding element of each *Bex* gene



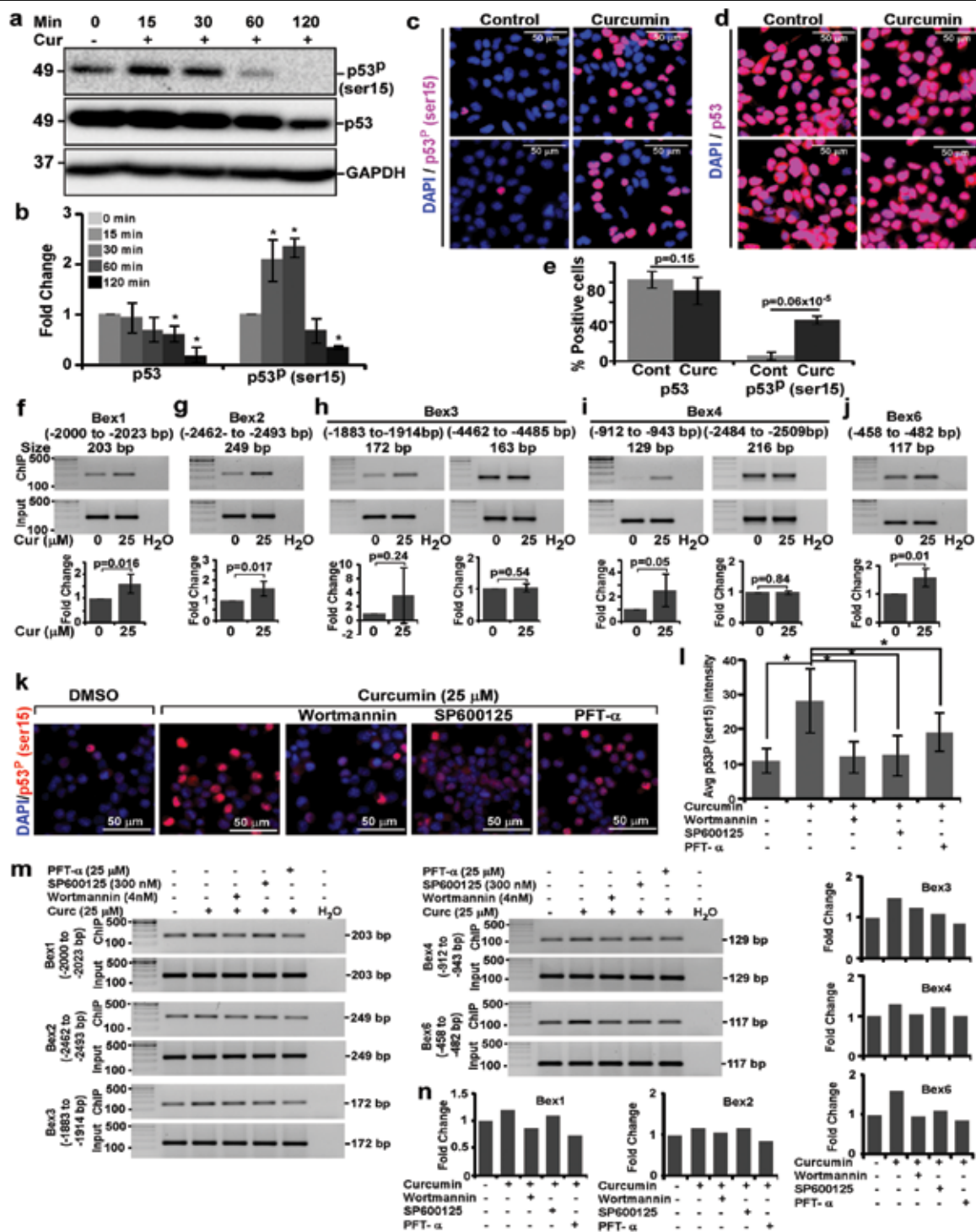


Figure 2: Hyperphosphorylation of p53 at ser15 and its binding to the promoter region of Bex genes by chromatin immunoprecipitation in curcumin-mediated Bex gene induction in N2a cells.

Figure 2: Hyperphosphorylation of p53 at ser15 and its binding to the promoter region of Bex genes by chromatin immunoprecipitation in curcumin-mediated Bex gene induction in N2a cells.

interact more with phospho-p53-ser15 in curcumin treated N2a cells than corresponding controls.

(k) Immunofluorocytochemical analysis demonstrates wortmannin, SP600125 and pifithrin- α reduces p53-ser15 phosphorylation at 30 minutes of curcumin treated N2a cells. **(l)** Average nuclear phospho-p53-ser15 intensities with or without inhibitors were measured and plotted as histograms from three independent experiments.

(m) Effect of wortmannin (4 nM), SP600125 (300 nM) and pifithrin- α (25 μ M) on phospho-p53-ser15 DNA binding activity to *Bex* genes at 30 minutes of curcumin (25 μ M) treated N2a cells. Chromatin immunoprecipitation was performed as described above. PCR amplification was performed corresponding to p53 binding element/s of *Bex1*, *Bex2*, *Bex3*, *Bex4* and *Bex6* gene promoters. Input

DNA PCR was also used as loading control. **(n)** Band intensities of ChIP PCR products were normalized with corresponding input DNA PCR products and fold change was calculated. Values were plotted as histograms. P-values displayed were calculated using two-tailed, unpaired Student's t-test and $*=p\leq 0.05$ is considered statistically significant.

PUBLICATION

- ❖ Himakshi Sidhar and **Ranjit K. Giri**, Induction of *Bex* genes by curcumin is associated with apoptosis and activation of p53 in N2a neuroblastoma cells. Scientific Reports, 7:41424, 2017.

PRESENTATION

- ❖ Himakshi Sidhar and **Ranjit Kumar Giri*** Curcumin-mediated induction of proapoptotic *Bex* genes is

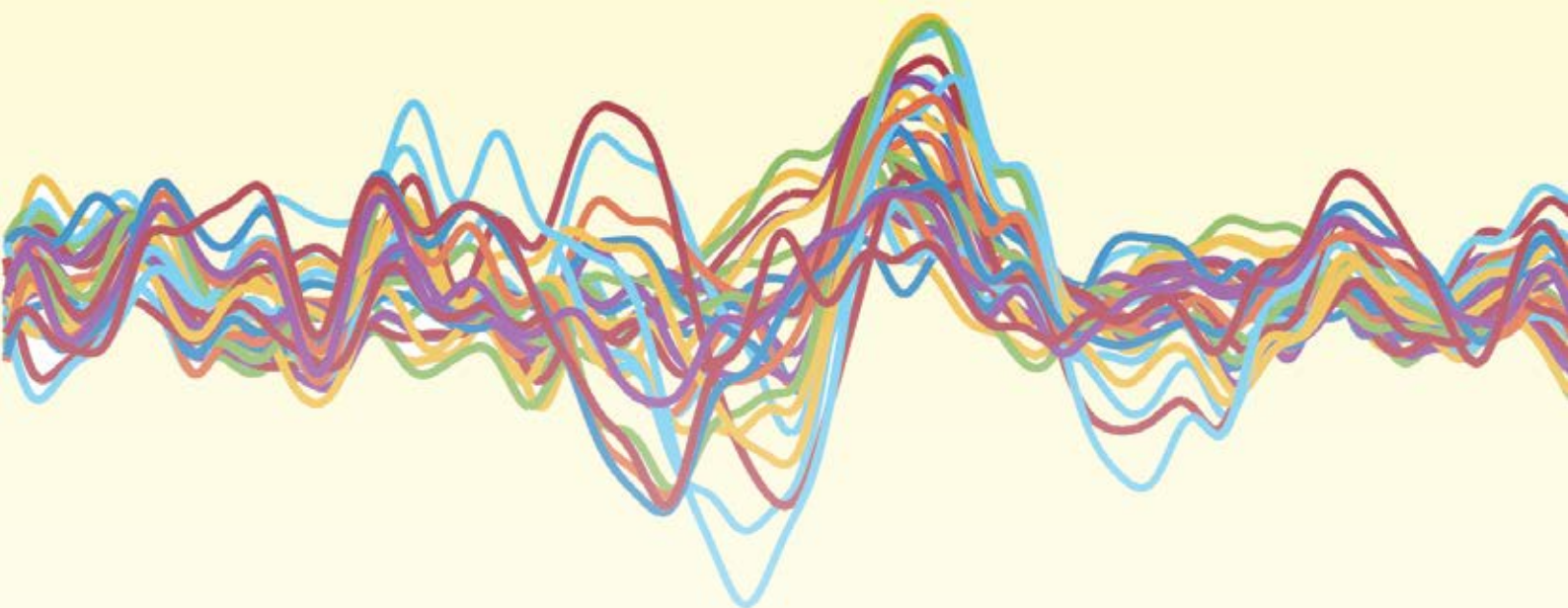
associated with apoptosis in mouse neuro 2a neuroblastoma cells and involves activation of p53. [*Corresponding Author]. First International Conference on Nutraceuticals and Chronic Diseases, Sep 9-11, 2016, Cochin, Kerala, India. Note: Himakshi was awarded with best young scientist award.

COLLABORATOR

Sathees C. Raghavan, Dept. of Biochemistry, Indian Institute of Science, Bangalore 560012 for proving MPTQ used in this project.

FUNDING

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Understanding the pathogenesis of neurodegenerative disorders involving protein aggregation

PRINCIPAL INVESTIGATOR

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TECHNICAL ASSISTANTS

Ankit Sharma, Mahendra Singh

One of the shared pathological hallmark of most age-related neurodegenerative disorders comprising Huntington's disease (HD) and Alzheimer's disease (AD) is the accumulation of mutant disease proteins as inclusion bodies. Appearance of aggregates of the misfolded mutant disease proteins suggest that cells are unable to efficiently degrade them, and failure of clearance leads to severe disturbances of the cellular protein quality control system. Therefore, it is believed that rescue of quality control system could be able to delay the progression of the disease.

In my laboratory, we primarily use HD as a model system to understand the mechanistic basis of impaired protein homeostasis and how that can be restored. At present,

my laboratory focused on the role of Ube3a in protein quality control and its involvement in progression of HD and AD. Now, we are screening small molecules activator or inducer of Ube3a as well as HSF1 and their effect of rescuing neurodegeneration on HD model systems. In addition, we are also using nanoparticle-based approach to prevent amyloid fibrillation and rescue neurodegeneration.

Earlier we have demonstrated that Ube3a function as a cellular protein quality control ubiquitin ligase and involved in the clearance of misfolded mutant huntingtin (causes HD) and mutant superoxide dismutase (causes ALS) [J. Biol. Chem., 2008, 2009 and Neurobiol. Aging, 2013]. 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). Recently we have demonstrated that removal of Ube3a selectively from HD mice brain resulted in augmented disease phenotype and shorter lifespan in comparison with HD mice (Hum. Mol. Genet., 2014). Since the paternally inherited Ube3a is epigenetically silenced in neuronal tissues, which can be reactivated by topoisomerase 1 inhibitors, we tested the effect of topoisomerase 1 inhibitor, topotecan on the progression of HD using mouse model. Topotecan is a semisynthetic water soluble derivative of plant alkaloid camptothecin that can cross the blood brain barrier and long been implicated for cancer chemotherapy. We have found that the treatment of topotecan to HD transgenic mice considerably improved their motor behavioural abnormalities along with significant extension of lifespan. Improvement of behavioural deficits are accompanied with the significant rescue of their progressively decreased body weight, brain weight and striatal volume (Hum. Mol. Genet. 2017). However, during our study, we observed that the permeability of topotecan into the normal mice brain is very poor. Interestingly, because of leakage of blood brain barrier in HD mice brain the drugs access to HD mice brain increased considerably.

In another project (in collaboration with scientist at Indian Association for the Cultivation of Science, Kolkata), we use nanoparticle based strategy to prevent fibrillation and

aggregation of mutant huntingtin as well as other amyloid proteins. We have demonstrated that nanoparticle form of green tea polyphenol (epigallocatechin) is about 10-20 times more efficient than its molecular form in preventing aggregation of amyloid protein like mutant huntingtin. Interestingly, we have also found that nanoparticle form of some of the sugar molecules can significantly enhance their chaperone performance in inhibiting protein aggregation and in lowering of amyloidogenic cytotoxicity. These nanoparticles have excitation dependent green/yellow/orange emission and surface property identical to respective sugar molecule.

UNDERSTANDING THE PHYSIOLOGICAL FUNCTION OF UBE3A AND PATHOGENESIS OF ANGELMAN SYNDROME

Ube3a was first identified as a cellular protein linked with ubiquitin-mediated proteolysis of tumour suppressor p53 in assistance with E6 oncoprotein of the human papilloma virus (HPV). Subsequently, it is characterized as an ubiquitin ligase, an E3 enzyme involved in targeting specific protein for ubiquitination and degradation through proteasome. Ube3a also acts as a transcriptional co-activator of steroid hormone receptors. Ube3a shows neuron specific imprinting and dysfunction 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 exhibit many features of AS, including cognitive and motor dysfunctions. These mice also display defects in hippocampal LTP, altered function of hippocampal CAMK-II α and abnormal dendritic spine morphology. Studies in these mice also provided further clue that Ube3a is perhaps necessary for development of synapse and experience-dependent synaptic plasticity.

Past several years we are involved in exploring the physiological function of Ube3a and how its loss of function is associated with AS using 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 aberrantly increased expression of HDAC1/2 found in AS mice brain might be directly linked with synaptic and cognitive dysfunctions in these mice. Reduced expression of some of the HDAC2 regulatory gene like BDNF and synaptophysin in the hippocampus of AS mice noted by us further supports our conclusion. We have also found that prolonged treatment of HDAC inhibitor, sodium valproate, significantly improved various

behavioural abnormalities (deficits in social interaction, cognitive and motor performances) in AS mice. We further continued our study and 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. 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. Currently, we are testing the effect of another HDAC inhibitor on the rescue to behavioural deficits in AS mice. In another project, we are studying the role of miRNA in the pathogenesis of AS. We performed genome wide analysis of altered miRNA using AS mice cortical areas. Several up-regulated and down-regulated miRNA were identified. Currently, we are characterizing one up-regulated and one down-regulated miRNA.

PUBLICATIONS

- ❖ N. Pradhan, S. Shekhar, **Nihar R. Jana*** and Nikhil R. Jana*. Sugar-Terminated Nanoparticle Chaperones Are 100-100000 Times Better Than Molecular Sugars in Inhibiting Protein Aggregation and Reducing Amyloidogenic Cytotoxicity. *ACS Applied Materials & Interfaces*, 9, 10554-10566, 2017. *Corresponding authors.
- ❖ S. Shekhar, N. Vatsa, V. Kumar, B.K. Singh, I. Jamal, A. Sharma and **N.R. Jana**. Topoisomerase inhibitor topotecan delays the disease progression in a mouse model of Huntington's disease. *Human Molecular Genetics*, 26, 420-429, 2017.
- ❖ I. Jamal, V. Kumar, N. Vatsa, B.K. Singh, S. Shekhar, A. Sharma and **N.R. Jana**. Environmental enrichment improves behavioural abnormalities in a mouse model of Angelman syndrome. *Molecular Neurobiology*, 2016 [DOI: 10.1007/s12035-016-0080-3].
- ❖ K. Debnath, S. Shekhar, V. Kumar, **Nihar R. Jana*** and Nikhil R. Jana*. Efficient inhibition of protein aggregation, disintegration of aggregates and lowering of cytotoxicity by green tea polyphenol-based self-assembled polymer nanoparticles. *ACS Applied Materials and Interfaces*. 10, 20309-20318, 2016. *Corresponding authors.
- ❖ V.K. Nelson, A. Ali, A. Dutta, S. Ghosh, M. Jana, A. Ganguli, A. Komarov, S. Paul, V. Dwivedi, S. Chatterjee, **N.R. Jana**, S.C. Lakhotia, G. C. Chakraborti, A. Mishra, S. C. Mandal, and M. Pal. Azadiradione ameliorates polyglutamine expansion disease in drosophila by potentiating DNA binding activity of heat shock factor 1. *Oncotarget*, 7, 78281-78296, 2016.
- ❖ D.J. Klionsky et al. (with more than 200 authors including **N.R. Jana**). Guidelines for the use and interpretation of assays for monitoring autophagy (3rd edition). *Autophagy*, 12,1-222, 2016.
- ❖ Neuroinflammation in Huntington's and related neurodegenerative disorders. In "Inflammation:the common link in brain pathologies ed. by **N.R. Jana**, A Basu and PN Tandon]" 171-184, 2016.

PRESENTATIONS

- ❖ **N.R. Jana**. Altered protein homeostasis and neuronal dysfunction in Huntington's disease. International Symposium on Neurodegenerative Disorders (ISND2017), NIMHANS, Bengaluru, March, 2017.
- ❖ **N.R. Jana**. Huntington's disease: Genetics and Pathogenic mechanisms. International Conference on Neurodegenerative Disorders (NDD2017), Kolkata, February, 2017.
- ❖ **N.R. Jana**. Impaired protein homeostasis and its rescue in a mouse model of Huntington's disease. International Symposium of Molecular Signalling (ICMS2017), Chennai, January, 2017.
- ❖ **N.R. Jana**. Proteostasis impairment in Huntington's disease, Annual meeting of the Indian Academy of Neurosciences, NBRC, Manesar, October, 2016.
- ❖ **N.R. Jana**. Impairment of protein homeostasis in Huntington's disease. All India Cell Biology Conferences, Jiwaji University, November, 2016.
- ❖ **N.R. Jana**. Popular talk at

several undergraduate colleges (Midnapore College, Goaltore College, RNLK Women's College at West Bengal) and Universities (Dibrugarh University, Tezpur University, Vidyasagar University).

FUNDING

Deregulation of micro RNA in cell and animal models of Huntington's

disease: role of altered micro RNA in neuronal differentiation and cell cycle regulation. A joint project with Biomedical Genomics Centre and SNIP, Kolkata. Department of Biotechnology, Govt. of India. Grant No: BT/PR7185/MED/30/910/2012.

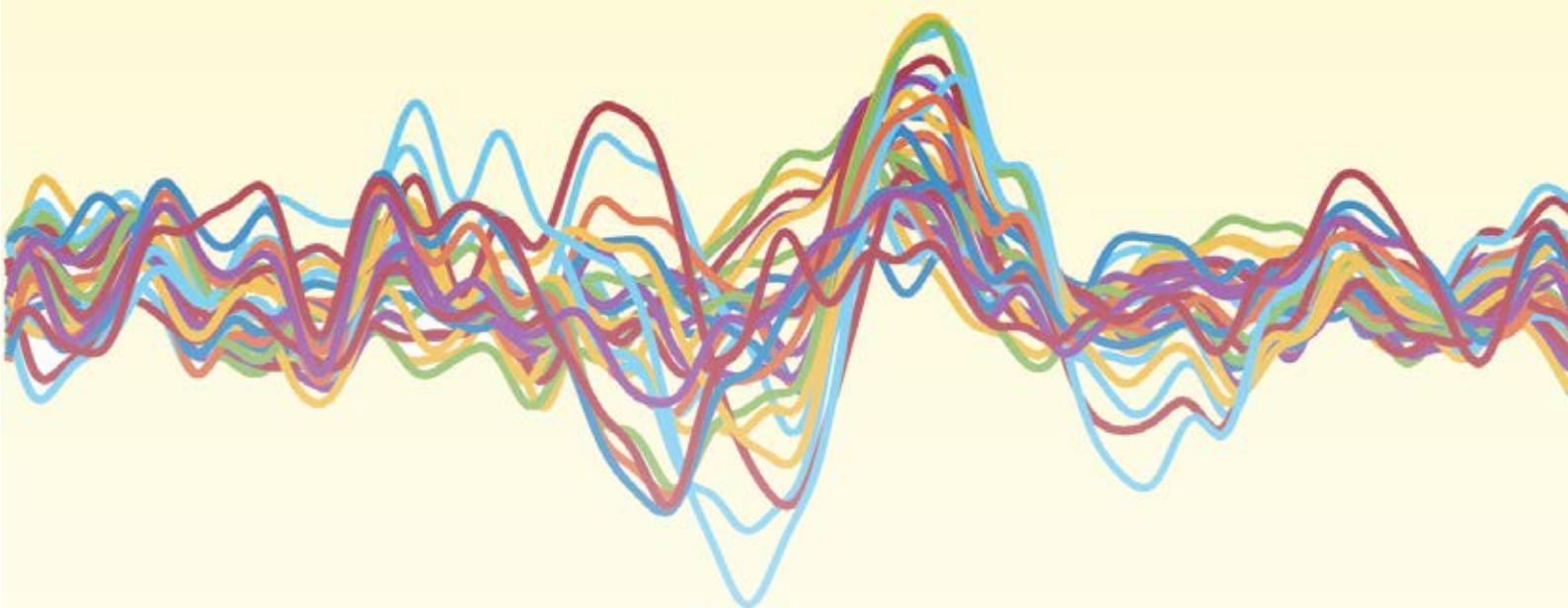
Ube3a as a therapeutic target of Huntington's disease. TATA Innovation project, Department of Biotechnology, Govt. of India. Grant No: BT/HRD/35/01/03/2013

COLLABORATORS

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

Dr. Subramanian Ganesh, IIT Kanpur.

Dr. Nitai Bhattacharya, Biomedical Genomics Centre, Kolkata.



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

PRINCIPAL INVESTIGATOR

Anindya Ghosh Roy

RESEARCH FELLOWS

Dharmendra Puri

Atrayee Basu

Harjot Kaur

Sibaram Behera

RESEARCH ASSOCIATE

Sandeep Kumar

PROJECT ASSISTANTS

Pankajam Thyagarajan

Titash Mukherjee

Keerthana P

Revathi Muthuvel

TECHNICAL ASSISTANTS

Sumit mahapatra

Yunis Khan

BACKGROUND

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, biochemistry and imaging in *Caenorhabditis elegans*.

CELL BIOLOGICAL MECHANISMS REGULATING NEURONAL POLARITY & MAINTENANCE

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 (Figure1). 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 (Figure1). None of the known microtubule stabilizing factors involving plus or minus end binding proteins, and centrosomal proteins suppressed klp-7 [0].

However, the drug Colchicine that destabilizes MTs suppressed the same. This indicated that our genetic screening might identify novel regulators neuronal cytoskeleton. By combining meiotic recombination and whole genome sequencing, we have mapped three suppressors in three individual genes. These genes encode metalloprotease, immunoglobulin like molecule and RNA binding protein. Loss of the RNA binding protein perturbs axon growth and its over expression causes overgrowth of axon indicating that it is necessary and sufficient for axon development. We are investigating the molecular mechanism by which these genes regulate microtubule cytoskeleton and thereby influence nerve cell development.

To understand how microtubules are maintained after axon development, we are studying posttranslational modification of tubulin involving. We found that simultaneous loss of two tubulin

carboxypeptidases suppresses the axon overgrowth phenotype caused due to lack of E3 family ligase rpm-1. This indicated that there is a link between neuronal homeostatic signalling and post-translation modification of tubulin. We are investigating the mechanistic link between these two pathways.

NEURONAL REGENERATION

We are interested in understanding how a given neural circuit is regulated after neuronal injury. We are particularly interested in mechanosensory and locomotion behavior. In order to pursue this question, we have established the femto-second laser injury assay in our 2-photon laboratory. Using this we have been able to sever neuronal processes across the worm body (Figure 2). Briefly we image using the 920 nm wavelength and cut the axons using 720 nm wavelength with 40 ms pulse duration and 28.5 mW laser power.

Using two femto-second lasers simultaneously 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 on both sides contribute to regain of gentle touch sensation. In collaboration with Sandhya Koushika's group at TIFR-Mumbai, we have shown that axonal fusion is also correlated with the restoration of axonal transport at the distal fragment (Figure 3).

We further showed that let-7 miRNA inhibits the establishment of cytoplasmic continuity in a cell autonomous manner, during late larval and adult stages. Loss of let-7

increases the level of ced-7 mRNA and the probability of fusion event is increased in late larval stage. As the worm ages, the axonal transport is perturbed and a key fusogen molecule EFF-1 becomes limiting at the growing tips of cut axon (Figure 3). Loss of let-7 overcomes these barriers by delaying neuronal aging and stimulating functional recovery. Our data reveal the functional property of a regenerating neuron. Axon fusion 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. This study addresses this question with quantitative behavioural assay (Basu et al 2017/under final revision in PNAS, USA).

We will be asking further whether the axons that are unable to fuse

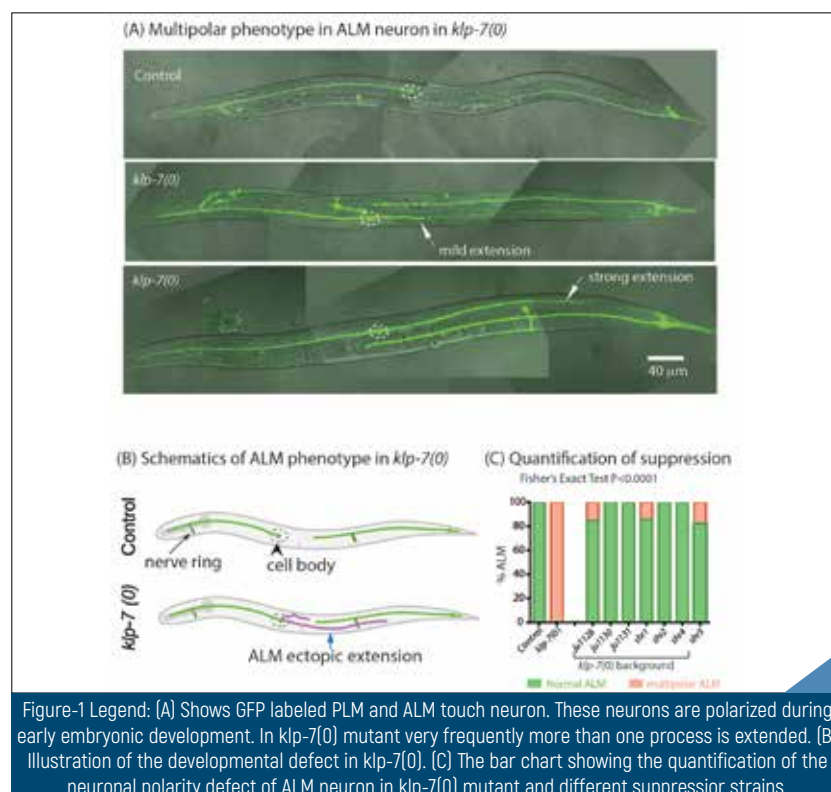
could reach their target cell or not.

PUBLICATIONS

- ❖ 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 (under final revision)

PRESENTATIONS

- ❖ **Anindya Ghosh Roy:** "Restoration of Functional Connectivity After Neuronal Injury" in CUSAT-NUS Joint International Conference on Biotechnology & Neuroscience at Cochin during 19-21st December, 2016



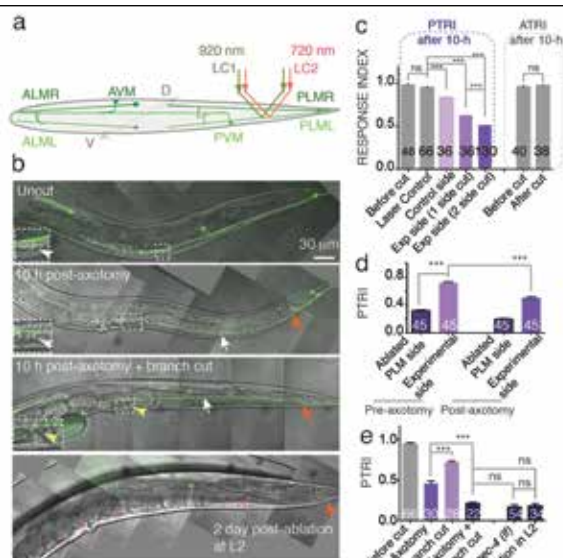


Figure-2 Legend: (A) Schematics of worm with 6 mechanosensory neurons highlighted in green. (B) Representative images of PLM neurons before and after axotomy. Arrows indicate the position of axotomy on the PLM neurons. (C)-(E) Represents bar charts showing the effects of axotomy and cell ablation on touch sensation.

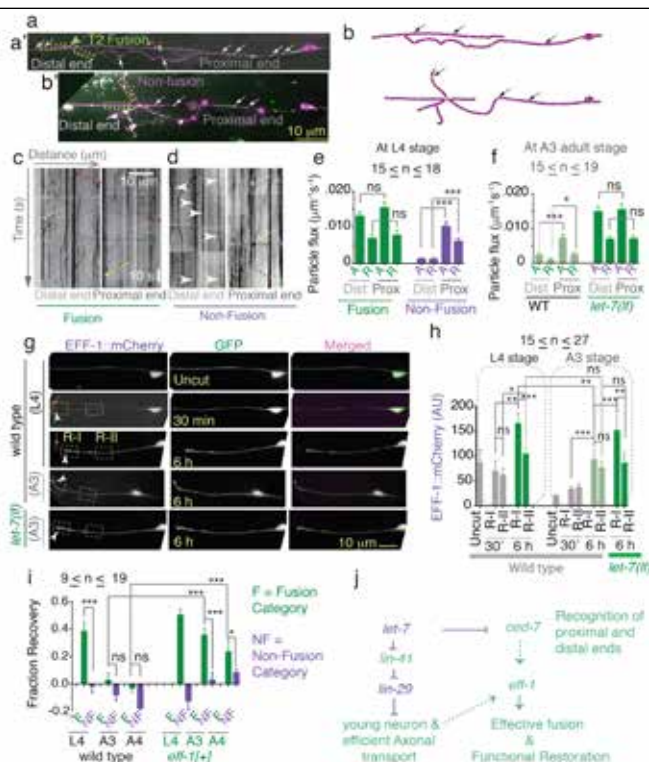


Figure-3 Legend: (a-a'-b') Still images from time-lapse movies of PLM with GFP::RAB-3 using spinning disc confocal at 24-h post-axotomy. (b) Schematic representation of images shown in (a). (c) Kymographs from the movies from the "ROIs" (yellow dotted box in a-a') placed on distal and proximal ends of fused neuron. Diagonal tracks represent events of anterograde (dotted yellow arrow trace) or retrograde (dotted red arrow trace) movements. (d)-(f) Bar charts represent particle flux in proximal and distal ends measured in fusion and non-fusion events. (g) Spinning disc confocal images of worms co-expressing GFP and EFF-1::mCherry. (h) Average intensity of EFF-1::mCherry in two ROIs, after axotomy. (i) EFF-1 is sufficient for functional restoration in aged worms. (j) Represents the working model depicting how let-7 miRNA pathway negatively regulates effective axon fusion in L4 and aged worms.

❖ **Anindya Ghosh Roy:** "A genetic screen for mutants affecting neuronal polarity" in C. elegans discussion meeting organized by TIFR-Mumbai during 10-11 Feb, 2017

❖ **Anindya Ghosh Roy:** "Restoration of Functional Connectivity After Neuronal Injury" in 21st International C. elegans Meeting being held June 21-25, 2017 at UCLA.

❖ **Dharmendra Puri:** "Regulation of neuronal microtubule cytoskeleton" in 21st International C. elegans Meeting being held June 21-25, 2017 at UCLA.

FUNDING

Wellcome Trust-DBT
NBRC Core

COLLABORATOR

Sandhya Koushika, TIFR, Mumbai, India

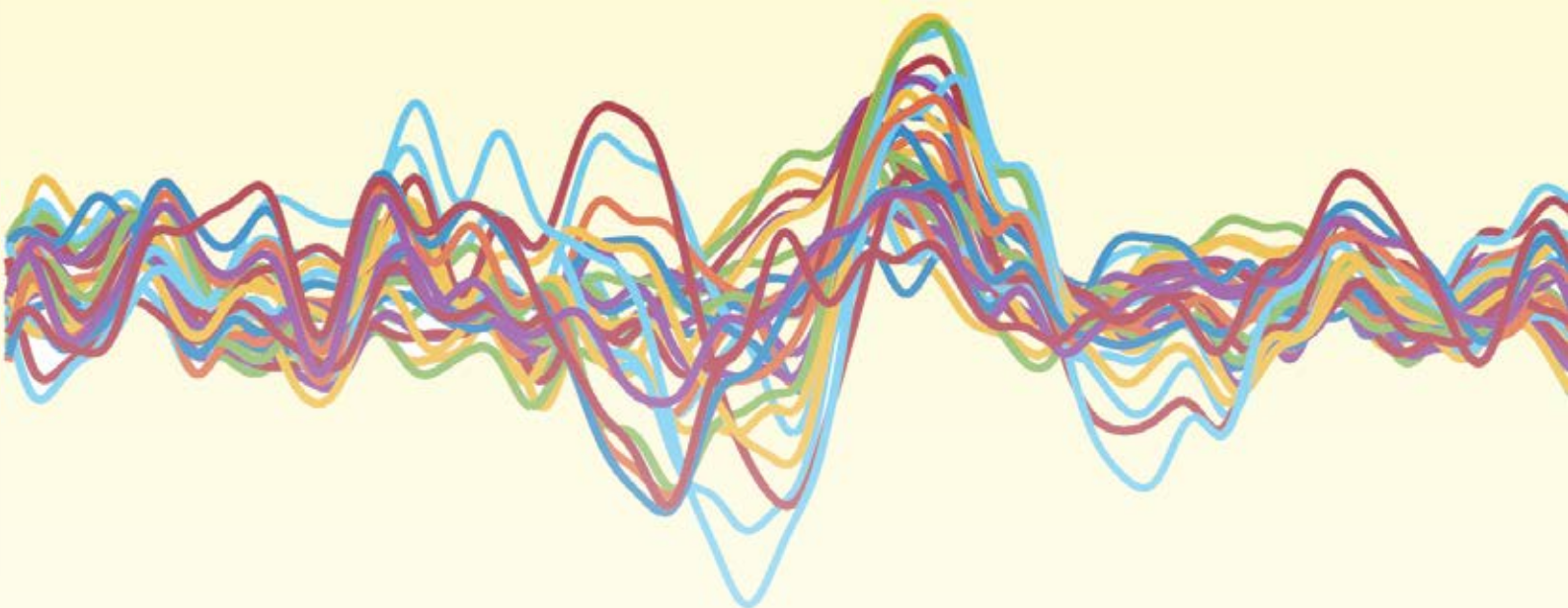
Shalini Gupta, IIT-Delhi, India
Sourav Banerjee, NBRC, India

AWARD

Wellcome Trust-DBT Intermediate fellowship-2013-2018
Ramalingaswami Fellowship-2013 [declined]

DEGREES AWARDED (Ph.D.)

Sanskriti Swami was awarded MSc degree.



Metabolic reprogramming in glioblastoma

PRINCIPAL INVESTIGATOR
Ellora Sen

RESEARCH FELLOWS
*Piyushi Gupta, Fahim Ahmad,
Touseef Sheikh, Pruthvi
Gowda, Shruti Patrick*

RESEARCH ASSOCIATE
Ankita Singh

TECHNICAL ASSISTANT
Shanker Datt Joshi

LAB ATTENDANT
Rajesh Kumar Kumawat

BACKGROUND

Glioblastoma multiforme (GBM) - the most malignant of brain cancers characterized by dysregulated metabolism, is largely refractory to current therapeutic regimens. Besides aberrant metabolism, global epigenetic abnormalities in conjunction with numerous genetic alterations promote glioma progression. The overall focus of our group is to understand the correlation between the epigenetic landscape of glioma and metabolic adaptation, and its consequence on the regulation of genes associated with resistance to chemotherapeutics, immune evasive responses and inflammation. Also, since tumor infiltrating monocytes play a crucial role in tumor immune surveillance, the effect of tumor metabolites on monocytes and its consequence on immune evasive responses is also being investigated.

(i) Our studies have highlighted

the previously unknown role of telomerase in (i) the regulation of Glucose-6-phosphate dehydrogenase (G6PD) and Transketolase (TKT) - two major nodes in the pentose phosphate (PPP) pathway; (ii) glycogen accumulation and (iii) the involvement of Nrf2 driven TERT in maintaining oxidative defence responses in glioma cells. Importantly, we have shown that GBM patient tumors bearing TERT promoter mutations (C228T and C250T) known to be associated with increased telomerase activity; exhibit elevated Nrf2 and TKT expression and decreased glycogen accumulation.

(ii). Epigenetic regulation by histone methyltransferase G9a is known to control autophagic responses. As the link between autophagy and metabolic homeostasis is widely accepted, we evaluated the efficacy of BIX-01294 - an inhibitor of G9aHMTase dependent H3K9me, on autophagic responses

in glioma cells. BIX induced increase in metabolic modelers TIGAR (TP53-induced glycolysis and apoptosis regulator) and PKM2 (Pyruvate kinase M2) were crucial for G9a induced autophagic responses changes, as transfection with TIGAR mutant or PKM2 siRNA reversed BIX-mediated alterations in LC3B expression. Taken together, our findings suggest that metabolic remodeling activates autophagic responses in glioma cells upon G9a inhibition.

(iii) As tumor lactate is known to disable immune surveillance, its effect on HLA expression on macrophages (crucial for adaptive immune responses against tumor) was investigated. Besides demonstrating the importance of lactate in the transcriptional regulation of HLAB, our studies have highlighted the role of protein arginine methyltransferase 1 (PRMT1)- the predominant arginine methyltransferase, in modulating chromatin landscape crucial for facilitating HLAB gene expression.

PUBLICATIONS

- ❖ Ahmad F, Dixit D, Sharma V, Kumar A, Joshi SD, Sarkar C and **Sen E** (2016). Nrf2-driven TERT regulates pentose phosphate pathway in glioblastoma. *Cell Death and Disease*; 7:e2213
- ❖ Ahmad F, Dixit D, Joshi SD, **Sen E** (2016). G9a inhibition induced PKM2 regulates autophagic responses. *Int J Biochem Cell Biol*; 2016;78:87-95.
- ❖ Gupta P, Singh A, Gowda P, Ghosh S, Chatterjee A, **Sen E** (2016). Lactate induced HIF-1 α -PRMT1 cross talk affects MHC I expression in monocytes. *Exp Cell Res*; 347(2):293-300.

PRESENTATIONS

- ❖ **Ellora Sen**. Link between pentose phosphate pathway and telomerase activity in Glioblastoma. IUBMB 18th July 2016, Vancouver (Invited Talk)
- ❖ **Ellora Sen**. SIRT6 regulates Hexokinase 2 expression and its function. IUBMB 20th July 2016, Vancouver (Invited Talk)
- ❖ **Ellora Sen**. Unraveling the link between dysregulated metabolism and telomerase in glioma. ISNOCON, Hyderabad, April 2016
- ❖ **Ellora Sen**. Decoding metabolic programming in glioblastoma. Indian Association of Cancer Research, New Delhi, April, 2016
- ❖ **Ellora Sen**. Dysregulated metabolism in glioblastoma: Involvement of telomerase. NIMHANS Bengaluru, August 2016
- ❖ **Ellora Sen**. Link between dysregulated metabolism and telomerase activity in Glioblastoma. 3rd International Meeting on Advanced Studies in Cell Signaling Network (CeSiN 2016), Kolkata, December 2016
- ❖ **Ellora Sen**. Metabolic networks: Implications in Cancer and Inflammation. SAP-UGC, Dept. of Biochemistry, University of Delhi March 2017
- ❖ **Ellora Sen**. Metabolic storms: Feeding the tumor black-hole. Regional Centre for Biotechnology, Faridabad, March, 2017

PHILOSOPHY

- ❖ **Ellora Sen**. Health and well being: Neurotheological perspectives.

International Vedic Conference, Special Centre for Sanskrit Studies, Jawaharlal Nehru University, New Delhi, Dec 2016

- ❖ **Ellora Sen**. Cognition of death and mortality awareness. The Nalanda Dialogues, Nava Nalanda Mahavihara, Nalanda, January 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

COLLABORATOR

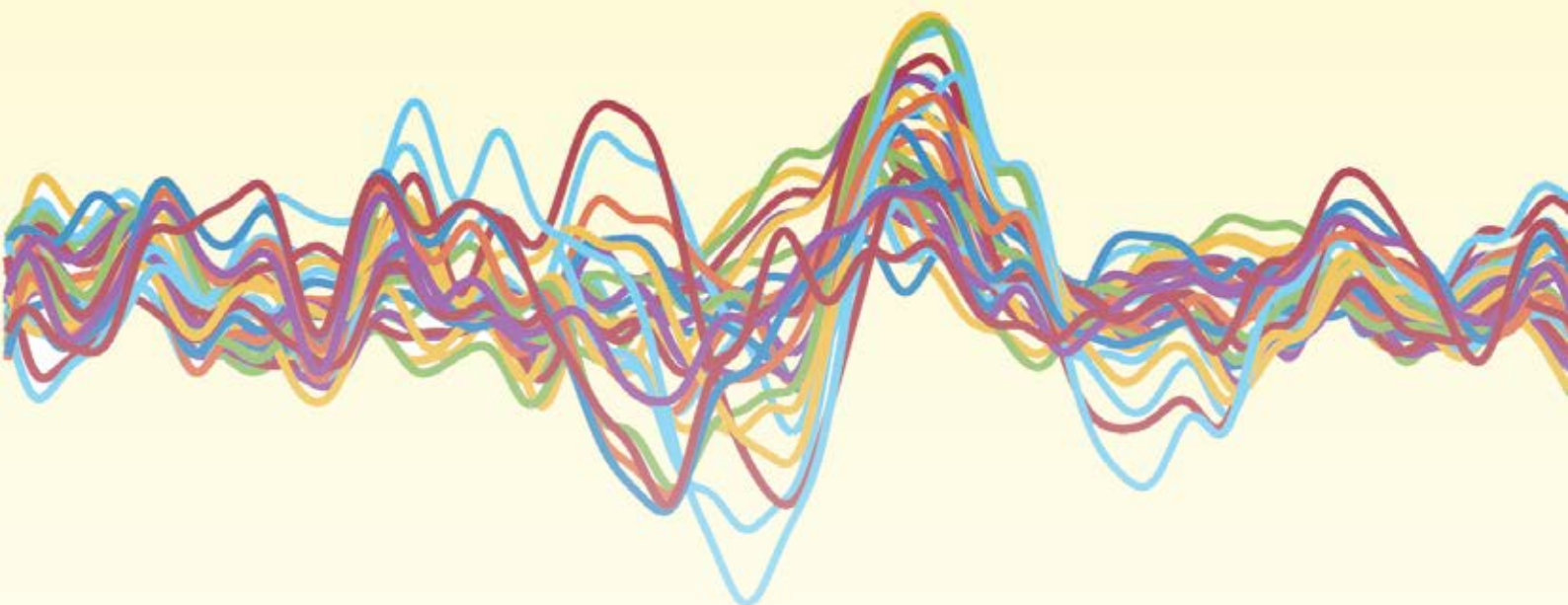
Dr. Chitra Sarkar, AIIMS New Delhi

AWARDS

- ❖ Kshanika Oration Award, Indian Council of Medical Research, 2016
- ❖ Indian Society of NeuroOncology ISNO Annual Award for outstanding work in neuro-oncology, 2016.

Degrees Awarded

- ❖ Piyushi Gupta (2016). IL-1 β signalling in metabolic adaptation, survival and immune evasive responses in glioma
- ❖ Fahim Ahmad (2016) Telomere in Metabolic Programming and Survival Responses in Glioblastoma Multiforme



Cellular and molecular mechanisms of HIV-1 neuropathogenesis

PRINCIPAL INVESTIGATOR

Pankaj Seth

RESEARCH FELLOWS

Manju Tewari, Mahar Fatima, Chitra MS Singal, Hriday S. Pandey, Reshma Bhagat and Priyanka Singh

PROJECT ASSISTANTS

Kanza Saleem, Anuradha Mehta

TECHNICAL ASSISTANTS

Durgalal Meena and Naushad Alam

The last decade has witnessed evolution in the field of neuroAIDS, as antiretroviral therapies have been able to maintain significantly low levels of HIV-1 in circulatory system and have almost ceased the continuous trafficking of HIV-1 virion into the brain. However, these drugs have failed to eradicate HIV-1 from the brain cells. In fact, this is one of the reasons why the HIV associated motor and cognitive deficits and HIV associated dementia have been renamed as HIV-1 associated neurological disorders (HAND) to cover a wide range of neurocognitive deficits. As a result, the focus of the field has shifted towards understanding the consequences of the remaining virus in brain of HIV/AIDS patients. Despite remarkable success of combinatorial anti-retroviral therapy (cART), HAND remains to affect up to 50% of

HIV/AIDS patients. In most of the AIDS patients, cART reduces circulating HIV-1 in systemic system to undetectable level however, that is not the case when it comes to the central nervous system (CNS) tissues. Human brain remains unchallenged by cART due to poor penetration of the cART drugs through the blood brain barrier. Furthermore, as cART challenges only actively replicating virus, it fails to tackle the latent virus in certain niche areas, including brain that serves as a "safe haven" for the virus. Recent literature suggests that the neurotoxic protein, HIV-1 Tat continues to be produced even by the latent virus and is detectable in CSF of AIDS patients. As HIV-1 Tat is secreted from infected cells it affects both the infected as well as non-infected cells in the vicinity, and due to this nature HIV-1 Tat has been clinically implicated in HIV-1

associated neurological disorders in the post cART era.

Neurocognitive deficits in HIV/AIDS patients occur due to damage to neuronal cells particularly in basal ganglia, sub cortical and frontal cortex regions. CNS responds to injury or neuronal loss by recruiting the multipotent neural precursor cells (NPCs) that reside in the sub-ventricular zone (SVZ) and the hippocampal dentate gyrus. Alterations in NPC microenvironment perturbs overall potential of the brain and may affect their ability to serve as emergency reservoirs after injury. Viral infections such as Human Immunodeficiency Virus-1 (HIV-1) modulate NPC homeostasis, affecting their proliferation and differentiation, which is affirmed by the loss of developmental milestones and impaired brain growth in HIV-infected infants and children.

Keeping pace with the field, we have made some novel discoveries in understanding the mechanisms as to how HIV-1 and its regulatory protein Transactivator of Transcription (Tat) affects the human neural stem cells.

In addition to our research findings in neural precursor cells, we gained novel insights into the mechanism of glia mediated neuronal damage. Using cell and molecular biology tools we discovered excessive release of ATP, the instant source of energy in cell, from glial cells may be the reason for neuronal damage. In fact the knockout studies from our laboratory implicate P2X7R as

one of the significant contributors in glia mediated neuronal death. Furthermore, we have now delineated mechanisms of enhanced ATP release in astrocytes in response to HIV-1 Tat. Previously, our lab has shown that ATP release in astrocytes is exacerbated with exposure to Tat which could result in glia-induced neuronal toxicity. Astrocytic network enwraps essentially all the synapses in the CNS and being extremely proximal to neurons, astrocytes are best suited to regulate neuronal homeostasis. Any disruption in astrocytic functionality can profoundly affect neighbouring neurons.

Recently, microRNAs have been shown to interfere with astrocytic functionality and cellular ATP levels were shown to be controlled through microRNAs. We performed real-time array to analyze miRNA perturbation in astrocytes and found miR-320a to be among highly dysregulated miRNAs. miR-320a was predicted to target voltage-dependent anion channel 1 (VDAC1) and miR-320a and VDAC1 interaction was reported to be of high confidence. VDAC1 is a porin channel present in the outer membrane of mitochondria that regulates efflux of ATP from mitochondria to the cytosol. VDAC1 presence has also been reported on other membranes including plasma membrane.

Interestingly, VDAC1 is reported to regulate ATP release from the cells. In our model system of human primary astrocytes, we observed that VDAC1 was indeed

regulating the ATP release. In astrocytes, we observed HIV-1 Tat dysregulates miR-320a and VDAC1 levels. We tested our hypothesis that VDAC1 transcripts act as a molecular substrate for miR-320a and observed that miR-320a mimic was down regulating VDAC1 both at transcript and protein level whereas functionally ablating miR-320a levels using LNA inhibitor against miR-320a, we observed that VDAC1 was up-regulated both at transcript and protein level. Additionally, we also demonstrated perturbed expression of miR-320a in the frontal cortex of HIV-1-infected individuals, suffering from mild cognitive impairment (MCI), as shown through *in situ* hybridization and real-time PCR. VDAC1 mRNA levels were also observed to be dysregulated in the frontal cortex of HIV-1-infected patients as compared to controls. We also observed that blocking the miR-320a-VDAC1 molecular axis can ameliorate the excessive release of ATP in HIV-1 Tat affected astrocytes and rescues the neurons from glia-mediated toxicity. Furthermore, these studies unravel a novel miRNA-regulated molecular pathway disrupted in astrocytes that perturbs ATP release. Under this project, we propose for the first time miR-320-VDAC1 molecular pathway as a mediator of HIV-1 Tat-induced neurodegeneration. The findings unravel few intricacies that would help to improve our understanding of glia neuron interactions in the normal and diseased brain, especially neuroAIDS. Our findings

are important and timely as it has gained novel insights into the effects of HIV-1 on primary human neural precursor cells and astrocytes and has two major observations.

These findings would help in better understanding of the cellular and molecular mechanisms of HIV-1 Tat-induced neuropathogenesis.

PUBLICATIONS

- ❖ Y. Adlakha and **P. Seth** (2017). The Expanding Horizon of MicroRNAs in Cellular Reprogramming. *Progress in Neurobiology* Jan 148:21-39.
- ❖ S. Mukherjee, N. Singh, N. Sengupta, M. Fatima, **P. Seth**, A. Mahadevan, SK Shankar, A. Bhattacharyya and A. Basu (2017). Japanese encephalitis virus induces human neural stem/progenitor cell death by elevating GRP78, PHB and hnRNPC through ER stress. *Cell Death Disease* Jan 19;8(1):e2556.
- ❖ M. Fatima, B. Prajapati, K. Saleem, R. Kumari, C.M.S Singal, and **P. Seth** (2017). Novel insights into role of miR-320a-VDAC1 axis in astrocyte-mediated neuronal damage in neuroAIDS. *Glia* 65(2):250-263.
- ❖ **P. Seth** (2016) *NeuroAIDS: Past, Present and Future*; EDITORIAL in *Current HIV Research* 14 (5): 372, 2016.
- ❖ P.N Tandon and **P. Seth** (2016). Cell Therapy for Neurological Disorders: The Elusive Goal: A Review. *Neurology India* 64: 612-623.
- ❖ M. Bhagat, JK. Palanichamy, P. Ramalingam, M. Mudassir, K. Irshad, K. Chosdol, C. Sarkar, **P. Seth**, S. Goswami, S. Sinha, P. Chattopadhyay (2016). HIF-2alpha mediates a marked increase in migration and stemness characteristics in a subset of Glioma cells under hypoxia by activating an Oct-4/Sox-2- Mena (INV) axis. *Int J Biochemistry and Cell Biology*, May; 74:60-71.
- ❖ M Fatima, R Kumari, JC. Schwamborn, A Mahadevan, SK. Shankar, R Raja, and **P. Seth** (2016). Tripartite Containing Motif 32 Modulates Proliferation of Human Neural Precursor Cells in HIV-1 Neurodegeneration. *Cell Death and Differentiation* May;23(5):776-786.

Book Chapter-

M. Tewari and **P. Seth** (2016). Astrocytes in Neuroinflammation and Neuronal Disorders: Shifting the focus from neurons. *In: Inflammation: the Common Link in Brain Pathologies*. Springer Eds. NR Jana and A. Basu; pp 43-70, 2016.

PRESENTATIONS

- ❖ **P. Seth** (Invited Speaker), *An ill fated relationship - HIV and Brain*. International Symposium on Neurodegenerative Disorders (ISDN-2017) at National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India, March 29-30, 2017.
- ❖ **P. Seth** (5th Sarath Chandran Memorial Lecture), *Novel*

Insights into NeuroAIDS, Sri Venkateshwara College, New Delhi, India, March 7, 2017.

- ❖ **P. Seth** (Guest Lecturer), *Neural Stem Cells: the amazing cells in brain*, on National Science Day at Kendriya Vidyayaya, NSG Campus, Manesar, India, February 28, 2017.
- ❖ **P. Seth** (Guest Lecturer), *Unique model of neural stem cells for understanding NeuroAIDS*. Government Girls College, Gurgaon, India, February 13, 2017.
- ❖ **P. Seth** (Invited Speaker), *Neural Stem cells as model system for understanding brain damage by HIV-1*. Delhi Technical University, New Delhi, India, February 11, 2017.
- ❖ **P. Seth** (Invited Speaker), *Understanding neuron-glia crosstalk in HIV-1 Neuropathogenesis*. Brain Storming Session on DBT National Initiative-Glial Research on Health and Disease, Jiwaji University, Gwalior, India, February 2-3, 2017.
- ❖ **P. Seth** (Invited Speaker), *HIV-1 Modulates Properties of Neural Stem Cells*. NeuroCON 2017, ICARE Institute of Medical Sciences and Research (IIMSR), Haldia, West Bengal, India, January 19-22, 2017.
- ❖ **P. Seth** (Invited Speaker), *Consequences of HIV-1 Infection in Human Neural Stem Cells*, Indo-US symposium on Central Nervous System

Viral Infections and its therapy,
Doars, Chalsa Hilltop, India,
November 14-17, 2016.

- ❖ **P. Seth** (Invited Speaker), *Molecular insights into HIV-1 neuropathogenesis*, Department of Pathology Seminar Series, Uniformed Services University of Health Sciences, Bethesda, USA, November 1, 2016.
- ❖ **P. Seth** (Invited Speaker), *Novel Molecular pathway of ATP perturbation of ATP release in human astrocytes contributes neuronal death in HAND*, 14th International Symposium of International Society of Neurovirology (ISNV) and HIV Endgame, Toronto, Canada, October 24-28, 2016.
- ❖ **P. Seth** (Invited Speaker), *HIV-1 viral protein alters properties of human neural stem cells*, National University of Singapore, Singapore, September 1, 2016.
- ❖ **P. Seth** (Invited Speaker and Chairperson), *Neuron-*

Glia interactions: Friends turn foe in HIV-1 induced neurodegeneration, at Asia Pacific Society of Neurochemistry (APSN 2016), Kuala Lumpur, Malaysia, during August 26-30, 2016.

- ❖ M. Fatima, K. Saleem and **P. Seth** [2016] "*Novel molecular pathway of ATP release perturbed in astrocytes contributes to neuronal death in HIV-1 induced neurodegeneration*" at the 34th annual meeting of Indian Academy of Neurosciences (IAN), National Brain Research Center, India, October 19th-21st, 2016.

FUNDING

This work is supported by NBRC Core and DBT funds.

COLLABORATORS

S. Sharma, E. Sen, A. Basu and S. Sinha, NBRC, Manesar, India.
B. Sindhu, S. Sharma, and A. Singh, Civil Hospital, Gurgaon, India.
S. Shankar and A. Mahadevan,

NIMHANS, Bangalore, India.

M. Mukherjee, IGIB, New Delhi, India.

S. Sen, P. Chattopadhyay, AIIMS, New Delhi, India.

C. Mukhopadhyay, Jawaharlal Nehru University, New Delhi, India.

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

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

J. Schwamborn, University of Luxembourg, Luxembourg (EU).

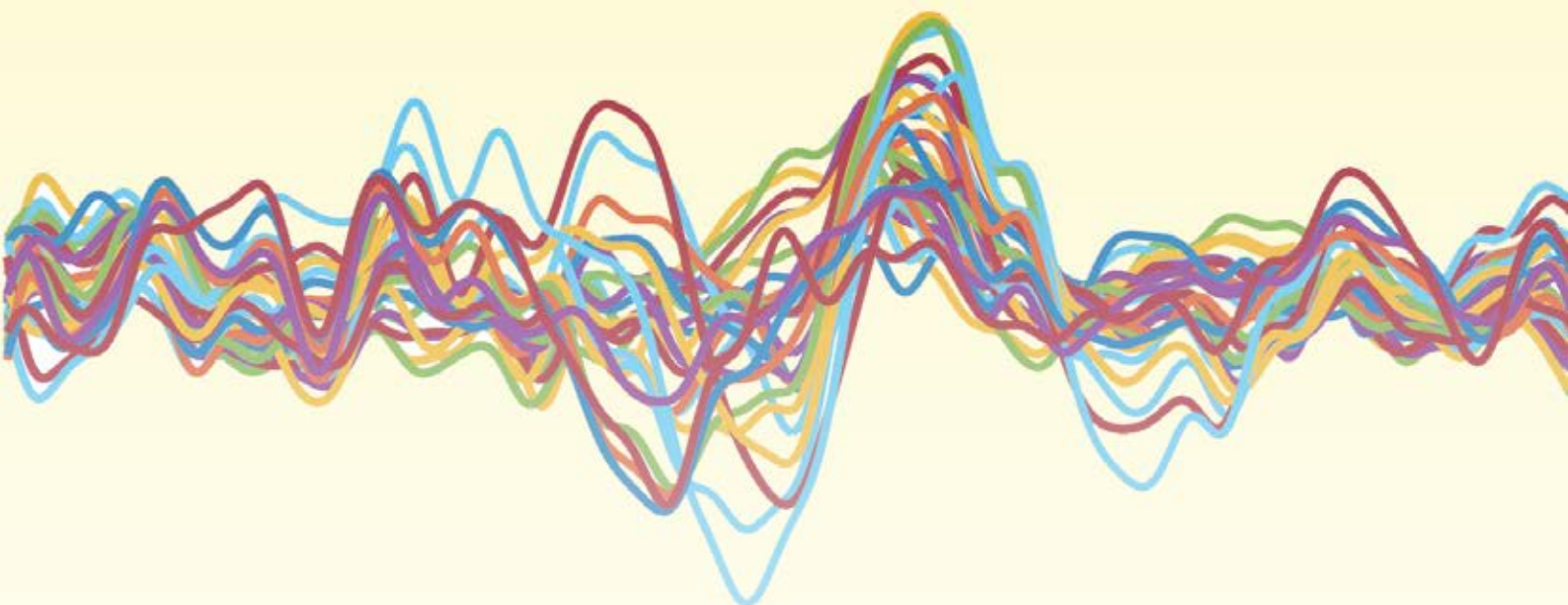
AWARDS

Chitra M.S. Singal - Awarded International Travel Grant from Society on NeuroImmune Pharmacology and Department of Biotechnology for presenting a poster in the 23rd Society on NeuroImmune Pharmacology meeting held in Philadelphia, PA from 29th March 2017 to 1st April 2017.

DEGREES AWARDED (PH.D.)

Manju Pant

Mahar Fatima



Therapy of glioma: Role of hypoxia and aberrant gene expression

PRINCIPAL INVESTIGATOR *Subrata Sinha*

The biology of tumours that arise from the supporting cells of the brain is 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. This work is in collaboration with Prof Parthaprasad Chattopadhyay and Dr Kunzang Chosdol, Department of Biochemistry, Prof Chitra Sarkar, Dept of Pathology and Profs P S Chandra and Deepak Gupta, Dept of Neurosurgery, AIIMS. Glioma are amongst the most hypoxic of human tumours. Hypoxia results in cellular adaptive mechanisms to counter the stress which also result in therapeutic resistance and changes in cell behaviour that make the tumour more aggressive. The best known mediator of hypoxia is HIF1 α , a key molecule at the centre of the pathway that results in the

up-regulation of critical genes, including angiogenic molecules like VEGF and osteopontin that result in the hypoxic response. We had earlier identified a molecule in the Cadherin family, FAT1 THAT up-regulates pro inflammatory pathways including IL6, MMPs and Cox 2. Since hypoxia is also accompanied by an increase in the expression of pro-inflammatory cytokines, we investigated the ability of this molecule to regulate HIF1 α . We have now identified FAT 1 as a new master regulator of HIF1 α in hypoxic conditions. The basal level of FAT1 varies within cell lines and also in primary brain tumours. We have shown that the relationship of FAT1 with HIF1 α and some of its target genes is also valid in primary human glioma. This also provides us with a means of molecular sub-classification of tumours within the same histological

grade and a means to explain the varying behavior of apparently similar tumours [Madan et al 2017].

We have also been looking at strategies for abrogating hypoxia induces therapeutic resistance, especially by using a combination of drugs that are already approved for therapy or in trials as single agents, but have not been shown to be very effective. After examining a number of such drug combinations, we have identified a combination of 2 deoxy glucose [2DG, which has been earlier used for human trials on glioma]) and Cisplatin (a previously used second line drug) that has a synergistic effect both in hypoxia and in normoxia. 2DG caused a strong autophagic response which is, after a point protective to tumour cells especially in hypoxia. Cisplatin is able to abrogate the same and push the cell to an apoptotic pathway. AKT inhibitors also have a similar synergistic effect and can replicate the effect of cisplatin and cause synergistic tumour cell death. This

opens up the possibilities of using newly introduced AKT inhibitors for the therapy of hypoxic gliomas along with 2DG.

PUBLICATIONS

- ❖ Madan E, Dikshit B, Gowda SH, Srivastava C, Sarkar C, Chattopadhyay P, **Sinha S**, Chosdol K. FAT1 is a novel upstream regulator of HIF1 α and invasion of high grade glioma. Int J Cancer. 2016 Aug 18. DOI: 10.1002/ijc.30386. Joint corresponding author
- ❖ Jalota A, Kumar M, Das BC, Yadav AK, Chosdol K, **Sinha S**. Synergistic increase in efficacy of a combination of 2-deoxy-D-glucose and cisplatin in normoxia and hypoxia: switch from autophagy to apoptosis. Tumour Biol. 2016 Jun 15 doi: 10.1007/s13277-016-5089-8
- ❖ Bhagat M, Palanichamy JK, Ramalingam P, Mudassir M, Irshad K, Chosdol K, Sarkar C, Seth P, Goswami

S, **Sinha S**, Chattopadhyay P. HIF-2 mediates a marked increase in migration and stemness characteristics in a subset of glioma cells under hypoxia by activating an Oct-4/Sox-2-Mena (INV) axis. The International Journal of Biochemistry & Cell Biology 74 (2016) 60–71.

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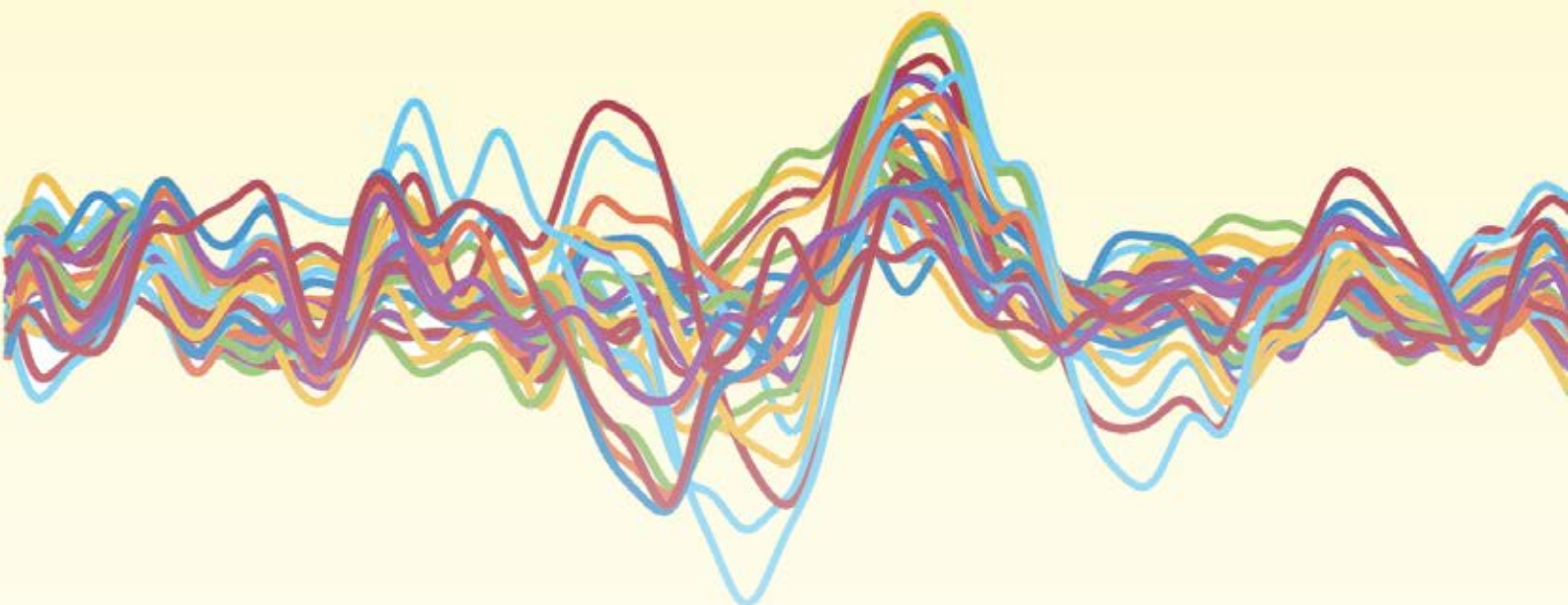
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Targeting of infectious diseases: Generation of neutralizing antibodies to HBV and HIV1 clade C

PRINCIPAL INVESTIGATOR *Subrata Sinha*

For Hepatitis B which today still remains the commonest cause of infectious encephalopathy in the world, we are generating neutralizing antibodies to the pre S1 region of the Hepatitis B surface antigen to target the epitopes responsible for attachment of the virus to Hepatocytes

Similarly HIV encephalopathy is increasing with the improvement in the outcome of HIV infections leading to more long term survivors, Here again cross clade neutralizing antibodies have an important role for reducing infectivity and in immunogen design.

PUBLICATIONS

- ❖ Sankhyan A, Sharma C, Dutta D, Sharma T, Chosdol K, Wakita T, Watashi W, Awasthi A, Acharya SK, Khanna N, Tiwari A and **Sinha S**. Inhibition of preS1-hepatocyte interaction by an array of recombinant human

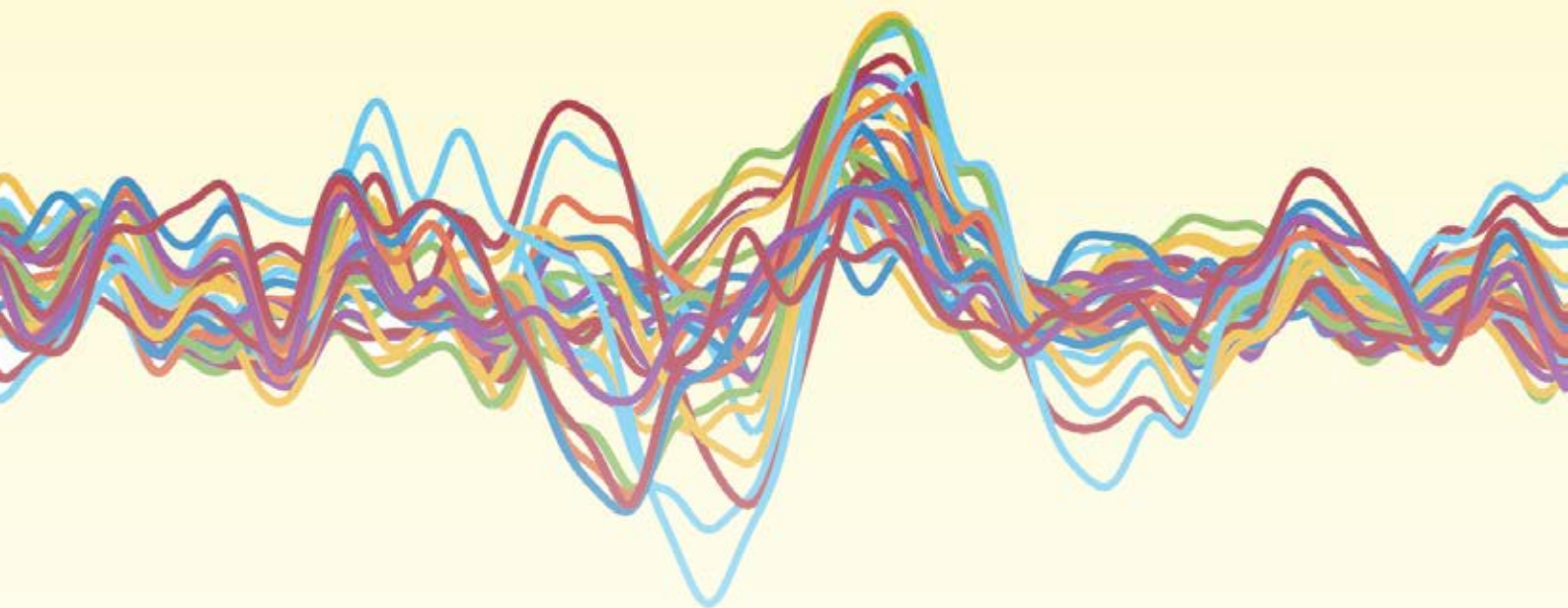
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- ❖ Khan L, Kumar R, Thiruvengadam R, Parray HA, Makhdoomi MA, Kumar S, Aggarwal H, Mohata M, Hussain AW, Das R, Varadarajan R, Bhattacharya J, Vajpayee M, Murugavel KG, Solomon S, **Sinha S**, Luthra K Cross-neutralizing anti-HIV-1 human single chain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

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Genetic analysis of dyslexia

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Dyslexia, (specific learning disorder) has a multifunctional origin with a strong familial pattern. Dyslexia affects 5-10% of the population, and could exist by itself or with other comorbidities, like ADHD. There are a number of genetic studies on dyslexic, both population and family based. Methods of classical genetics as well as next generation sequencing have been utilized. There have been a number of candidate genes demonstrated with varying degrees of replicability. Dr Nandini Singh has carried out screening and diagnosis of a number of cases of dyslexia, including a number of familial cases. Her group has identified three large extended multi-generational families from different endogamous groups, as well as nuclear families with one or two affected siblings.

We are studying three multi-

generational families for genetic studies. These are from 3 different endogamous groups. It is expected that the relative genetic homogeneity within the families would assist in the identification of susceptible genes. This is being done by next generation sequencing. In addition we are studying the inheritance in nuclear families with a candidate gene approach. While the candidate gene approach is being used for affected nuclear families, exome sequencing followed by validation used for the large extended families.

Distinct patterns of inheritance are observed in each family. While in one case the pattern is recessive, in another the pattern is dominant in nature. There is also a difference in the disease associated loci. The results are still being validated. The results

so far indicate that there are multiple pathways to a similar dyslexic phenotype, which however may have subtle variations that are not always possible to distinguish by routine testing. In some cases there appear to be quantitative effects of copy number variations. 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.

How different endophenotypes of dyslexia can be identified and what is the basis for the same is a key question in the field. It is hoped that the molecular genetic dissection of familial dyslexia will help in this effort.

COLLABORATORS

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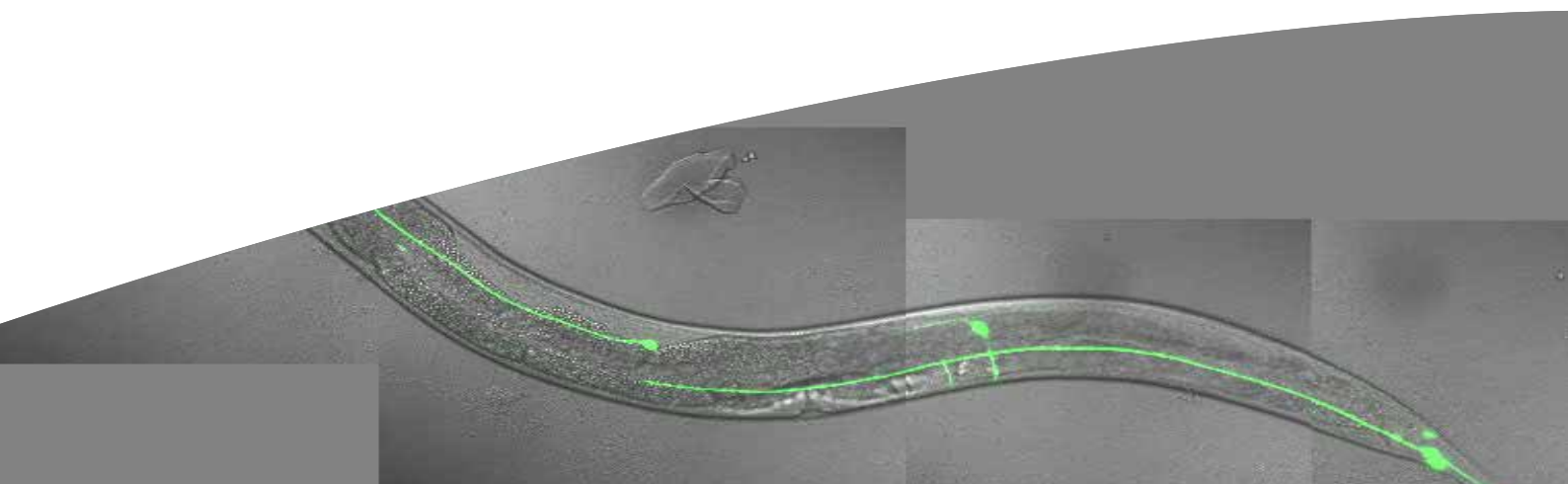
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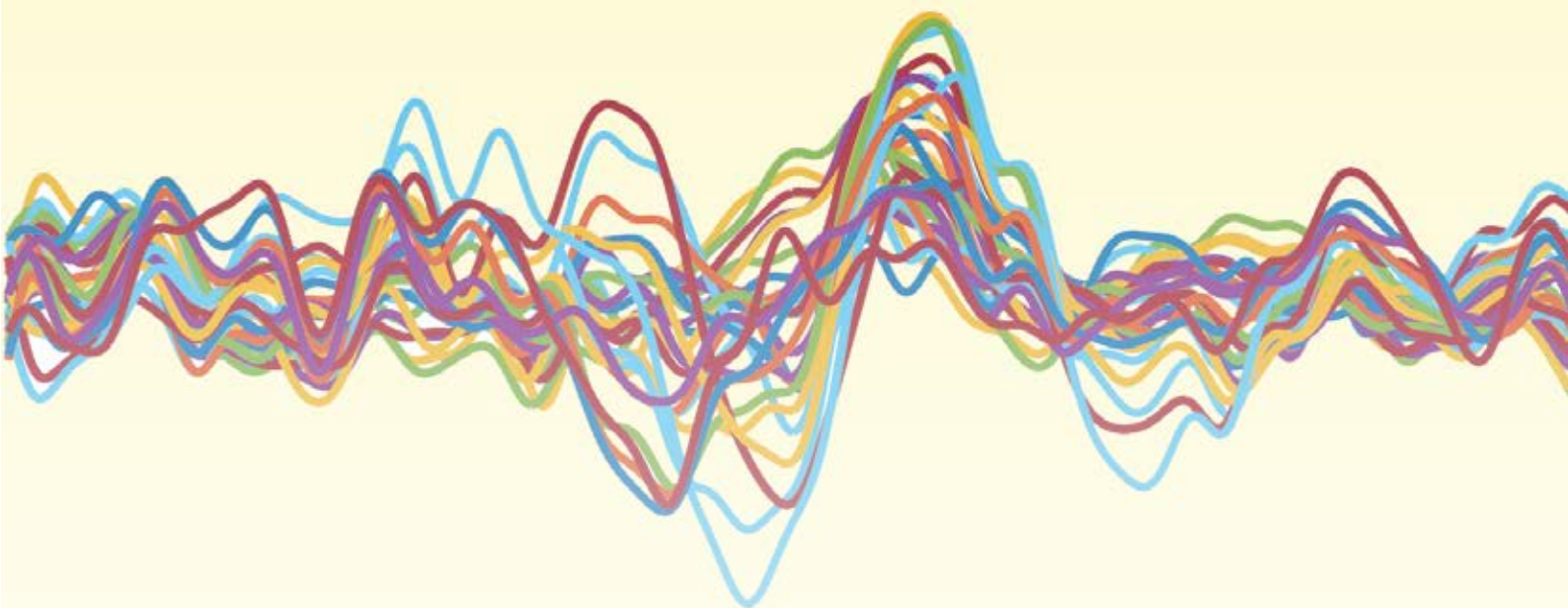
AWARDS

- ❖ J C Bose fellowship of the DST [2016]
- ❖ Sun Pharma Award Medical Sciences – Basic research, for 2015 (announced in 2016)



System & Cognitive Neuroscience Division





Neural mechanisms of spatial navigation

PRINCIPAL INVESTIGATOR

Yoganarasimha Doreswamy

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The research focus of our laboratory is to understand how the brain constructs an internal representation of the outside world and how those representations are stored and recalled as conscious memories, thus forming a spatial relation between an organism and its environment. 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.

Exploratory behaviour in rodents reveal self-organized criticality, wherein a system dealing with information flow pose itself

at a critical point where loss of information is minimized and processing is facilitated, and has been suggested to be a scale free phenomenon. In light of interactions between neural representations of location and direction (the place cells and head direction cells), we tested the hypothesis that heading dynamics may be a scale invariant phenomenon. To address this question, rats were allowed to freely explore on a completely novel elevated platform for 90 minutes in the experimental room, illuminated with a ceiling mounted light source, and surrounded with a black circular curtain having four salient distal landmarks hanging on it. Rats performed Lateral Head Scans (LHS) during intermittent pauses structured within animal's movement profile. LHS events were detected by processing the video data of the animal behavior and time series of these events were analyzed offline. Angular distance covered in a continuous clockwise or counter-clockwise head span (defined as events) were identified and analysed for criticality. Self-organized criticality was quantified through power law distributions of event measures. We observed that the distributions of 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 have analysed the LHS dynamics in two other behavioural states where the spatial exploration was altered, as power law

distributions are not uncommon in various natural phenomenon and mere observation of power law distribution may not necessarily prove that the LHS behaviour is an example of criticality. We conducted experiments 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, thus providing an opportunity to compare the LHS dynamics in various behavioural states. The exploratory architecture under normal behaviour 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 behavioural 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 behavioural states provided strong evidence for LHS behavior as an example of criticality during normal spatial exploration.

Through *in vivo* neurophysiology studies, the network dynamics of neural representation in subicular complex region was assessed in various experimental conditions to understand the

functional properties of subicular complex neurons during spatial navigation. We observed an attractor-like network activity in subicular complex region, wherein different types of cells encode the environmental novelty as an ensemble showing strong coherence between place cells, head direction cells and place x direction cells in various experimental conditions. Subicular network representations showed switching of directional bearings to stable landmarks, thus impacting the orientation of the spatial representations, suggesting integration of directional information onto the spatial framework at the subicular complex region. Further, we also observed dominance of salient landmarks in reorienting the spatial representations in familiar environments due to a shift in reference frame anchoring, indicating a distinct way of information processing in subicular complex region.

In order to understand one of the most fundamental cognitive properties of mammals for survival, i.e. establishing a spatial relation between self and the surrounding environment, we have carried out *in vivo* neurophysiology studies to assess the specific role of hippocampal sub regions. The CA2 region has been acknowledged as an important part of the hippocampal circuitry, much more than a mere 'transition zone' between CA3 and CA1 regions. Its unique connections and striking differences in its biophysical and synaptic properties along

with different morphological characteristics and gene expression pattern, makes CA2 a very important and strategic region to modulate both CA3 and CA1 firing, thus influencing the spatial navigation mechanisms within the hippocampus. Analysis of in vivo neural activity from different sub regions of the hippocampus in awake behaving rodents is under progress, to understand synchrony between hippocampal sub regions and replay of firing sequence during sleep.

Network communication between Hippocampus and neocortex is involved in transfer, storage, organization and retrieval of information associated with learning and memory. Bidirectional interactions between these two regions are necessary for cognitively demanding tasks such as decision making. The temporal interaction between these regions during learning, memory and in decision-making is still not very

clear. We have initiated studies to understand interaction between hippocampus and Orbitofrontal Cortex (OFC) regions during spatial memory and decision making, through in vivo multitetrode single-unit recordings from OFC and hippocampus during specific behavioral experiments in rodents. As the Hippocampus is a critical brain region involved in spatial learning and memory, the place cells encode spatial information by firing at specific location of an environment when the animal moves through that area. Whereas, the neurons in the Orbitofrontal Cortex (OFC) region encode various parameters of reinforcement, like the magnitude, expectation and flavor of the reward. OFC activity thus exerts a strong influence on behavior and plays a key role in decision making. Information transfer between OFC and hippocampus is required for successful output of behavior during spatial decision making and

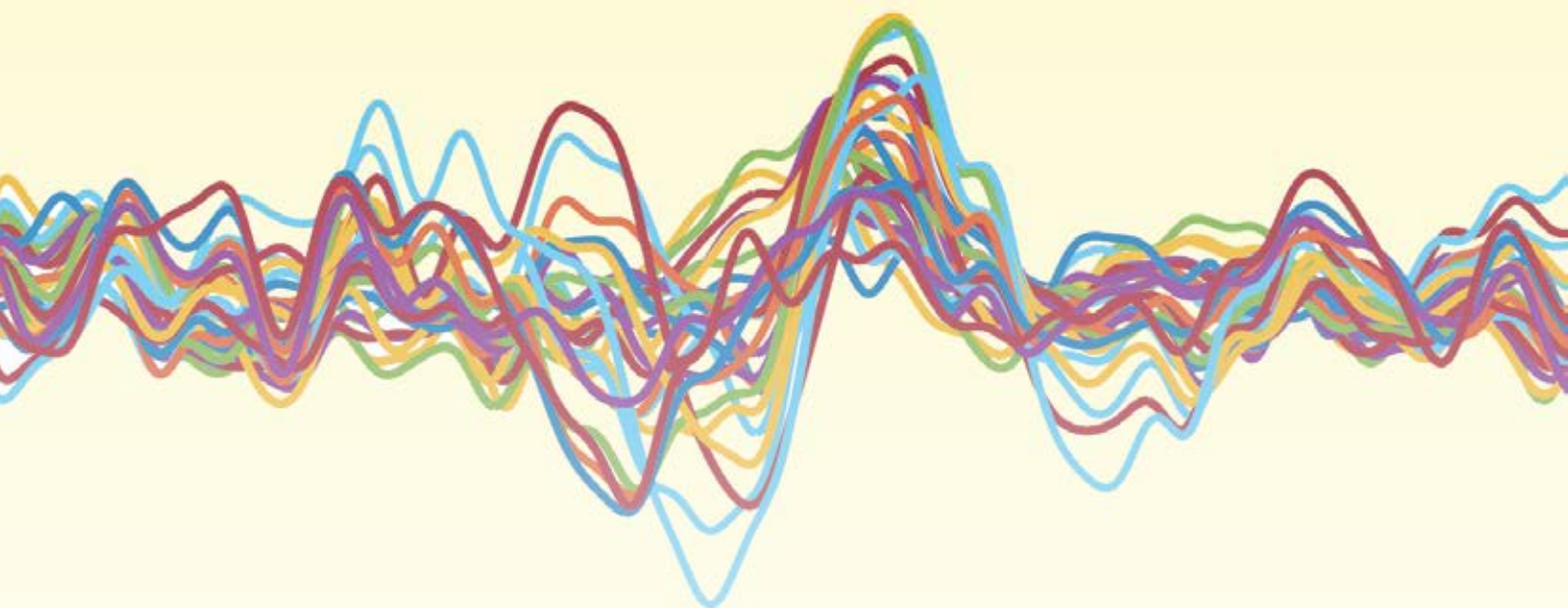
memory. To understand how exactly these brain regions interact, we are recording neural activity from these brain regions simultaneously under different behavioral scenarios. Studying the nature of interaction of these specific brain regions will help us understand how information from one region is integrated into other regions and how these regions encode mnemonic properties of the task. These studies can shed light into how different brain regions interact during cognitive processes and help build computational models on the network interaction.

PUBLICATION

- ❖ Chetan K. Yadav and **Yoganarasimha Doreswamy** [2017] Scale invariance in lateral head scans during spatial exploration. *Physical Review Letters* 118(15), 158104(6)

FUNDING

NBRC Core Funds



Opioid Modulation of song learning in male zebra finches

PRINCIPAL INVESTIGATOR
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Songbirds such as zebra finches are excellent models to study vocal learning during a sensitive period early in their development. Only male birds sing and use their songs in adulthood for courtship. Songs of zebra finches consist typically of 5-7 syllables which are highly stereotyped. Juvenile male zebra finches initially produce soft sounds which are similar to human babies' babbling. During the sensory phase, (~20d - 40d posthatch), a 'template' or copy of their fathers' songs is created in their brains. By ~25d, young males also start vocalizing and begin to practice their songs during what is called a 'sensorimotor phase'. Between ~80-120d post-hatch, songs are perfected and do not change thereafter. No two songs are exactly alike and each male will add to, modify or improvise on the model song (generally his father's song) to create his own signature tune.

Singing, song learning, song perception and hearing are controlled by interconnected regions in songbirds' brains. Interestingly, earlier studies in our lab had shown that each of these brain regions in adult male zebra finches express both μ - and δ -opioid receptors (ORs, Khurshid et al., 2009). Further, we also showed that the endogenous opioid system modulates singing and the motivation to sing in adult male zebra finches (Khurshid et al., 2010).

We have recently started studying the role of the endogenous δ -OR system on song learning in male zebra finches. Pairs of ~35d old male juvenile siblings were used for these experiments. Systemic injections of the δ -OR antagonist naltrindole were injected into one set of birds for a period of ten days (~35d-45d) whereas the other set of siblings received the vehicle and acted as controls

during the sensorimotor phase of song learning. Songs of both birds were recorded while singing to females at ten day intervals from 90d to 120d posthatch. We had earlier shown that the motivation to sing does not change with naltrindole treatment during development since there was no significant difference in the number of songs sung by controls and treated birds. However, there was a significant decrease in syllable duration in naltrindole-treated birds compared to those of controls. Naltrindole-treated male zebra finches produced lower-pitched songs compared to controls. The range of pitch that zebra finches could produce was also higher in controls versus treated birds. We also found that control birds produced more complex syllables which were highly frequency modulated compared to treated birds. Further, these frequency modulations were repeated accurately each time control birds sang, which was not seen in treated birds. We have now confirmed these findings which demonstrate that opioid neuromodulation by the δ -OR system is important for song learning since blocking these receptors for a very short period (10 days) during the sensitive period can have long-term effects on singing.

Earlier literature has demonstrated that different song control nuclei show large-scale changes in volume during the sensitive period for vocal learning. Since the quality of singing in naltrindole-treated birds is different from that in controls,

we wondered whether there was any effect of blocking δ -ORs on the volume of different regions which control vocal learning. However, there were no significant changes in the volumes of song control nuclei in control versus treated birds, suggesting that naltrindole does not change neuronal density or dendritic arbors surrounding neurons in these regions. Our preliminary findings also show that the number of DARPP-positive medium spiny neurons (which also express δ -ORs) was higher in Area X in naltrindole-treated birds compared to controls. DARPP-32 is a protein which is expressed in dopaminergic neurons and is involved in signalling cascades downstream of dopamine receptors. Taken together, these results suggest that blocking δ -OR may lead to an increase in the production or survival of medium spiny neurons in Area X during development.

PUBLICATIONS

- ❖ **Iyengar S, Parishar P, Mohapatra AN (2017):** Avian Cognition and Consciousness - from the Perspective of Neuroscience and Behaviour. Chapter, In press: "Self, Culture and Consciousness: Interdisciplinary Convergences on Knowing and Being". Eds: Sangeetha Menon, Nithin Nagaraj and VV Binoy, Springer Nature.

PRESENTATIONS

- ❖ **S. Iyengar:** Cognition in Corvids - an Avian Model System. Invited lecture at the Cognitive

Science workshop and NBRC-IITD workshop, January 2016.

- ❖ **S. Iyengar:** The Effects of Opioids on Vocalization and Vocal learning using Songbirds as a Model System. Invited lecture presented at the IBRO-APRC (Asia Pacific Regional Committee) School, NBRC "Theme: Development and Functions of Brain Circuits: From Molecules to Behaviour", March 2016.
- ❖ **S. Iyengar:** Mirror, Mirror on the Wall and some other aspects of Corvid Brain Structure and Cognition. Invited talk presented at IISER, Pune, July 2016.
- ❖ **S. Iyengar:** The Role of Mu-Opioid receptors in modulating the songs of Adult Male Zebra Finches, talk presented at the NeuroGroup Meeting, Khandala, Pune, September 2016.
- ❖ **S. Iyengar:** Effects of Mu-opioid Receptor Modulation on Singing in Adult Male Zebra Finches. Invited lecture presented at the XXXIV Annual Conference of Indian Academy of Neurosciences, NBRC, Manesar, October 2016.
- ❖ **S Sen, P Raghunathan, SS Kumaran and S Iyengar:** A Three-Dimensional Digital Atlas of the Indian House Crow (*Corvus splendens*) Brain. Poster presented at the XXXIV Annual Conference of Indian Academy of Neurosciences, NBRC, Manesar, October 2016.

- ❖ S Sen, S Paul, P Raghunathan, SS Kumaran and **S Iyengar**: A Three-Dimensional Stereotaxic MRI Brain Atlas of House Crows (*Corvus splendens*). Poster presented at the

Annual Meeting of Society for Neuroscience, San Diego, CA, USA, November 2016.

FUNDING

NBRC Core and DST funds (Grant

entitled "Effects of the δ -Opioid Receptor System on Singing and Song Learning in Zebra Finches", EMR/2015/001422, received September 2016).

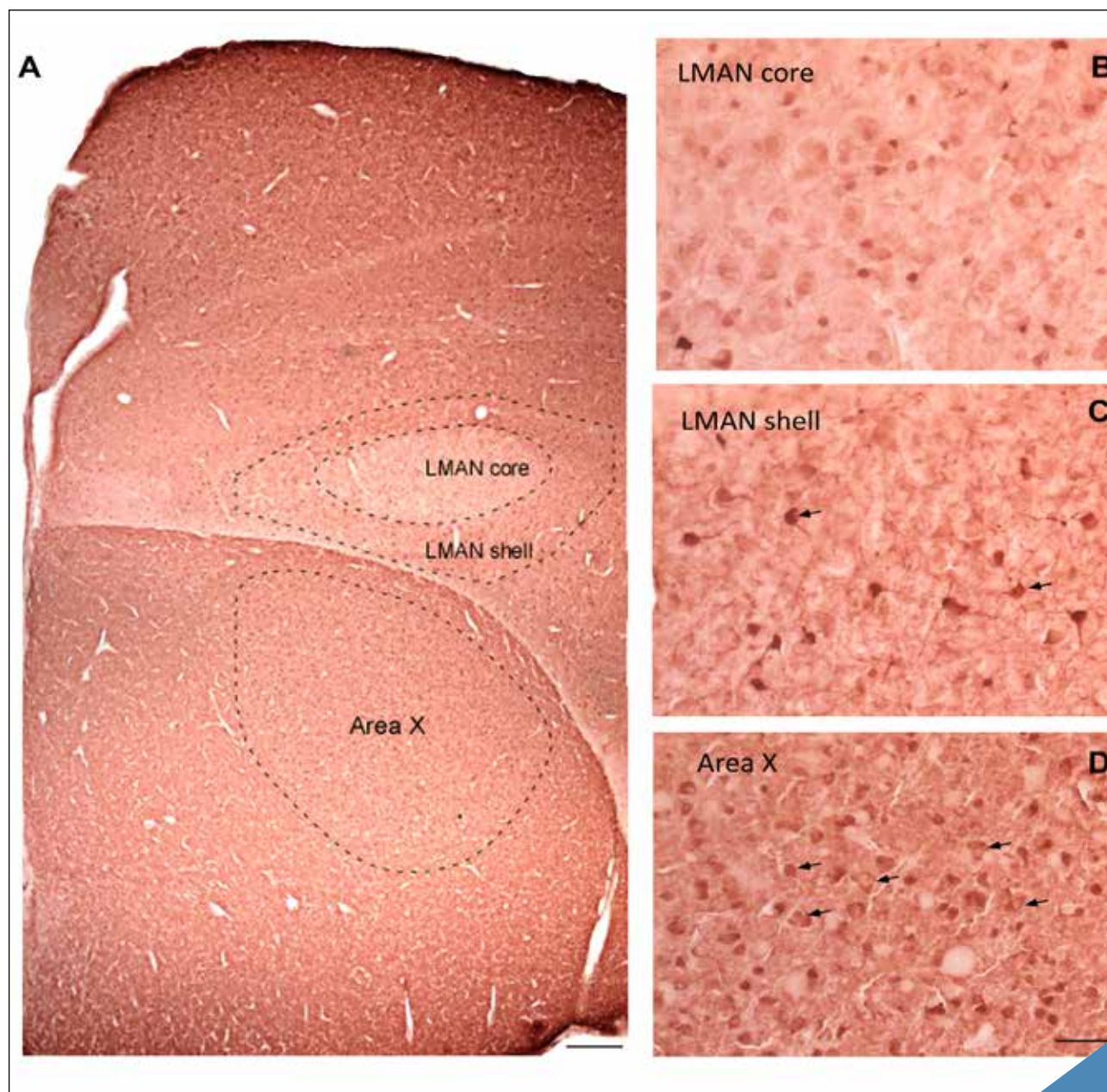
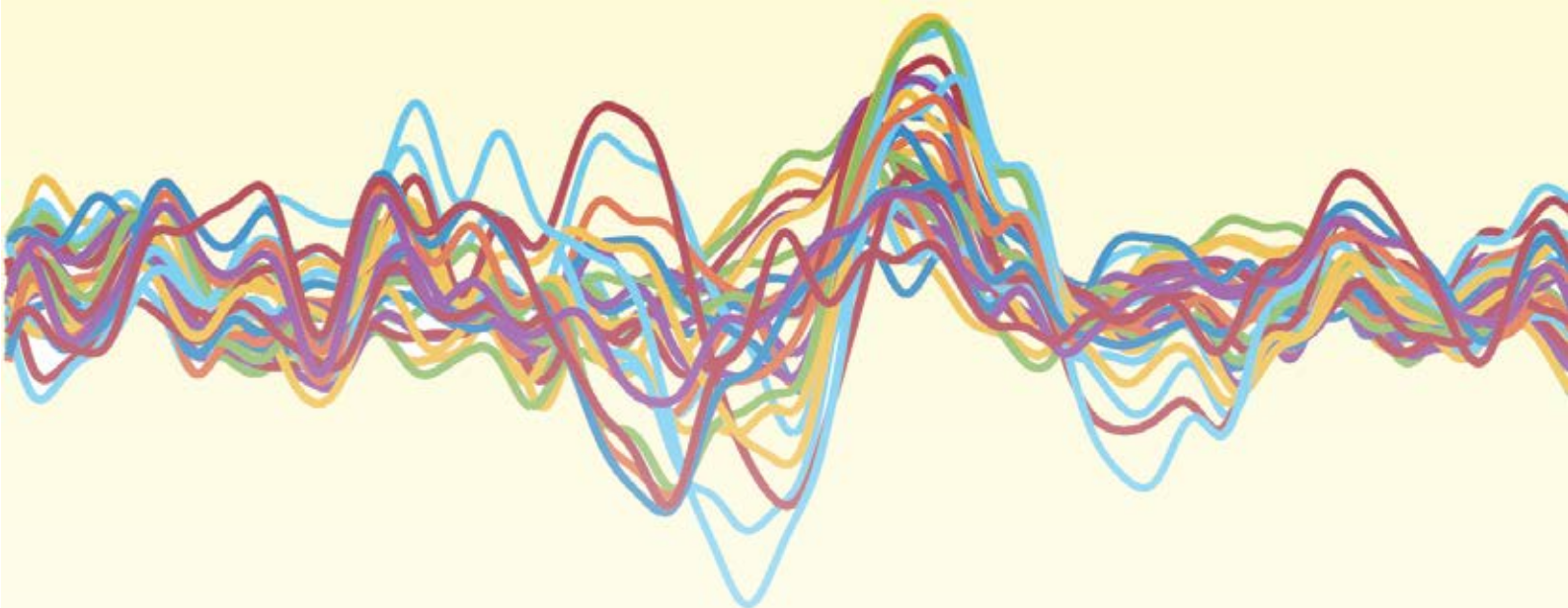


Figure 1: (A) A cross-section of the anterior forebrain in an adult male zebra finch stained for DARPP-32. With the exception of LMAN_{core}, all other subregions of the brain are immunoreactive for DARPP-32. Scale bar, 500 μ m. High-power images demonstrate (B) low levels of DARPP-32 staining in LMAN_{core} and DARPP-32-positive neurons (arrows) in (C) LMAN_{shell} and (D) Area X. Scale bar, 25 μ m.



Organization of somatosensory and motor systems and the effects of spinal cord injuries

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Our research focus is to understand the organization and information processing in the somatosensory and motor systems of the brain, and how spinal cord injuries affect parts of the brain that control movements and enable sense of touch. It has been proposed that brain plasticity mediates spontaneous as well as physiotherapy-induced recoveries of function after spinal cord injuries. However, mechanisms of brain plasticity are not known, thus hindering our efforts to devise more effective interventions. We use a variety of model systems to understand the effects of spinal cord injuries including non-human primates, rats and mice. We have previously shown in monkeys that lesions of the dorsal spinal cord result in large-scale reorganization of the somatosensory areas of the

brain [Dutta et al., Brain Structure and Function, 2014; Tandon et al., Journal of Neuroscience, 2009], and a more limited but specific reorganization of the movement representation in the motor cortex [Kambi et al., Journal of Neuroscience 2011]. In rats similar lesions cause changes in the movement representation such that the movements of the de-efferented body parts are evoked from larger regions of the motor cortex [Tandon et al., European Journal of Neuroscience 2013]. Our efforts are now focused towards understanding mechanisms of brain plasticity [Kambi et al., Nature Communications, 2014; Chand and Jain, Journal of Neuroscience, 2015]. Recent advances in the development of genetically modified mouse lines have provided an invaluable tool

to understand cellular and synaptic mechanisms of brain plasticity. Mouse lines are available that have fluorescently labeled specific neuronal cell types, which also permit calcium imaging in these specific cell types. We are using such mouse lines to understand synaptic mechanisms of brain plasticity. We are developing a mouse model of spinal cord injuries based on our previous studies in rats and monkeys.

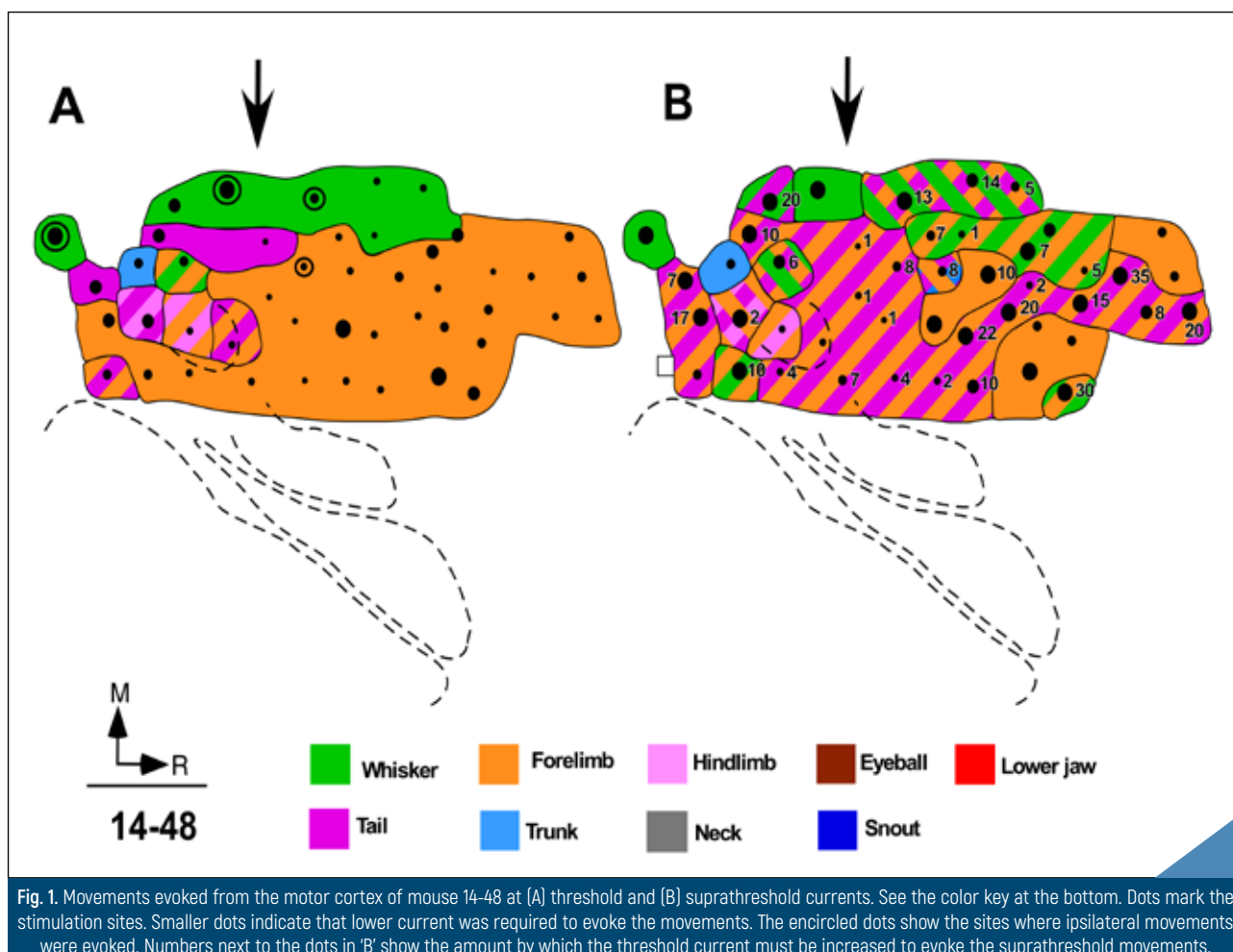
Topographic organization of the motor cortex is usually determined

by intracortical microstimulation (ICMS). ICMS involves using microelectrodes to inject small amounts of current to stimulate layer 5 neurons. The stimulating current is reduced to the smallest threshold value that elicits a visible movement of a body part. We used ICMS to determine organization of the motor cortex in mice. We determined normal organization of the mouse motor cortex, since such reports are few.

We found that although the overall topography of the mouse motor

cortex is similar to rats, there are significant differences. There is a medial whisker movement area, which is bordered on the lateral side by the forelimb area. Caudally there are small trunk and hindlimb movement regions, and a rather large tail area. Within these representations, there are scattered patches of neurons from where movements of other body parts, particularly the tail could be evoked (Fig. 1).

Interestingly, stimulation at currents that were slightly higher



than the threshold currents (i.e. suprathreshold currents) evoked movements of additional body parts at nearly all the sites (Fig. 1 and Fig. 2). The increase in threshold currents required for additional movements was generally as low as 1 μ A. For example, at suprathreshold currents whisker movements could be evoked from the forelimb area and vice versa. The number of tail movement sites increased throughout the motor cortex. The additional movements were unlikely to be due to the point-spread of the current, because these movements were observed not just at the boundaries of the representations, but throughout the motor cortex. Moreover, the movements evoked at suprathreshold currents could be of non-adjacent and distant

body parts. In rats, in contrast, suprathreshold currents do not evoke movements of additional body parts, except that movements of the neck muscles are evoked from the whisker area [Tandon et al., European Journal of Neuroscience, 27:228, 2008]. We conclude that the mouse motor cortex has a mosaic representation of movements of different body parts.

PUBLICATIONS

- ❖ Hisham Mohammed and **Neeraj Jain** (2016) Ipsilateral cortical inputs to the rostral and caudal motor areas in rats. *Journal of Comparative Neurology* 524:3104-3123.
- ❖ Hui-Xin Qi, Jamie L Reed, Joao G Franca, **Neeraj Jain**, Yoshinao Kajikawa and Jon H Kaas (2016). Chronic recordings reveal

tactile stimuli can suppress spontaneous activity of neurons in somatosensory cortex of awake and anesthetized primates. *Journal of Neurophysiology*. 115: 2105-2123. doi: 10.1152/jn.00634.2015.

PRESENTATIONS

- ❖ Priyabrata Halder and **Neeraj Jain** (2016). Reorganization of cuneate nucleus in macaque monkey following chronic partial spinal cord injuries. Neuroscience 2016, Annual Meeting of the Society for Neuroscience, USA.
- ❖ Kalpana Gupta, Manika Arora, Mithlesh K.Singh and **Neeraj Jain** (2016). 'Sensory and motor changes in ageing rats'. 34th Annual Meeting of Indian Academy of Neurosciences, National Brain Research Centre, Manesar.
- ❖ Shanah Rachel John, Priyabrata Halder and **Neeraj Jain** (2016). 'Topographic representations in the mouse motor cortex is not well defined'. 34th Annual Meeting of Indian Academy of Neurosciences, National Brain Research Centre, Manesar.
- ❖ Prem chand and **Neeraj Jain** (2016). 'Cortico-cortical and thalamocortical connections between the hand and face regions of area 3b are unaffected following dorsal spinal cord injuries in macaque monkeys'. 39th Annual Meeting of the Japan Neuroscience Society, Pacifico Yokhama, Japan.
- ❖ **Neeraj Jain**, Leslee Lazar, Prem Chand, Radhika Rajan

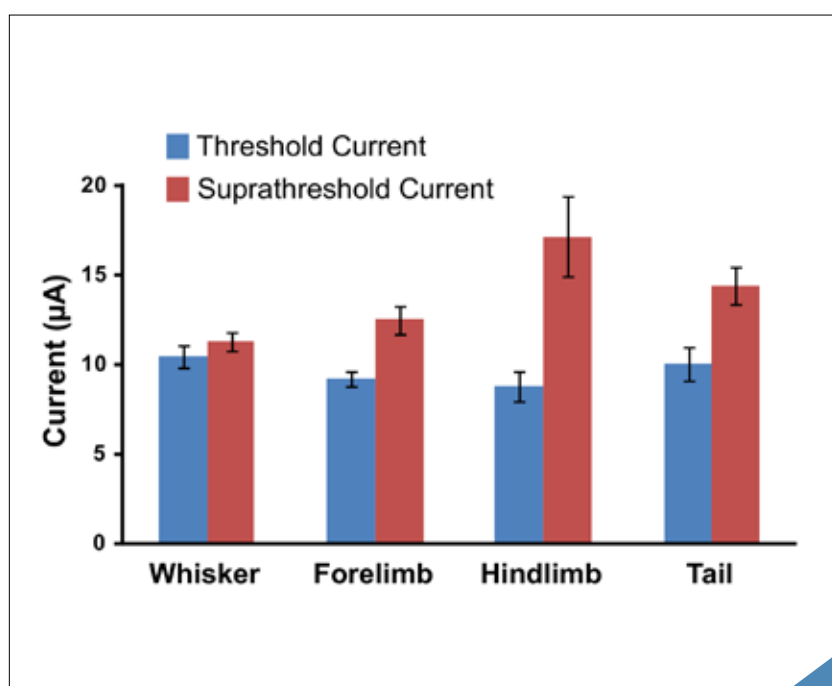


Fig. 2. A bar graph showing currents required to evoke movements of the whiskers, forelimb and tail at threshold currents, and the movements of these body parts evoked at additional sites at suprathreshold currents. The data show mean $\pm$ SEM from six animals.

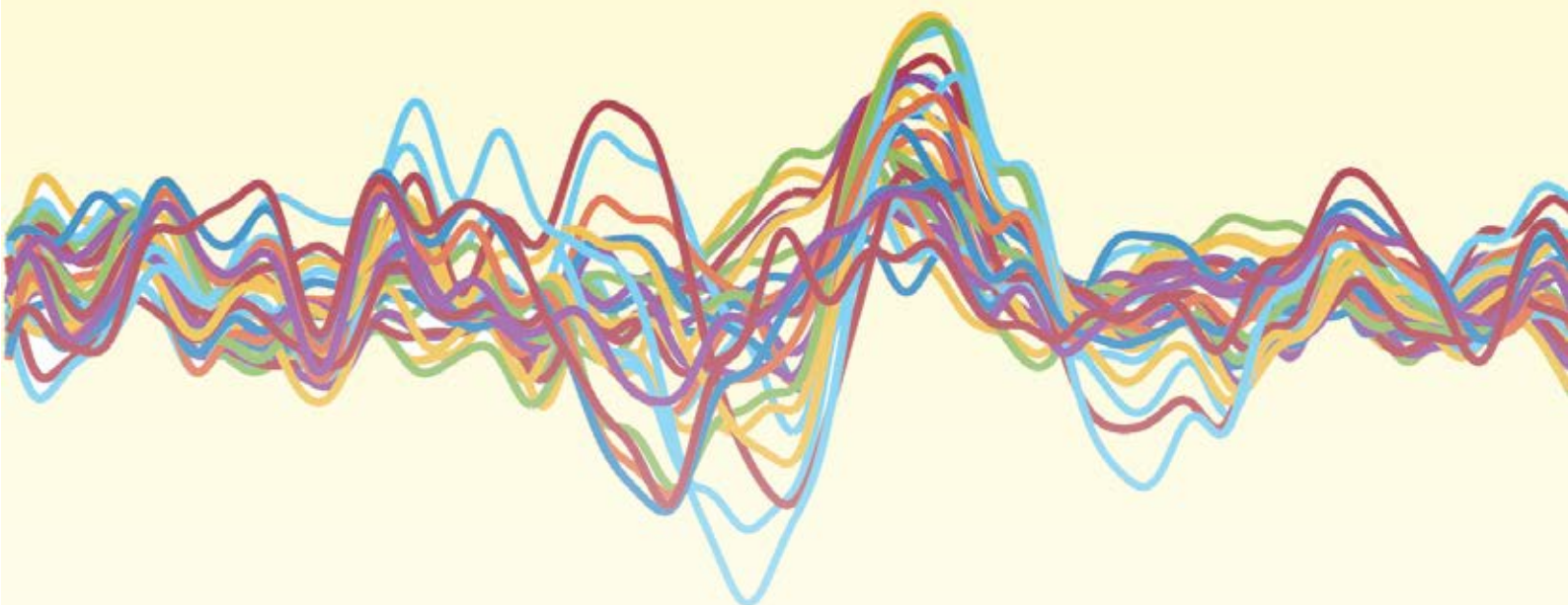
- (2016). 'Neurophysiological and neuroanatomical correlates of independent use of opposable thumb in macaque monkeys'. 39th Annual Meeting of the Japan Neuroscience Society, Pacifico Yokhama, Japan.
- ❖ 'How spinal cord injuries affect the brain: some mechanistic insights', at Indian Institute for Science Education and Research Mohali, March 31, 2017.
 - ❖ 'How spinal cord injuries affect the brain', at Seventh Symposium on Frontiers in Molecular Medicine, Jawaharlal University, New Delhi, March 23-24, 2017.
 - ❖ 'Spinal cord injuries and brain reorganization - what have we learnt', at Centre for Neuroscience, Indian Institute of Science, Bangalore, March 21, 2017.
 - ❖ 'Somatosensory information processing in the brain and effects of injuries', at a workshop on 'Brain Science and Technology: Tools and Techniques to understand human Brain', Indian Institute of Technology Delhi; December 14-18, 2016.
 - ❖ 'Spinal cord injuries and brain reorganisation', at Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel, December 8, 2016.
 - ❖ 'The Somatosensory Information Processing and Spinal Cord Injuries' at Israel - India Neuroscience Symposium, December 3-4, 2016, Eilat, Israel.
 - ❖ 'Somatosensory cortex is designed for opposable thumb', at the 1st NeuroGroup Meeting, September 27-28, 2018, Khandala.
 - ❖ 'How modular organization of the brain contributes to information processing' a Plenary Talk at the 3rd Annual Conference of Association for Cognitive Science, IIT Gandhinagar; October 3-5, 2016.
 - ❖ 'Brain-Computer Interface: Challenges in designing a useful motor and sensory prosthetic' at Special Session on 'Brain Computer Interface' in 8th ISSS National Conference on MEMS, Smart Materials, Structures and Systems, IIT Kanpur, September 30, 2016.

FUNDING

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Molecular changes relevant to synaptic plasticity and memory

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Narayan

The ability to form memories and recall them at a later time is a fundamentally important function of the brain. Perhaps the importance of memory is better appreciated when they are impaired or lost. Synaptic plasticity, the ability of synapses to change in response to experience is considered to be the cellular process contributing to memory formation. One aspect of the research in my laboratory is to understand the processes that are involved in synaptic plasticity and memory. The other aspect of our research involves Alzheimer's disease and Down syndrome. The research personnel mentioned above are working on different projects related to these aspects. One aspect of the work going on in my laboratory is described below.

One kind of synaptic plasticity, long-term potentiation (LTP)

of synapses, is thought to play critical roles in memory formation. Plethora of studies have shown that long-term potentiation as well as memory are regulated by molecular events including phosphorylation. Protein kinases bring about phosphorylation of proteins. The role of one particular kinase, the extracellular signal-regulated kinase (ERK), in synaptic plasticity and memory has been investigated extensively. Studies have shown that ERK activity is induced by stimuli relevant for LTP and memory. Importantly, blocking the activity of this kinase blocks LTP as well as memory.

Although several research groups have examined the critical role of ERK in LTP and memory, the mechanisms of ERK activation are not fully understood. Previously, we

have shown that KCl-induced depolarization of hippocampal slices induces sustained activation of ERK. We also investigated the molecular mechanisms involved in KCl-induced sustained ERK activation. An important finding in that study was that brain-derived neurotrophic factor plays a critical role in KCl-induced sustained ERK activation. In another study, we showed that activation of the cAMP pathway also induces sustained ERK activation. In this study also we investigated the processes involved in sustained ERK activation.

We are now examining whether other pathways having important roles in synaptic plasticity and memory induce sustained ERK activation. For these studies, we are pharmacologically activating a particular kinase that regulates ERK activation. We prepare

the hippocampal slices from young adult rats and treat them pharmacologically to induce activation of the kinase under investigation. We examine ERK activation using antibodies that react with only the phosphorylated and thus activated form of ERK. To accurately assess ERK activation, we normalize phosphorylated ERK level with the total level of ERK. Our results show that activation of the kinase under investigation significantly activates ERK. This is consistent with the previous findings. Importantly, we found that activation of this kinase induces ERK activation that lasts much beyond the duration of pharmacological agent treatment that activates the kinase. Thus, activation of this particular kinase induces sustained ERK activation in the hippocampal slices.

Sustained ERK activation could play an important role in synaptic plasticity and memory formation. We are now investigating the mechanisms of this sustained ERK activation.

PRESENTATION

❖ Tushar Arora and **Shiv K. Sharma**. Targeting amyloid aggregation using a novel peptide. Poster presentation in the 34th annual meeting of Indian Academy of Neurosciences. October 19-21, 2016, NBRC, Manesar, Haryana.

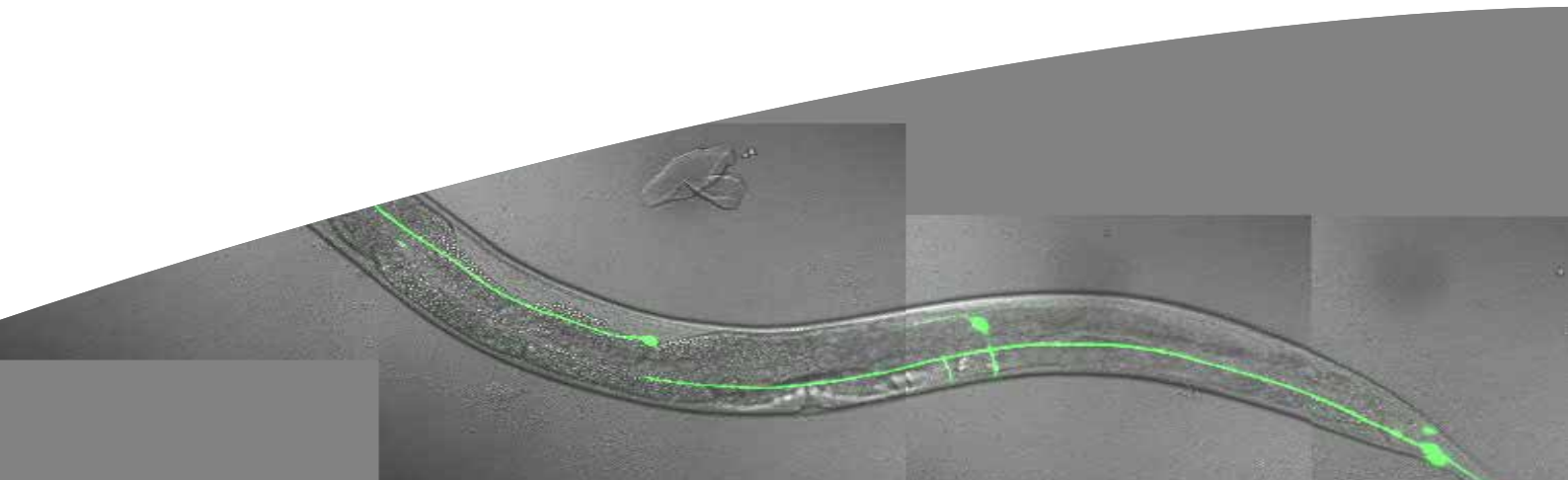
FUNDING

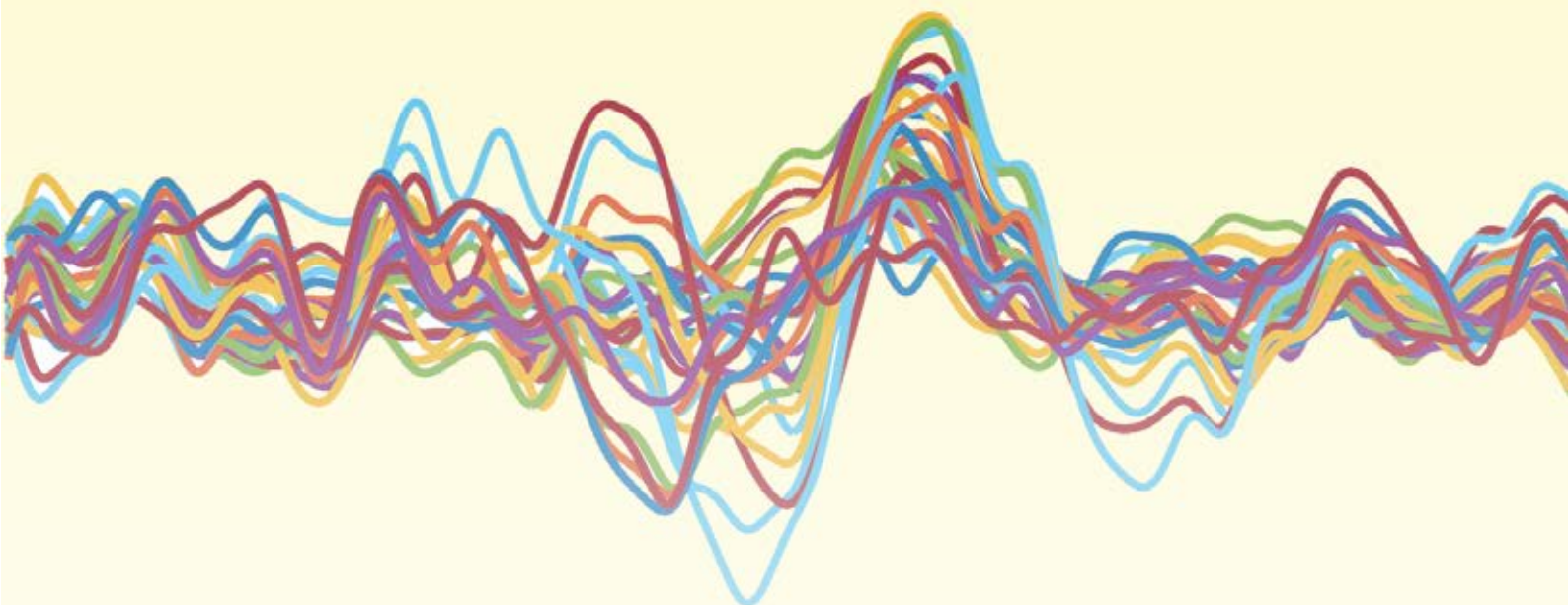
This work is supported by NBRC Core.

DEGREE AWARDED (PH.D.)

Kaushik P Sharma

Computational Neuroscience & Neuroimaging Division





Investigating neuro-cognitive network mechanisms using multimodal neuroimaging

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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, 2016 - March, 2017. The overarching goal of these projects is to develop an understanding for the neurobiological mechanisms of multisensory integration and basic sensory function. The

three projects on which we have focussed are related to determining efficient tools for cortical source localization from EEG/ MEG data, investigating the network structure of neuronal entrainment and identifying the network level correlates of multisensory processing using spectro-temporal techniques.

IDENTIFYING EFFICIENT TOOLS FOR SOURCE LOCALIZATION OF EEG/ MEG BASED ON GROUND-TRUTH VALIDATION TECHNIQUES AND EMPIRICAL MEASUREMENTS

Oscillatory brain electromagnetic activity is an established tool to study neurophysiological mechanisms of human behavior using electro-encephalogram (EEG) and magneto-encephalogram (MEG) techniques. Often, to extract source level information in the cortex, researchers have to rely on inverse techniques

that generate probabilistic estimation of the cortical activation underlying EEG/ MEG data from sensors located outside the body. State of the art source localization methods such as exact low resolution electromagnetic tomography (eLORETA), Dynamic Imaging of Coherent Sources (DICS) and Linearly Constrained Minimum Variance (LCMV) has over the years been established as the prominent techniques of choice. These algorithms produce a distributed map of brain activity underlying sustained and transient responses during neuroimaging studies of behavior. The volume conduction effects and noise of the environment play a considerable role in adding uncertainty to source localization. There are very few comparative analysis that evaluates the "ground truth detection" capabilities of these methods. In this Project, we compared the aforementioned techniques to estimate sources of spectral event generators in the cortex using a two-pronged approach. First, we use simulated EEG data with distributed dipole modelling to validate the accuracy and sensitivity of each one of these methods of source localization. eLORETA performed better for distributed dipole localization out of the three for both oscillatory activity (e.g., band-specific enhancement of signal power) and transient responses (e.g., event related potentials) using three different performance metrics. Second, we used empirical EEG data where 40 Hz brain response was evoked during rhythmic presentation of an auditory tone

at 40 Hz frequency. The tone itself consisted of fundamental frequency of 1000 kHz. Localization spreads for transient N100/ P100 component of the auditory evoked potential response as well as for the 40 Hz evoked auditory responses were compared among eLORETA, LCMV and DICS. Interestingly a mixed set of results indicates there is no one-stop solution for source localization. For example for point sources LCMV and DICS were equally good as eLORETA for source localization, in fact for higher noise and at physiologically valid noise levels LCMV seems to be the best method for time-lock analysis. For distributed source estimation eLORETA yielded more favorable results (more details in Fig 1).

ENTRAINMENT OF LARGE-SCALE CORTICAL NETWORKS UNDERLIE THE PROCESSING OF PERIODIC AUDITORY STIMULUS

Several electroencephalogram (EEG) studies have shown that stimulation by periodic auditory stimuli evokes a steady state response at the corresponding frequency, with 40Hz eliciting maximum response. Despite having enormous potential for clinical applications from measuring hearing threshold to characterizing the alteration of diseased state in Alzheimer's, the underlying network mechanisms are poorly understood. Present study exploits this paradigm to characterize the network mechanisms underlying binaural and monaural auditory stimulation.

EEG data was collected from 20 healthy volunteers who signed informed consents, approved by

the Institutional Human Ethics Committee of National Brain Research Centre, India. The participants had to stay still in a sitting position while their EEG was recorded during rest (200 s) and monaural (200 s each for left and right) and binaural (200 s) auditory stimulation. Pure tones at 1kHz frequency were presented at 40 cycles a second during the periodic stimulation period in 1 s On and 1s Off (silent) blocks.

We observed the enhancement of spectral power at individual participant and group level at 40 Hz in distributed scalp sensor locations (see details in Fig 2). Maximum 40 Hz spectral power found in mastoid sensors and frontal central areas. Subsequently, we computed global coherence, an average of all of the pairwise coherences, to identify the presence of a large-scale brain network. Task-specific enhancement of global coherence specifically at 40 Hz indicate the entrainment of a large-scale neuronal network in monaural and binaural conditions. Hemispheric analysis revealed the ipsilateral dominance in the processing of monaural stimuli. Subsequently, measurement of pairwise imaginary coherence to detect sub-networks were carried out. Statistical testing of interaction among channel pairs was done using non-parametric tests. Bilateral long range interactions involving centro-frontal and temporal sensors and parietooccipital sensors were significant. These interactions were ipsilateral dominant in monaural conditions. To identify the causal influence

in all significantly interacting channel pair we employed Granger causality (GC) analysis. In both monaural and binaural conditions, GC revealed the influence of right temporal region to the frontal areas, but in binaural and monaural left condition GC indicate the unidirectional influence of frontal regions to left mastoid region. In conclusion, we establish the presence of large-scale effective networks encompassing bilateral auditory and frontal areas that get entrained during the processing of 40 Hz auditory stimuli.

SEGREGATION AND INTEGRATION OF CORTICAL INFORMATION PROCESSING UNDERLYING CROSS-MODAL PERCEPTION

Visual cues from the speaker's face influence the perception of speech. An example of the influence is demonstrated by the McGurk-effect where illusory (cross-modal) sounds are perceived following presentation of incongruent audio-visual (AV) stimuli. Previous studies

report the engagement of specific cortical modules that are spatially distributed during cross-modal perception. However, the limits of the underlying representational space and the cortical network mechanisms remain unclear. In this combined psychophysical and electroencephalography (EEG) study, the participants reported their perception while listening to a set of synchronous and asynchronous incongruent AV stimuli. We identified the neural representation of subjective cross-modal perception at different organizational levels - at specific locations in sensor space and at the level of large-scale brain network estimated by between-sensor interactions. This was achieved by examining the markers of illusory perceptual processing in the event-related responses and spectro-temporal evolution of EEG signals at each sensor location and at large scale network level estimated by computing the pairwise imaginary coherence

underlying the cross-modal perception during synchronous and asynchronous AV speech. We identified an enhanced positivity in the event-related potential (ERP) peak at 300 ms post stimulus onset associated with cross-modal perception. At spectral level, cross-modal perception involved an overall decrease in power at the frontal and temporal scalp regions at multiple frequency bands and at all AV lags, along with an increased power at the occipital scalp region for synchronous AV stimulus. At the level of large scale neuronal networks, enhanced functional connectivity with the frontal regions at gamma band serves as a marker of AV integration. Concomitantly, we report in a single study, the segregation of information processing at individual brain locations and the mechanisms by which integration of information takes place in candidate brain networks underlying multisensory speech perception.

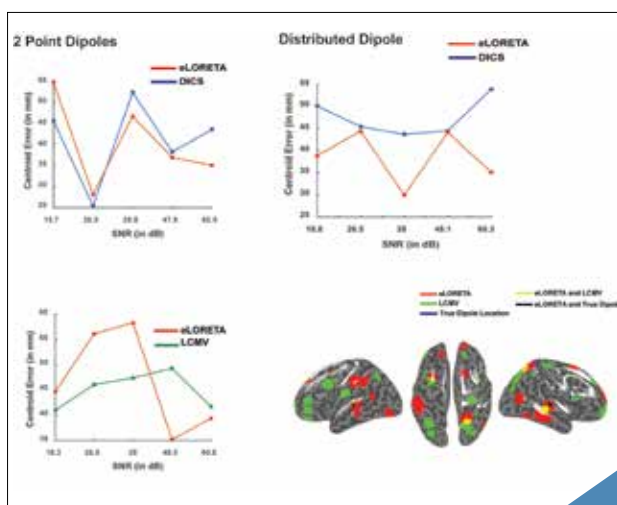


Fig1: Comparison of results from using source analyses (eLORETA, LCMV, DICS) from simulated data

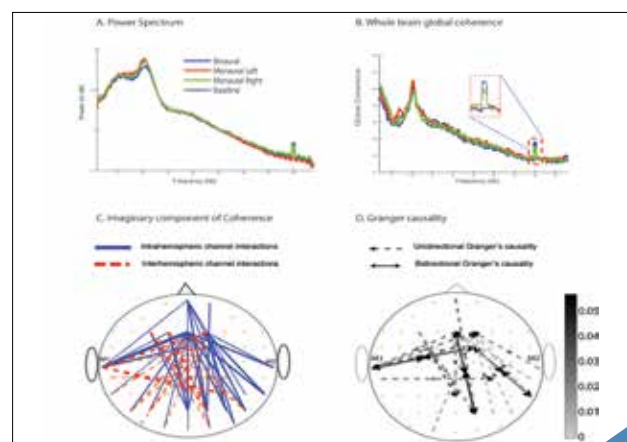
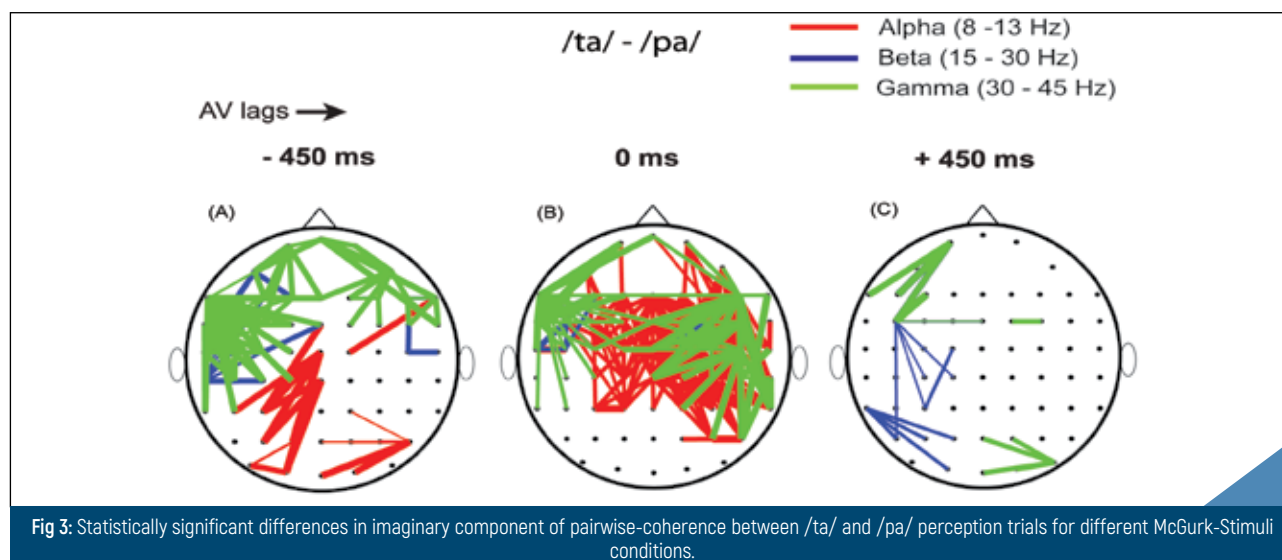


Fig 2: Understanding the networks underlying auditory steady state response (ASSR) at 40 Hz stimulation using EEG sensor level analyses. A) Power spectrum B) Whole brain global coherence analysis C) Pairwise coherence analysis D) Granger causality analysis



PUBLICATIONS

- ❖ Kumar, V. G. , Halder, T., Jaiswal, A. K., Mukherjee, A., Roy, D. & **Banerjee, A.** [2016] Large scale functional brain networks underlying temporal integration of audio-visual speech perception: An EEG study. *Frontiers in Psychology* 7:1558.
- ❖ Ghosh, S., Mukherjee, S., Sengupta, N., Roy, A., Dey, D., Chakraborty, S., Chattopadhyay, D., **Banerjee, A.** & Basu, A. [2016] Network analysis reveals common host protein/s modulating pathogenesis of neurotropic viruses. *Scientific Reports* 6:32593.
- ❖ Thakur, B., Mukherjee, A., Sen A., & **Banerjee, A.** [2016] A dynamical framework to relate perceptual variability with multisensory information processing. *Scientific Reports*:31280.
- ❖ Vattikonda, A., Raju, S.B., **Banerjee, A.**, Deco, G. & Roy, D. [2016]: Does the regulation of local excitation-inhibition balance aid in recovery of functional connectivity?

A computational account. *NeuroImage* 136:57-67.

PRESENTATIONS

- ❖ Kumar, V. G., Halder, T., Jaiswal, A., Mukherjee, A., Roy, D. & **Banerjee, A.** Large-scale functional brain network underlying perceptual variability during multisensory speech perception, IMRF, June 15-18, 2016, Suzhou, China
- ❖ **Banerjee, A.**, Kumar, V. G., Mukherjee, A., Thakur, B. Neurocognitive networks underlying multisensory perception. Japan Neuroscience Society Meeting 2016, Yokohama, Japan.
- ❖ **Banerjee, A.** Multimodal correlates of Multisensory Perception. Neuroimaging Workshop 2016, INMAS-DRDO, Timarpur, Delhi
- ❖ **Banerjee, A.** Multimodal correlates of Multisensory Perception. 3rd Bangalore Cognition Workshop 2016, IISc Bangalore.
- ❖ Ray, D., Hajare, N., **Banerjee, A.** Dual stream hypothesis of visual processing: model comparison and exploration of

functional plasticity. ACCS 2016 Meeting Gandhinagar.

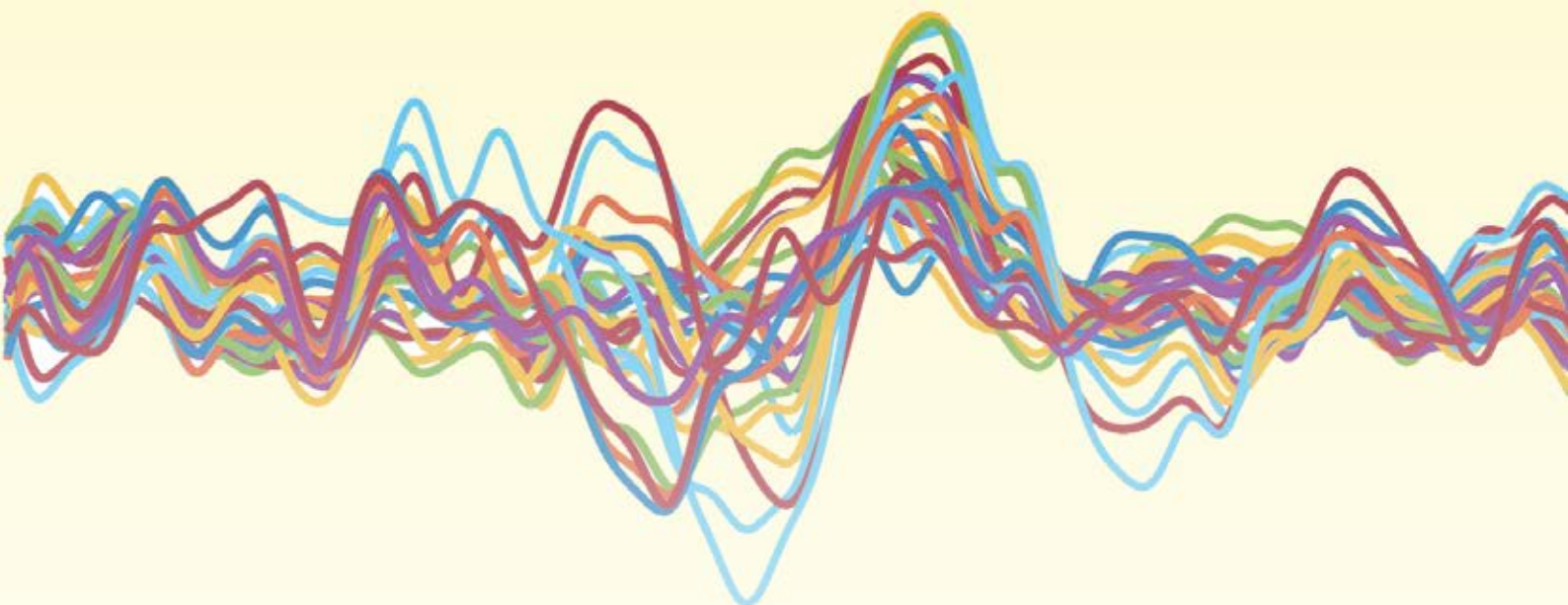
- ❖ Talwar, S. Kumar, V. G., **Banerjee, A.** Comparative Analysis of Cortical Sources Underlying P300 Complex Across Multiple Sensory Modalities. ACCS 2016 Meeting Gandhinagar.

FUNDING

- ❖ NBRC Core
- ❖ Ramalingaswami Fellowship, Department of Biotechnology
- ❖ Innovative Young Biotechnologist Award (IYBA), Department of Biotechnology
- ❖ Cognitive Science Research Fellowship, Department of Science and Technology
- ❖ National Postdoctoral fellowship, Department of Science and Technology

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Bhumika Thakur Institute for Plasma Research (IPR), Gandhinagar
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Dipanjana Roy CBCS, Allahabad



Development of novel brain signal processing toolbox 'KALPANA' for clinical application

PRINCIPAL INVESTIGATOR

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RESEARCH FELLOWS

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BACKGROUND/OBJECTIVE

To develop a user-friendly signal processing toolbox for an efficient analysis of magnetic resonance spectroscopic data to perform an absolute quantitation of neurochemicals/brain antioxidants/neurotransmitters from various brain regions. The development of such a tool shall ease the quantitation outcome with normal and clinical conditions as well as disease severity.

The Neuroimaging and Neuro Spectroscopy (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). The alarming exponential increase of this severe mental illness has catapulted the research to detect and diagnose the disease at its incipient stages. An understanding of the underlying molecular mechanisms that transform a healthy brain into a diseased condition would help us learn the causal molecular process of this disease.

Our lab is focusing on assessment and quantification of the brain pH, gamma-aminobutyric acid (GABA) and glutathione (GSH) levels in various study groups: normal healthy control (HC), mild cognitive impaired (MCI), and AD. This assessment shall not only elucidate the etiology and pathophysiology of AD but also aid in understanding the staging of AD.

GSH, a predominant brain

antioxidant responsible for neutralization of reactive oxygen species (ROS), has been correlated with cognitive impairment and emerging as a potential biomarker in AD. The impact of GABA, the chief neurotransmitter in the central nervous system (CNS) is implicated in AD but has never been correlated or quantified under clinical settings. Variations in brain pH is another indicator of the brain neuronal health and neuron degeneration and could become a potential biomarker of AD. These neurochemicals are being evaluated by proton (^1H) and phosphorous (^{31}P) MRS. Hence, for reliable outcome and enhanced signals, we have been employing MEScher-GARwood-PRESS (MEGA

PRESS) spectral editing techniques for GSH/GABA as well as specially designed ^{31}P MRS techniques for pH measurement.

Furthermore, absolute quantitation of neurochemicals from the measured MRS signals is required for meticulous processing of these small signals. Currently available software tools have limitations in terms of experimental design, processing mode and the post-processing schemes. These tools are being developed in different labs and for specific purposes. Our lab has therefore developed a novel comprehensive MATLAB-based software package called 'KALPANA' for processing, visualization and absolute quantitation of magnetic resonance spectroscopy data.

A complete framework for MRS processing using KALPANA package is given in Figure 1.

KALPANA PRESENTS THE FOLLOWING KEY FEATURES

- ❖ It allows to define and customize the preprocessing and analysis workflows using various time- and frequency-domain algorithms.
- ❖ Implementation of iterative peak fitting and baseline estimation methods allows maximizing the accuracy.
- ❖ Predefined routines optimized separately for different data types e.g. single voxel (SV), Magnetic Resonance Spectroscopic Imaging (MRSI)

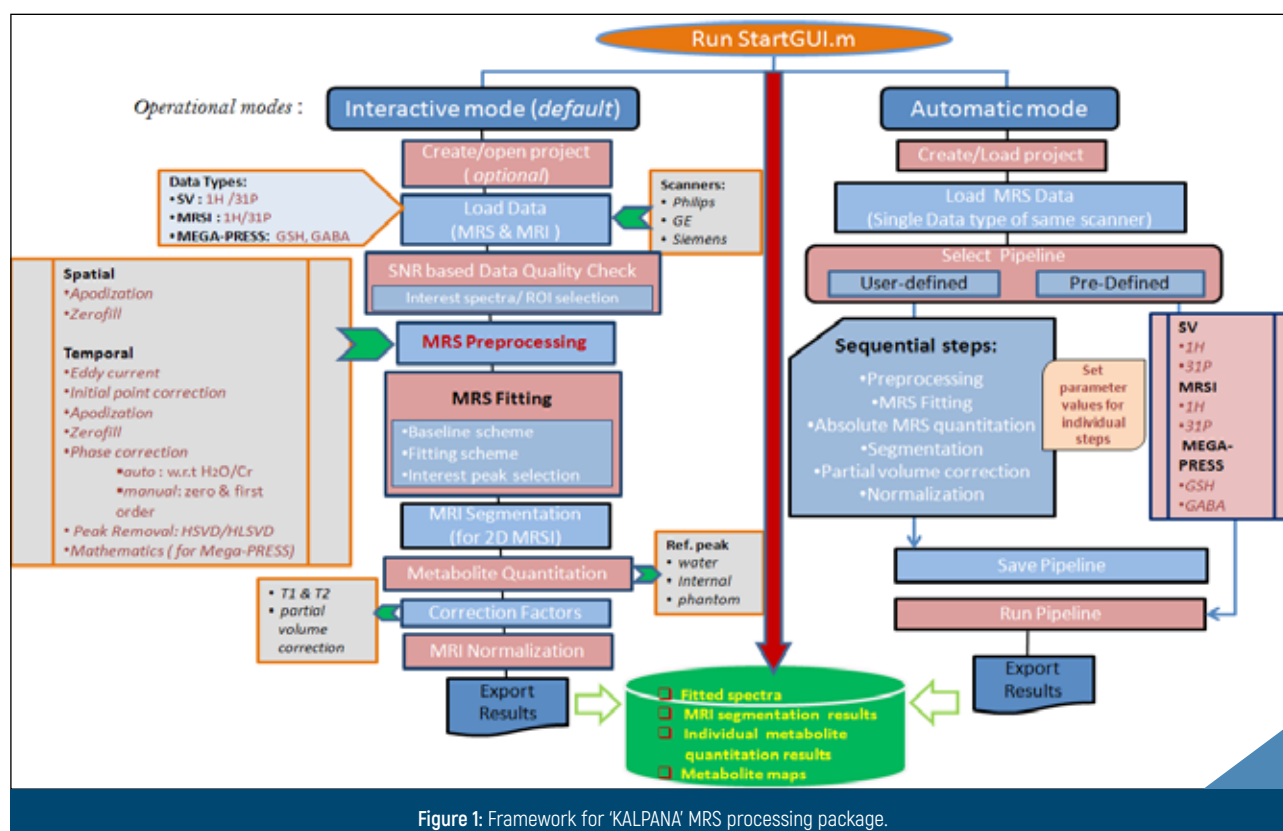


Figure 1: Framework for 'KALPANA' MRS processing package.

and MEGA-PRESS are available.

- ❖ It can efficiently process signals obtained from both ^1H and ^{31}P MRS methods.
- ❖ The package will ease the MR spectroscopy data analysis as it offers very flexible processing modes, automatic and semi-automatic.
- ❖ It has robust post-processing features as the tool provides absolute quantitation of neurochemical levels.
- ❖ It also provides an intuitive user-interface specifically tailored to meet the requirements of both clinical as well as laboratory research settings.

Validation and Testing: Our package KALPANA has been tested with simulated ^1H MR spectra with varying signal to noise ratios and baseline corrections. We have found that KALPANA achieves high quantitation accuracy as compared to the commonly used

signal processing packages, i.e. LCModel and jMRUI. The developed toolbox has been successfully employed for the data processing of both in vivo ^1H MRS spectra of brain in two published manuscripts GABA quantitation [1,2] in normal and diseased conditions.

Brain pH levels: For ^{31}P MRS clinical brain pH data obtained from healthy control, MCI and AD patients, we employed KALPANA toolbox to quantify the brain pH values and mapped them to specific brain regions (Figure 3). The pH of the brain, which is normally ~ 7.02 , was found to be alkaline in the left hippocampus regions of AD brain as compared to healthy control subjects in the same anatomical region.

Brain GABA levels: To assess regional and hemispheric differences among young healthy subjects, brain GABA concentrations were measured in vivo using ^1H magnetic resonance spectroscopy.

KALPANA toolbox was used extensively for quantitation of GABA levels. We found a significant regional dependence of GABA levels with lower concentrations in the frontal cortex (FC) as compared to both parietal cortex (PC) and occipital cortex (OC) regions. However, no significant hemispheric differences in GABA levels.

PUBLICATIONS

- ❖ **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*, (In Press).
- ❖ **Pravat K. Mandal***, Kriti Kansara and Aroma Dabas "The GABA-Working Memory Relationship in Alzheimer's Disease" *Journal of Alzheimer's disease Reports* (In Press)
- ❖ M. Grewal, Aroma Dabas, Sumiti Saharan, Peter B. Barker, Richard A.E. Edden, **Pravat K Mandal***, 'GABA Quantitation using MEGA-PRESS: Regional and Hemispheric Differences', *Journal of Magnetic Resonance Imaging*, Volume 44, no. 6, Pages 1619-1623, Dec 2016, DOI: 10.1002/jmri.25324.
- ❖ Suvarnalata Xanthate Duggirala, Sumiti Saharan, Partha Raghunathan, **Pravat K. Mandal***, 'Stimulus-dependent modulation of working memory for identity monitoring: A functional MRI study', *Brain and Cognition*, Volume 102, Pages 55-64, February 2016,

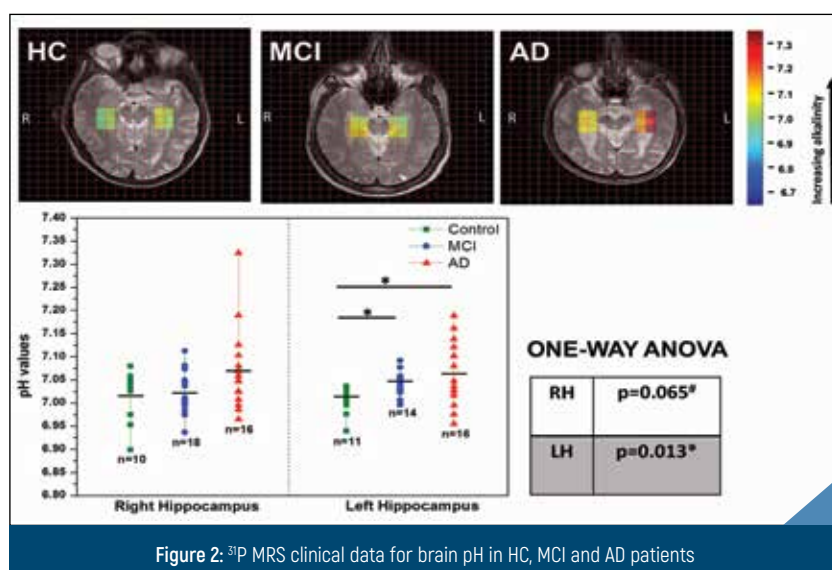


Figure 2: ^{31}P MRS clinical data for brain pH in HC, MCI and AD patients

PATENT APPLICATIONS DETAILS

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).

❖	<i>International</i>		<i>Patent</i>
	Application	No.	PCT/

IB2016/054978 dated 19th August, 2016.

- ❖ *National Patent* Application No. 20161100194 Published on 21st July 2017.

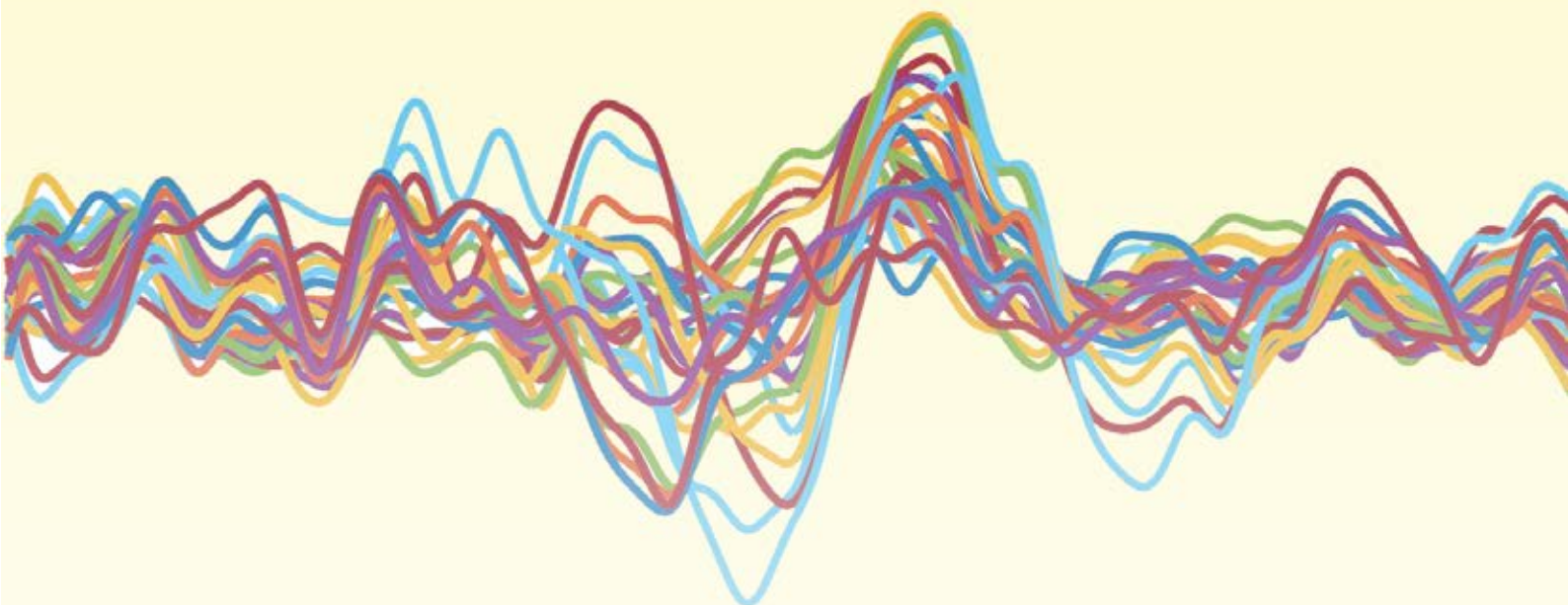
FUNDING

- ❖ Department of Biotechnology, Government of India
- ❖ Department of Information Technology, Government of India

- ❖ Department of Science and Technology, Government of India

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Spatiotemporal processing and signal transmission in brain

PRINCIPAL INVESTIGATOR

Prasun Kumar Roy

RESEARCH FELLOWS

*Vikas Pareek
Aftab Alam*

RESEARCH ENGINEER

V P S Rallabandi

An overarching issue in both basic and translational neuroscience is to comprehend how flow or transport processes occur, whether that of energy, information, current, drugs, cells or tissue displacement. The recent advance of multimodal neuroimaging, beyond simply scalar imaging, implies a broad general perspective towards pathophysiological processes, wherein one can study the various transport processes in the brain parenchyma. Hence, one needs a quantitative computational approach that can clarify, model, simulate, and predict the various transport processes and their modulation across the brain. The overall objective of this program is to obtain basic insights and translational implications, regarding the physiological or pathological change of the various transport or flow processes in the 3D spatially-extended brain tissue, that can also take into account

dynamical and plasticity processes. We pursue this aspect in the extreme ranges of age: Older age [degenerative/involuntary stage] and early age [regenerative/developmental stage].

INFORMATION FLOW AND CAUSATIVE CONNECTIVITY USING STRUCTURAL & FUNCTIONAL INTERACTION: SCREENING TEST FOR ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN CHILDREN (ADHD)

Identifying connection network among different brain regions in patients is a basic problem in neuroscience, especially for therapy planning in neurology or neurosurgery. The customary available methods assume linear interactions between regions (e.g. Granger method) or presume continuous fMRI sampling (Markovian method). However, in neuroanatomical reality, one finds that the interactions are non-linear with discrete sampling/mis-recorded latent sampling occurring

during signal acquisition from the brain. To deal with this reality, we develop a novel Hidden Markov autoregressive approach that can be applicable to situation where there is data missing. We test our approach using fMRI ground truth signals where neural connectivity has been known from anatomical studies on patients. We find that the error rate in identifying source nodes and neural connectivity by our method is only 23% and 39% of the error rate by Markovian method and autoregressive method. We then apply our technique to identify Resting state fMRI connectivity network in patients with Attention Deficient/Hyperactivity Disorder (ADHD) vis-a-vis healthy subjects of same age group [21 subjects with ADHD and 20 control subjects].

We find that our proposed method can diagnose ADHD disorder with sensitivity and specificity rates of 94% and 96% respectively (these rates for diagnosis by available methods are 72-84%), and the proposed method also can identify 9 and 6 extra source nodes/neural connectivity paths more, respectively in ADHD and healthy subjects (when compared to the paths that can be found by the standard available Granger method). Our technique also reveals the "Saliency - Network" linking the Insular vortex and the Cingular cortex, and also shows that the saliency connectivity lessens in ADHD when compared to normal (all these changes cannot be revealed by the classical Granger method). Our observation of this decline of Insular - Cingular

connectivity is validated well by collateral neuroanatomical findings of other investigators which show that there is diminution in Insular and Cingular cortical thickness and decrease in their interlinkage in ADHD. Delineating correctly the functional neural connections in the brain noninvasively by imaging, can have important application

in radioablative or neurosurgical approaches to epilepsy, the source nodes obtained by our method can accurately identify which nodes need to be ablated for arresting the seizure.

PUBLICATION

❖ Shilpa D, Chaudhry S, Lall B, Roy P. K. Learning Effective

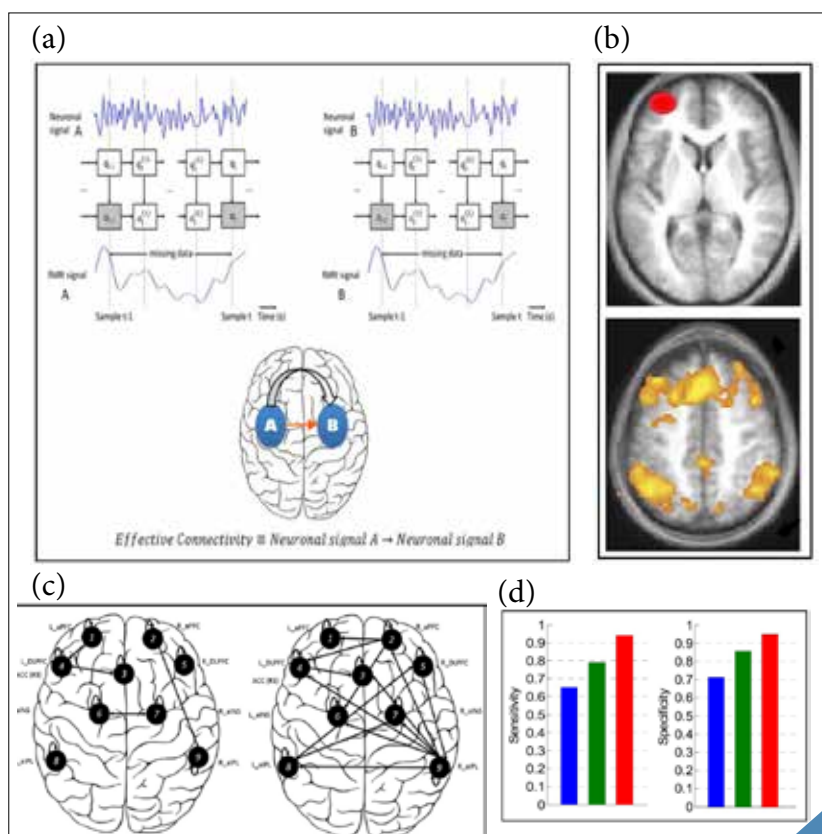


Fig. 1: [a]. Methodological Schema for delineating the interaction and directionality among brain regions under cognitive tasks.

[b]. Elucidating the actual cause-effect connectivity between different anatomical regions using Resting state fMRI signals. *Upper panel:* Reference node is shown in red. *Lower panel:* Areas correlated with node activity shown in yellow.

[c]. Attentional Deficit Hyperactivity Disorder (ADHD) paediatric patients. *Left panel:* Functional connections between anatomical nodes demarcated by the customary Granger method. *Right panel:* Connections obtained the new method developed. Note the extra functional connections obtained by the new method, the majority of the new connections have validation by invasive methods in literature.

[d]. Utilizing the actual connectivity method developed for diagnosis of ADHD patients from controls. Note the increased specificity and sensitivity rate for this method when compared with conventional connectivity analytics [Red: Rate for proposed method developed. Blue: Granger method. Green: Modified Granger method].

Connectivity from fMRI using Autoregressive hidden Markov model with missing data, *J. Neuroscience Methods*, 278, 87-100, 2017.

- ❖ Shilpa D, Chaudhry S, Lall B, **Roy P. K.** Dynamic Programming of High-order Dynamic Bayesian Networks for Identifying Effective connectivity in Brain. *J. Neuroscience Methods*. 285, 33-44, 2017.
- ❖ Shilpa D, Chaudhry S, Lall B, **Roy P. K.** Autoregressive Hidden Markov Model with Missing Data for Modelling fMRI Data, *Proc. Computer Vision & Image Processing*, 2016. DOI: 10.1145/3009977.3010021
- ❖ Alam A, Rallabandi V, **Roy P. K.** Systems biology of Immunomodulation for post-Stroke Neuroplasticity: Multimodal implications for Pharmacotherapy and Neuro-rehabilitation, *Frontiers in Neurology*, 7[94], 1-16, 2016 (showed as accepted last year).

PRESENTATIONS

- ❖ Pareek V. Tissue Mechanisms Involved in Recovery of Traumatic Brain Injury and its Validation using Diffusion Tensor Imaging (DTI), International Neuro-Trauma Workshop, All-India Institute of Medical Sciences (AIIMS), New Delhi, Aug. 2016.
- ❖ Kapoor, S. Endogenous plasticity mechanisms as therapy for Stroke. Annual Meeting of Japanese Neuroscience Society, Yokohama, Japan, July 2016.
- ❖ **Roy, P. K.** Neuroinformatics in India, Council of Training, Infrastructure and Science in Neuroinformatics, University of Reading, Reading, U.K., Sept. 2016.

FUNDING

Tata Innovation Award Fund.

Dept. of Electronics & Information Technology, Govt. of India.

COLLABORATORS

- ❖ Dr Jyotirmoy Bannerjee & Dr

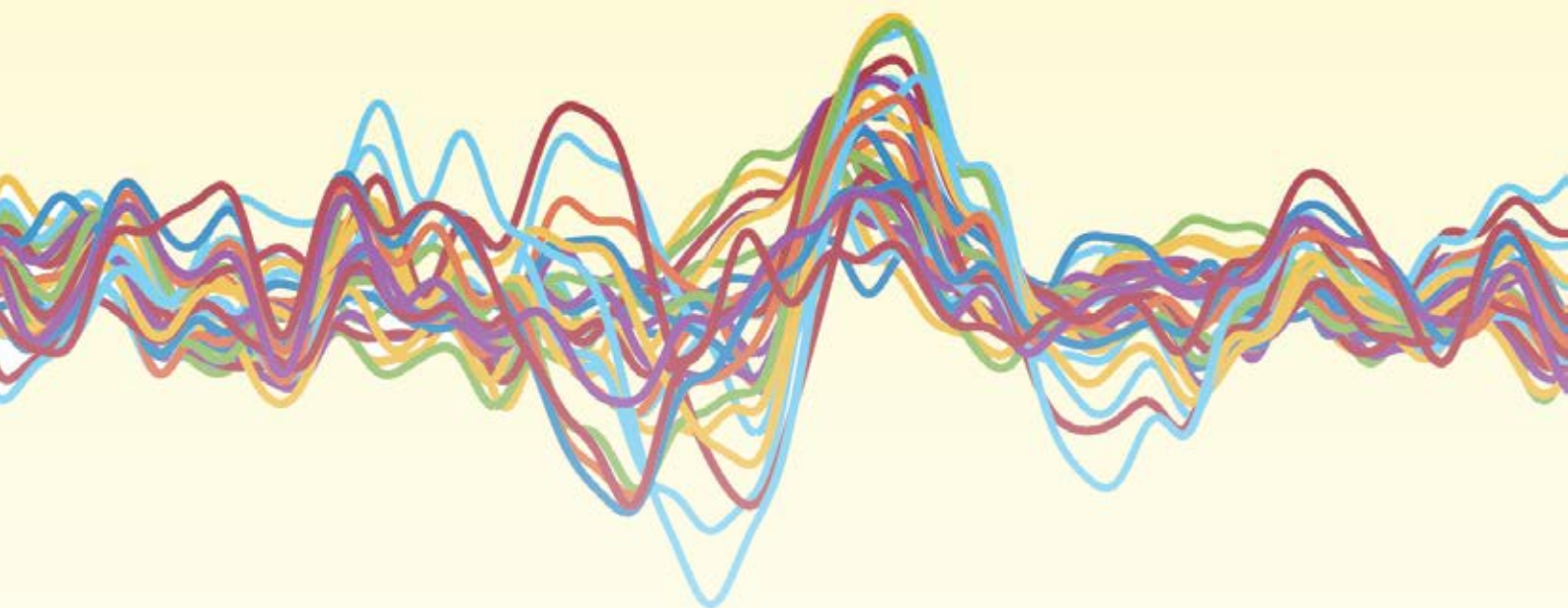
Aparna Dixit, Epilepsy Centre, NBRC.

- ❖ Dr Alan Evans, Montreal Neurological Institute, McGill University
- ❖ Dr. P Sarat Chandra & Dr Manjari Tripathi, All-India Institute of Medical Sciences, Delhi.
- ❖ Dr Ralph Martins, Edith Cowan University & CRC Mental Health Instt., University of Melbourne.
- ❖ Dr Sashibala Singh & Dr Sunil Hota, Defense Research & Development Organization, Delhi.

AWARDS

Pareek V, Training Program Fellowship Award, International Brain Research Organization, School on Neuroinformatics & Brain Network Analysis. Petronas University of Technology, 2017.

Alam A. Team project awarded Best Presentation prize. Route 28 Workshop on Adult Neurogenesis - Frauenchiemsee, Munich, 2016.



Stochastic activation and stability analysis for brain imaging & therapy

PRINCIPAL INVESTIGATOR

Prasun Kumar Roy

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*Suhela Kapoor
Vikas Parekh*

RESEARCH ENGINEER

Rajiv Ramaswamy

A challenging objective in applied neuroscience is the enhancement of the efficiency of clinical performance, such as that of neuroimaging processes, whether diagnostic or therapeutic. An innovative approach is afforded by the process of perturbation-induced activation, an emerging research field in computational neuroscience and biomedical engineering. This methodology of stochastic activation, noise-aided resonance or fluctuation-induced diffusion, is a general principle of nonlinear behaviour applicable to various systems, whether physical or biological, and takes place basically due to the statistical kinetic nature of the components that exhibits probabilistic fluctuations of parameters. The practical utility of the principle of stochastic diffusive activation (e.g. diffusion MRI) is yet to be fully utilized

for diagnostic or therapeutic neuroimaging. Probing the feasibility of such applications is the aim of our program.

NEW COLLATERAL NETWORK FORMATION IN THE AGEING HUMAN BRAIN AS A COPING NEUROPROTECTIVE MECHANISM: MYELINATION AND GENDER DIFFERENCES

As the brain journeys across the life-span progression, we aim to study the relationship between Micro-scale integrity and Macro-scale integrity. These two integrity processes are respectively white matter's molecular diffusivity indices (MDI) and integrated white matter volume (WMV). We investigate the Microscale ↔ Macroscale interaction, along each the individual's development and ageing process, by studying diffusion scans of 292 normal subjects, 20-95 years age. We observed that Fractional Anisotropy (FA) in the young

was higher than the middle aged, especially in regions of superior corona radiata and corpus callosal body. We correlate this age-induced transition due to the process of white fibre-based migration of neuronal progenitor cells and synchronized interhemispheric development in the young. Furthermore, we found that the number of connected network per anatomical node region maximizes at the 6th decade for men and the 7th decade for women, the number of connected networks are less in younger age as well as in older age. This study is an innovative endeavour to investigate of the interaction between Microscale integrity and Macroscale integrity of brain whilst ageing-induced neurodegeneration occurs.

Unexpectedly, we observe an inverted-U trend (optimal parabolic model) for fractional anisotropy in males as ageing occurs. However in females, we note a monotonic decreasing trend with ageing. We elucidate that, in males, the maximization in fibre anisotropy and relative conduction during middle-age corroborates with increased oligodendroglial myelination process in mid-life (5th decade), in other words there is a peaking of the myelination process in middle aged men. Nevertheless, in females there is anatomical evidence of less intensity of myelination in mid-age (due to hormonal transition during the menopausal process), hence the peaking of myelination or of AxD does not occur robustly. The formation of new connected but spatially-

separated networks in advanced age shows that the brain's intrinsic neuroplasticity takes recourse to distributed transmission of information (spatial multiplexing) across several channels as a novel information transmission strategy, so as to cope against the onslaught of senile neurodegenerative changes that occurs in the fibres as ageing occurs.

PUBLICATIONS

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- ❖ Subhadip Pal, **Roy, PK.** The consequence of day-to-day

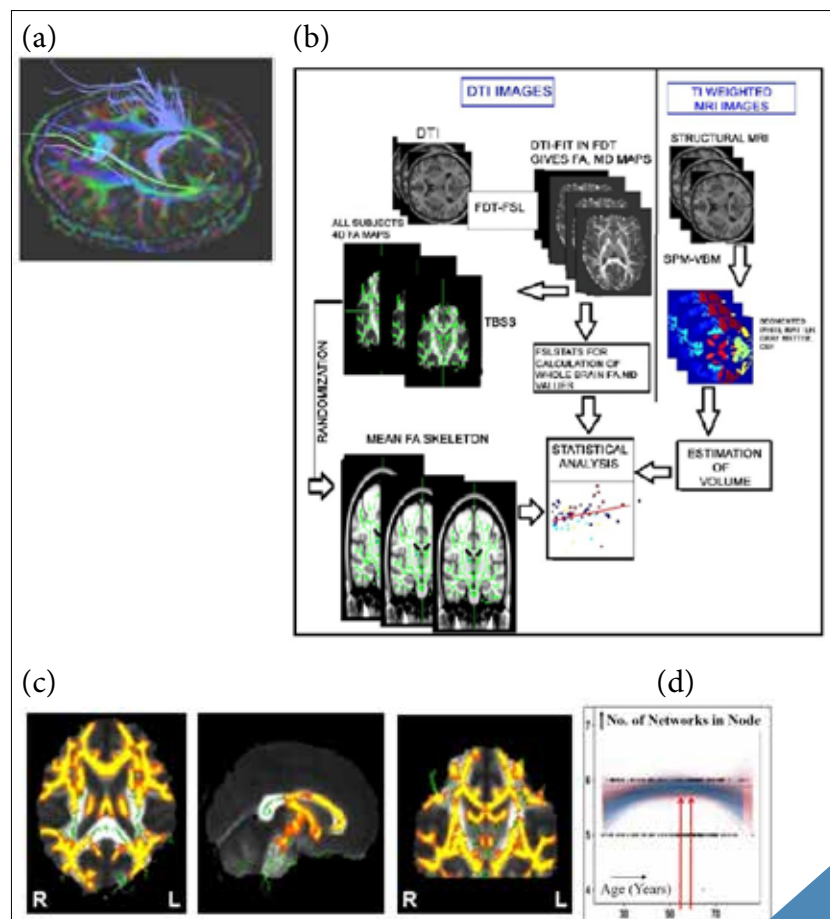


Fig. 2: (a):Diffusion Tensor Imaging motif of brain.

(b) Development of the Image Processing pipeline for performing the connectomics analysis

(c) The red coloured areas shows the brain regions that have more connectivity efficiency and myelination in the older age than in younger age.

(d) The average number of connected network per anatomical node region of the brain maximizes at the 6th and 7th decade for males and females respectively (brown and blue coloured graphs), whilst the ageing processes occurs.

stochastic dose deviation from planned dose in fractionated radiation therapy, *Mathematical Biosciences and Engineering*, 13 (1), 159-170, 2016 (mentioned as accepted last year).

PRESENTATIONS

- ❖ Rathee, R. Structural Integrity Changes of the Brain in Healthy Aging, Workshop on Imaging the Brain and Behaviour. Indian Institute of Technology - Delhi, July 2016.
- ❖ Kapoor, S. A multidisciplinary systems approach to

neural remodeling post ischaemic stroke injury using endogenous adult neural stem cells, Int. Conf. Cerebral Blood Flow & Metabolism: Brain & Brain PET 2017, Berlin, Jan 2017.

FUNDING

Tata Innovation Award Fund.

Dept. of Electronics & Information Technology, Govt. of India.

COLLABORATORS

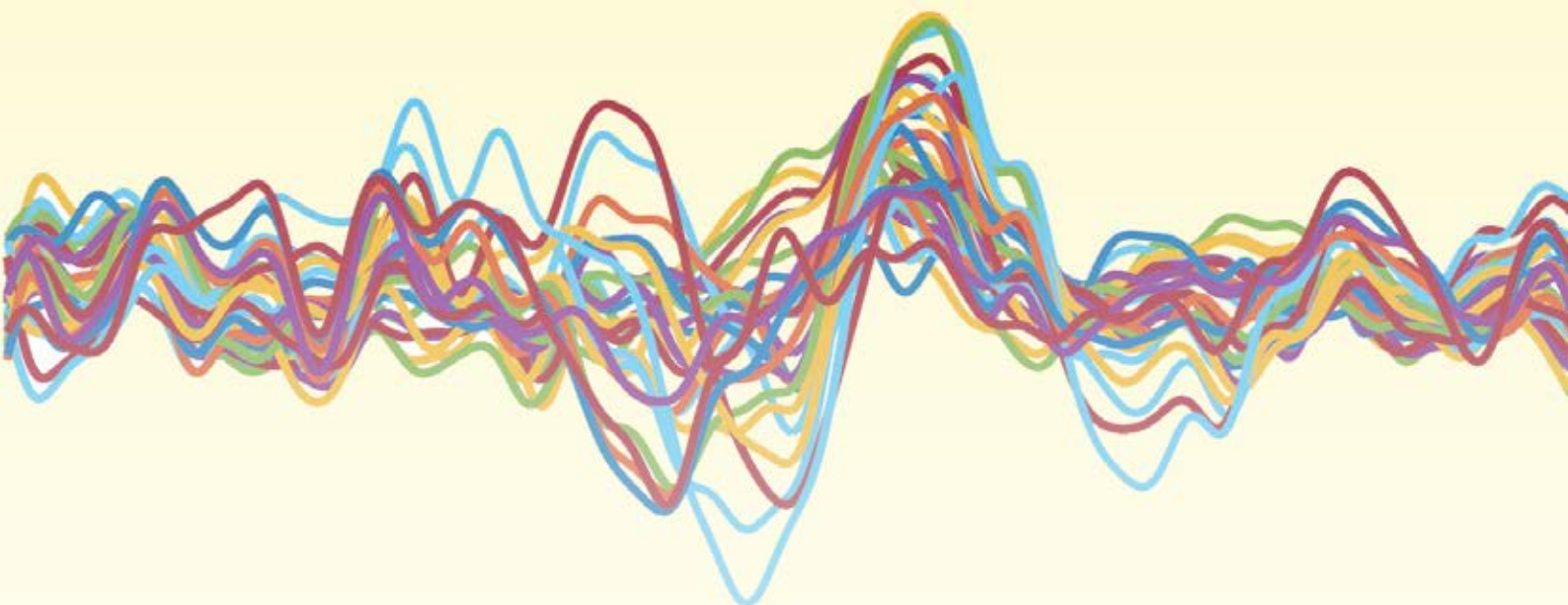
- ❖ Dr. Anirban Basu & Dr. Partha Raghunathan, National Brain Research Centre.
- ❖ Dr. Peter Luijten, Dutch Centre

for Translational Molecular Medicine & Utrecht University.

- ❖ Dr. M. V. Padma & Dr. T. S. Roy, All-India Institute of Medical Sciences, Delhi.
- ❖ Dr. Santanu Chaudhuri and Dr. Raj Khanna, Indian Institute of Technology - Delhi.
- ❖ Dr. Shinjini Bhatnagar, Translational Health Science & Technology Institute, Gurgaon.

AWARDS

Kapoor S, Japanese Neuroscience Conference, Travel Fellowship Award, Yokohama, 2016.



Microstructural anatomical differences between bilinguals & monolinguals

PRINCIPAL INVESTIGATOR
Nandini Chatterjee Singh

RESEARCH FELLOW
Archith Rajan

BACKGROUND

Bilingualism is a global phenomenon (Grosjean, 2010). There is therefore much interest in understanding how bilingualism affects brain and cognitive development including functional and structural neural plasticity (Bialystok et al, 2012). While past research has shown that bilingual and monolingual speakers differ in gray matter volume (GMV) (Mechelli et al., 2004) comparatively less research has explored changes in the brain's wiring/roadmap; namely the white matter (WM) fibre bundles that connect different gray matter regions, facilitating communication and the formation of structural and functional networks. White matter microstructure is estimated through measures of fractional anisotropy (FA) and mean diffusivity (MD). While FA is a measure of tract integrity, MD has emerged as a measure of tract geometry. In particular, MD has been postulated to reflect tissue changes such as astrocyte swelling,

synaptic changes, dendritic spine changes and angiogenesis that have been attributed to neural plasticity.

Our goal was to compare white matter geometry between bilingual and monolingual adults. Detailed information about diffusivity, requires, in addition to MD, two other measures of water diffusion namely axial diffusivity (AD) and radial diffusivity (RD) (Mori & Zhang, 2006). Higher AD values reflects greater ellipsoidal relative to spherical geometry whereas higher RD values reflect faster diffusion of water molecules (Mori & Zhang, 2006).

METHODS

Participants were eighteen early Hindi-English female bilingual speakers (mean age and SD: 23.94 ± 1.5 years) and eighteen female monolingual Italian speakers (mean age and SD: 23.45 ± 2.1 years). Bilingual participants were recruited from a tertiary institution in Delhi and monolingual

participants were recruited from a tertiary institution in Milan. Participants were matched for age, level of education, handedness and socio-economic status. All bilingual speakers spoke Hindi as their L1 and English as L2. Bilingual participants were residing in the National Capital Region of India (New Delhi) and were proficient in reading, writing and conversation in Hindi and English and with similar educational backgrounds. The study was approved by the Ethics Panels of the National Brain Research Centre, India and University of San Raffaele, Milan.

DATA ACQUISITION

DTI images from all participants were transferred to a workstation and checked for motion artifacts

and basic preprocessing like eddy current distortion correction and brain extraction were done. Using FMRIB's diffusion toolbox (FDT), a diffusion tensor was fitted onto corrected images using FDT toolbox to generate diffusion image maps with eigenvalues (λ_1 , λ_2 , and λ_3), fractional anisotropy (FA) and MD, $AD \lambda_{||} = \lambda_1$, $RD (\lambda_{\perp} = (\lambda_2 + \lambda_3)/2)$. Tract-based spatial statistics (TBSS) method (Smith et al., 2006) were employed, wherein the nearest most relevant tract centre in spatially normalized DTI images for each participant is projected onto a skeleton containing the centre of all major tracts that are common to all participants; thereby allowing voxel-wise statistics to be carried out at tract centres

only, thus minimizing the effect of misregistration. Maps of all DTI measures were then generated for voxel-wise statistical analysis comparisons. Significant group differences were projected as cluster voxels with different colors for the purpose of illustration.

Figure1: TBSS results showing group differences (BL > ML) in mean diffusivity (MD) (red), radial diffusivity (RD) (yellow), axial diffusivity (AD) (blue), expressed in 1-P values ($p=0.05$, corrected) and overlaid onto MNI152 template. BL=Bilinguals, ML=Monolinguals.

RESULTS AND CONCLUSIONS

Tract Based Spatial Statistics revealed higher mean MD for bilinguals in forceps minor and

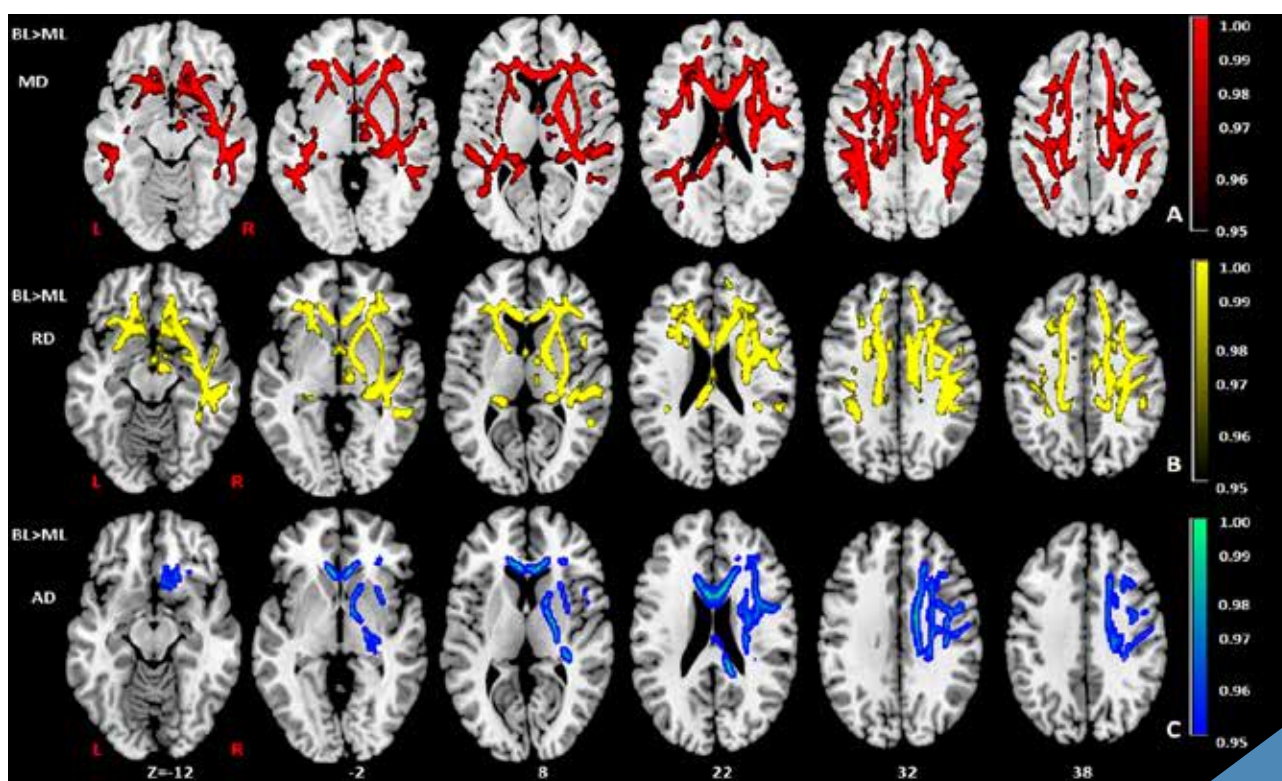


Figure 1 - TBSS results showing group differences (BL > ML) in mean diffusivity (MD) (red), radial diffusivity (RD) (yellow), axial diffusivity (AD) (blue), expressed in 1-P values ($p=0.05$, corrected) and overlaid onto MNI152 template. Superior Longitudinal Fasciculus (SLF) and forceps minor (FM) in the right hemisphere have also been indicated. BL=Bilinguals, ML=Monolinguals

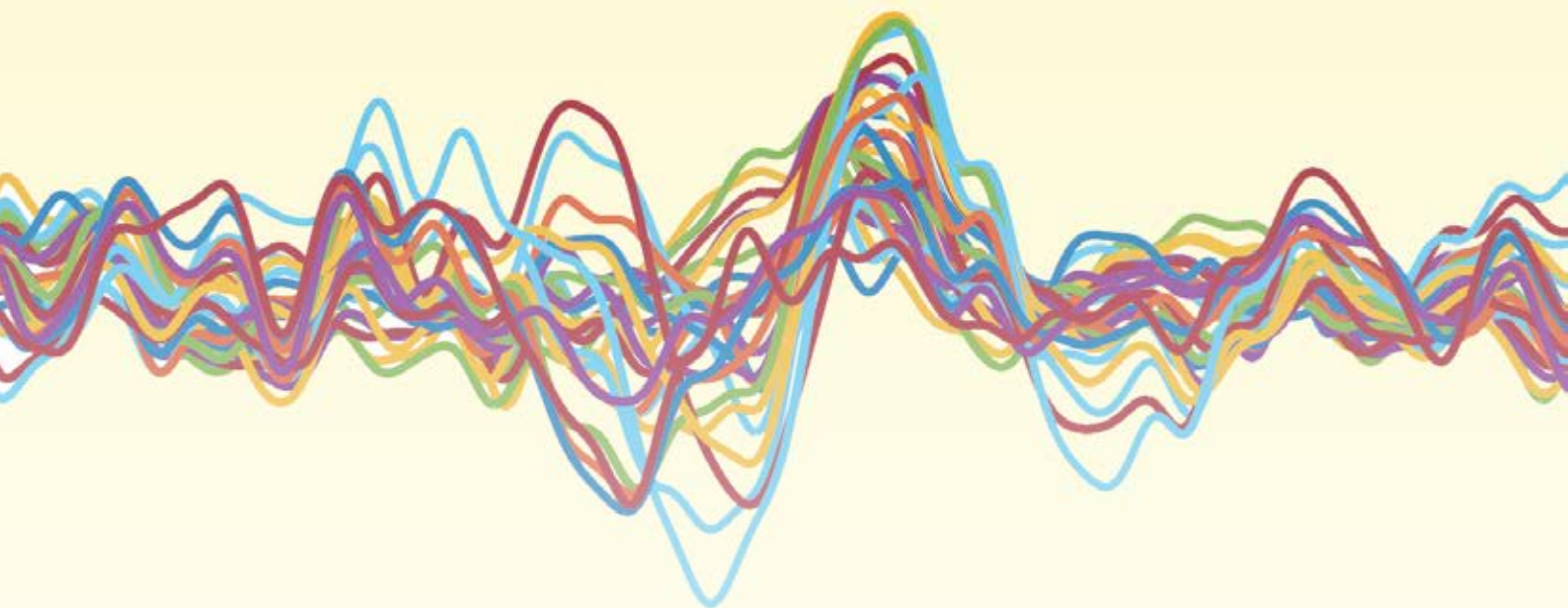
bilateral Superior Longitudinal Fasciculus (SLF). (Figure 1, Panel A). Bilinguals also had higher mean RD in forceps minor, right SLF, Inferior Longitudinal Fasciculus (ILF) and the right anterior thalamic radiation (Figure 1, Panel B) and higher mean AD in forceps minor, right SLF and right anterior thalamic radiation (Figure 1, Panel C). Comparisons between monolingual and bilingual speakers (Monolingual > Bilingual) found no significant differences in mean MD, RD or AD ($p > 0.05$). We postulate that higher MD and RD in forceps minor and SLF reflects cognitive control used to balance the non-overlapping sets

of articulatory gestures in regular discourse for bilingual speakers. The higher mean AD, RD and MD reflects differences in diffusion of water molecules in specific white matter tracts including the forceps minor and right SLF and is a consequence of the neuroplasticity that is necessarily generated by the linguistic load for bilingual discourse. According to our hypothesis, we can expect differences in SLF for bilingual speakers to be correlated with the complexity of the articulatory repertoire of multilingual individuals, as in related studies showing increased grey matter

volume in regions that are necessary for articulation for bilingual speakers (Abutalebi et al., 2013). Our study suggests that language environments shape the brain into myriad and diverse structures.

LONG TERM GOALS

Our long term objective is to not only integrate analysis of white matter organization in our imaging studies but to also conduct longitudinal studies that allow us to assess how short term and long term neuroplasticity emerges in learning.



Investigating emotional responses to ragas across cultures

PRINCIPAL INVESTIGATOR
Nandini Chatterjee Singh

SENIOR RESEARCH FELLOW
Avantika Mathur

BACKGROUND

Communication of emotions is crucial to social relationships and survival (Eckman, 1992). Besides facial expression, the two modalities that are often regarded as effective means of emotional communication are vocal expression and music that rely on acoustic signals for their transmission of messages. Neuroimaging studies in our laboratory have shown that children with autism respond more typically to music as opposed to speech. Given that emotion processing in faces and voices is impaired in children with autism our long term objective is to investigate how emotion contagion as applied music, is processed in children with autism. In view of the cultural setting of India, we focused on understanding emotion processing using

Indian Classical ragas as stimuli.

In Indian classical music, ragas constitute specific combinations of tonic intervals potentially capable of evoking distinct emotions. A raga composition is typically presented in two modes, namely, *alaap* and *gat*. *Alaap* is the note by note delineation of a raga bound by a slow tempo, but not bound by a rhythmic cycle. *Gat* on the other hand is rendered at a faster tempo and follows a rhythmic cycle. Our primary objective was to (1) discriminate the emotions experienced across *alaap* and *gat* of ragas, (2) investigate the association of tonic intervals, tempo and rhythmic regularity with emotional response.

Our first study focused on investigating the characterizing the different emotional responses elicited by different

ragas. We showed that (1) different ragas elicit distinct emotions across the two presentation modes, namely 'alaap' and 'gat' (2) specific tonic intervals are robust predictors of emotional response. (3) Tonality determines the emotion experienced for a raga whereas rhythmic regularity and tempo modulate levels of arousal.

(Emotional responses to Hindustani raga music: the role of musical structure, Avantika Mathur, Suhas H. Vijayakumar, Bhismadev Chakrabarti and Nandini C Singh, Frontiers in Psychology (Emotion Science), 2015

The second part of this study has focused on studying

emotion perception across different cultures. While, a comparison between enculturated (Indian) and non-enculturated (non-Indians) participants indicate similar emotional responses to ragas, factor analysis revealed cultural differences amongst the two populations in the way emotion labels were grouped together, in that, 'longing' was grouped with 'negative' factor (i.e. sad, tensed and angry emotions) by enculturated individuals whereas it was grouped with 'positive' factor (i.e. happy, romantic, calm, devotional) by the non-enculturated group. A correlation analysis between acoustic features and emotional responses revealed that non-

enculturated participants relied more on cues of rhythm (tempo, attack time, pulse clarity and event density) and tonality (minor/major ratio) as compared to enculturated participants. Further, within the same mode of the raga (gat in this case) we found that participants with musical expertise irrespective of culture relied significantly on tonality cues for emotion experienced.

Our results suggest that the recognition of emotions in music relies on two factors namely (1) the existence of psychoacoustic cues that are employed in similar fashion across cultures to convey emotions and (2) culture specific cues that supplement psychoacoustic

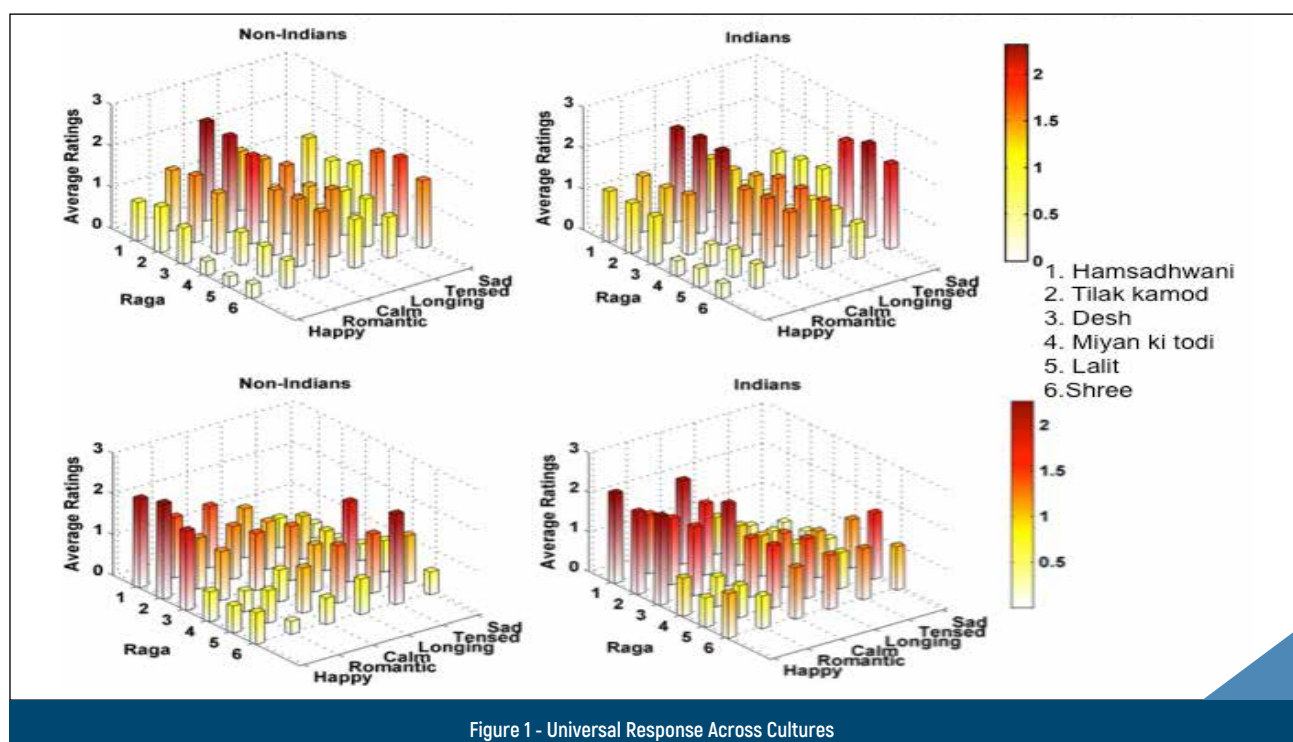


Figure 1 - Universal Response Across Cultures

cues to determine the affective character of unfamiliar music.

Further work is focused on investigating the cortical circuits underlying such emotion perception in music.

PRESENTATIONS

- ❖ Invited talk on 'The Rasa in the raga – characterising emotion in Indian Classical Music', Plenary lecture at Presidency College, Kolkata, India, March 2016.
- ❖ Invited talk on 'The development of *language specific* reading networks in biliterate bilinguals, International Conference on Language', University of Hyderabad, March 2016.
- ❖ Invited talk 'Screening and assessment of dyslexia in India', Un Learn workshop, UNESCO Mahatma Gandhi Institute of Education for Peace and Sustainable Development, IIT New Delhi, April [2016].
- ❖ Invited talk on 'Dyslexia Assessments in Indian Languages', Dyslexia Association of Singapore, June 2016
- ❖ Invited talk on 'The biliterate reading brain – implications for classroom and dyslexia', National Centre of Educational Research and Training, New Delhi, November 2016.
- ❖ Invited talk on Literacy, Global Literacy Meet at Yale University, New Haven, Connecticut, USA, December 2016.

PUBLICATIONS

- ❖ A role for putamen in phonological processing in children, Sarika Cherodath, Chaitra Rao, T. Sumathi, Rashi Midha and **Nandini C Singh**, Bilingualism: Language and Cognition, (in press), 2016.
- ❖ Reading skills in children provided simultaneous

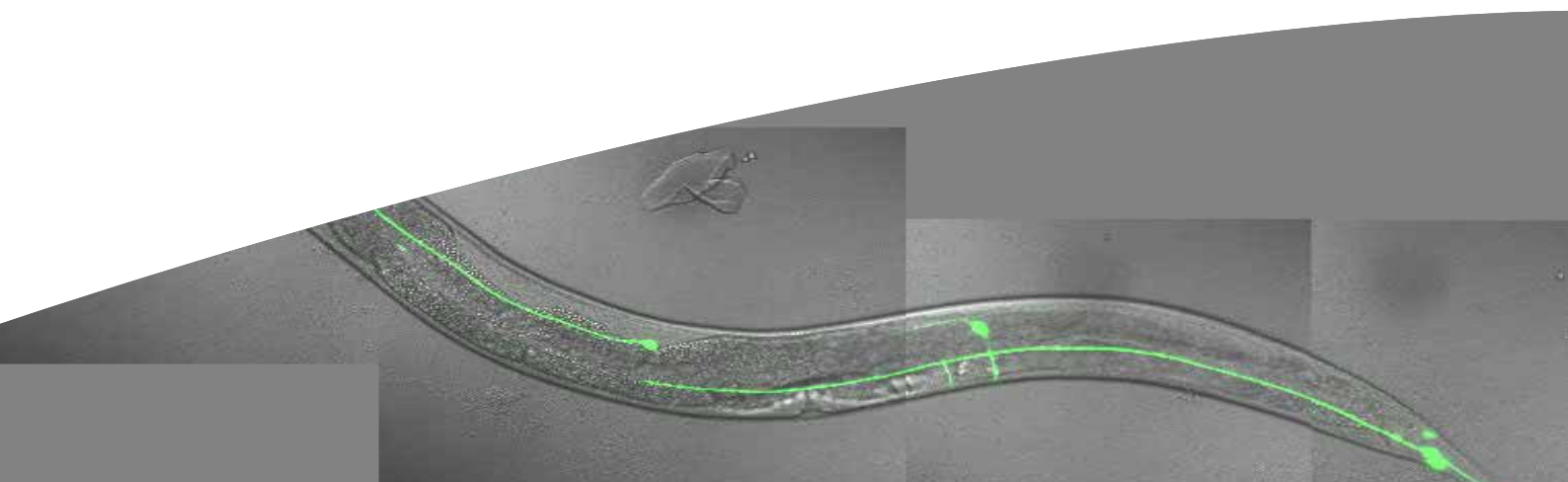
instruction in two distinct writing systems - Insights from behaviour and neuroimaging, **Nandini C Singh**, Sarika Cherodath, T A Sumathi, R. Koseira, K. Currawala, B. Kar, G. Oberoi, Multilingualism, Literacy and Dyslexia: Breaking Down Barriers for Educators (2016)

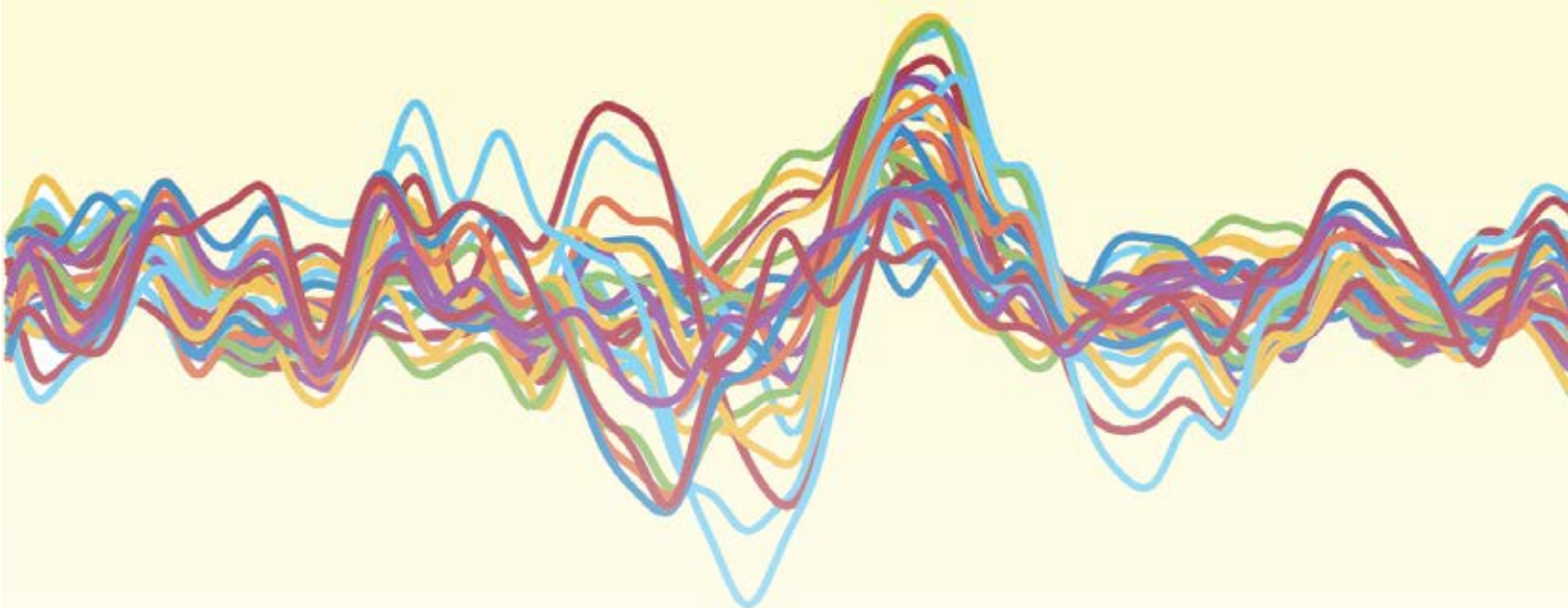
FUNDING

"Deciphering the cognitive and neural mechanisms underlying auditory learning in: the general population, musicians, and individuals with dyslexia,"- co-investigator with Dr. Robert Zatorre of McGill University, and Dr. Merav Ahissar of Hebrew University of Jerusalem, Canadian Institutes of Health, Canada.

The neurobiology of dyslexia: integrating brain and behaviour, Principal Investigator, Department of Science and Technology, Govt. of India.

Publications, Patents & Presentations





Publications

1. M Nain, S Mukherjee, S Karmakar, A Paton, J Paton, M Abdin, A Basu, M Kalia, and S Vрати [2017] GRP78 is an important host-factor for Japanese encephalitis virus entry and replication in mammalian cells. *Journal of Virology*, Feb 28; 91(6). pii: e02274-16.
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3. S Mukherjee, N Singh, N Sengupta, M Fatima, P Seth, A Mahadevan, S K Shankar, A Bhattacharyya, A Basu [2017] Japanese encephalitis virus induces human neural stem/progenitor cell death by elevating GRP78, PHB and hnRNPC through ER stress. *Cell Death & Disease*; 8(1):e2556.
4. P Mall, A Verma, A Basu, Chandrakanta, S F Khan, A Jain, P Tripathi, S Jain, A Parihar, R Kumar [2016] Clinical and magnetic resonance imaging features in survivors of acute encephalitis syndrome in Uttar Pradesh, India. *Curr Pediatr Res* 2016; 20 (1&2): 245-249.
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REVIEW

A Basu, and K Dutta (2017) Recent advances in Japanese encephalitis. *F1000Res*. 2017 Mar 13;6:259.

COMMENTARY

S Ghosh, and A Basu (2016) Acute Encephalitis Syndrome in India: The changing scenario. *Ann Neurosci* 2016; 23:131-133.

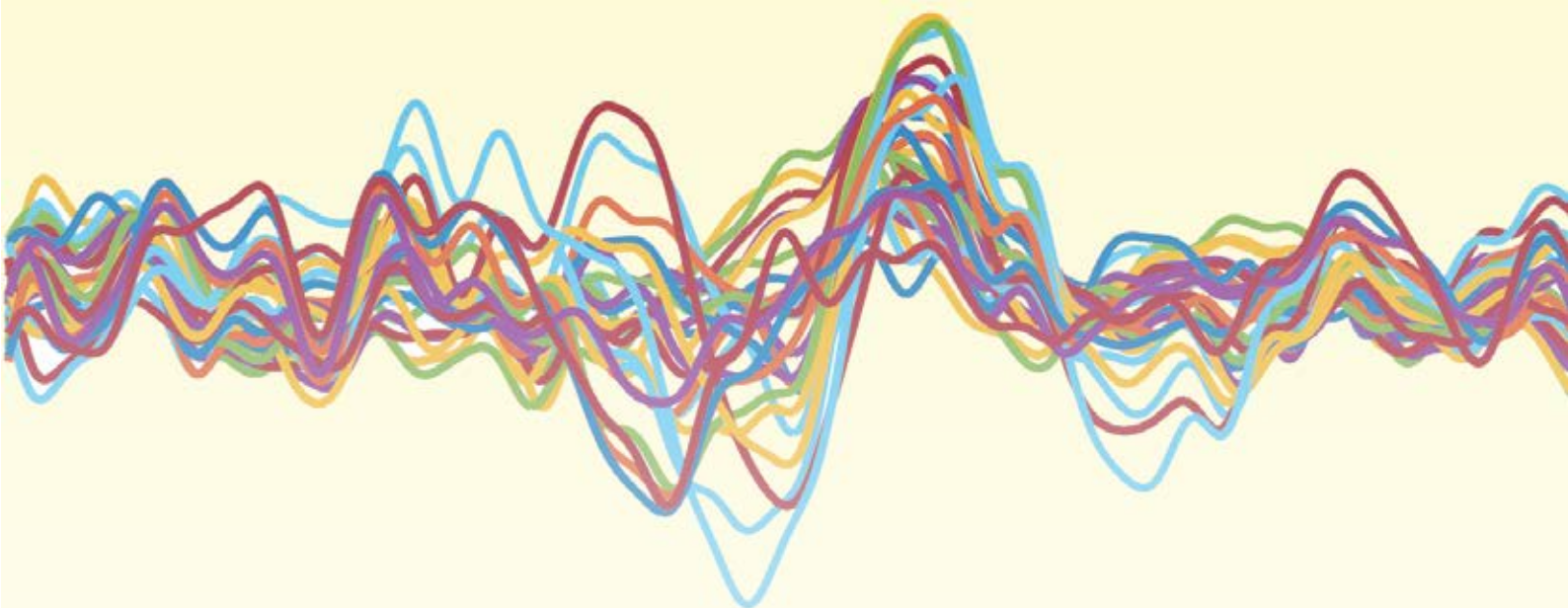
BOOK CHAPTER

M. Tewari and P. Seth (2016). Astrocytes in Neuroinflammation and Neuronal Disorders: Shifting the focus from neurons. In: *Inflammation: the Common Link in Brain Pathologies*. Springer Eds. NR Jana and A. Basu; pp 43-70, 2016.

PATENT

Pravat 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. *Pushpa Kumari, Balakumar Srinivasan and Sourav Banerjee* "A novel non-canonical function of E3 ubiquitin ligase in synapse formation" Janelia Farm / HHMI meeting on Molecular mechanisms at the synapse : Experiments and Modelling, USA, May, 2016
2. *Balakumar Srinivasan and Sourav Banerjee* "Burn your fat: Glial control of high fat diet induced modulation of feeding circuitry" Asia Pacific Society for Neurochemistry Annual Meeting, Kuala Lumpur, Malaysia, August 2016.
3. *Sarbani Samaddar and Sourav Banerjee* "Creative Destruction: Regulation of synaptic plasticity by selective degradation of miRNAs at the synapse" WE-Heraeus-Seminar on Neuronal Mechanics, Physikzentrum Bad Honnef, Germany, August 2016.
4. *Pushpa Kumari, Balakumar Srinivasan and Sourav Banerjee* "A novel non-canonical function of E3 ubiquitin ligase in synapse formation" Bangalore Microscopy Course, Bangalore, September 2016.
5. *A Basu* [2017] Neural stem/progenitor cell response to Japanese encephalitis virus infection. Microbial Pathogenesis, UGC-SAP, Dept. of Microbiology, DU South Campus. 23rd January, 2017
6. *A Basu* [2016] Insights into the neural stem/progenitor cell response to Japanese encephalitis virus infection. INDO-US Symposium on CNS Viral infection, 14-17th Nov, 2016, Sinclairs Retreat Dooars, Chalsa, West Bengal.
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8. *A Basu* [2016] HSP60 Plays a Regulatory Role in IL-1 β Induced Microglial Inflammation via TLR4-p38 MAPK Axis. July 17-21st, IUBMB 2016, Vancouver, BC.
9. *A Basu* [2016] Deciphering Mechanism of Neuronal Death in Chandipura Virus (CHPV) Infection: From Molecules to Network. Biology and Pathogenesis of Virus; Microbiology and Cell Biology Department, IISC, Bengaluru, 20-21st June, 2016.
10. *Himakshi Sidhar and Ranjit Kumar Giri*®, Curcumin-mediated induction of proapoptotic Bex genes is associated with apoptosis in mouse neuro 2a neuroblastoma cells and involves activation of p53. First International Conference on Nutraceuticals and Chronic Diseases, Sep 9-11, 2016, Cochin, Kerala, India. [© Corresponding Author.]
11. *N. R. Jana*. Altered protein homeostasis and neuronal dysfunction in Huntington's disease. International Symposium on Neurodegenerative Disorders (ISND2017), NIMHANS, Bengaluru, March, 2017.
12. *N.R. Jana*. Huntington's

- disease: Genetics and Pathogenic mechanisms. International Conference on Neurodegenerative Disorders (NDD2017), Kolkata, February, 2017.
13. *N. R. Jana*. Impaired protein homeostasis and its rescue in a mouse model of Huntington's disease. International Symposium of Molecular Signalling (ICMS2017), Chennai, January, 2017.
14. *N. R. Jana*. Proteostasis impairment in Huntington's disease, Annual meeting of the Indian Academy of Neurosciences, NBRC, Manesar, October, 2016.
15. *N.R. Jana*. Impairment of protein homeostasis in Huntington's disease. All India Cell Biology Conferences, Jiwaji University, November, 2016.
16. *N.R. Jana*. Popular talk at several undergraduate colleges (Midnapore College, Goaltore College, RNLK Women's College at West Bengal) and Universities (Dibrugarh University, Tezpur University, Vidyasagar University).
17. *Anindya Ghosh Roy*: "Restoration of Functional Connectivity After Neuronal Injury" in CUSAT-NUS Joint International Conference on Biotechnology & Neuroscience at Cochin during 19-21st December, 2016
18. *Anindya Ghosh Roy*: "A genetic screen for mutants affecting neuronal polarity" in C. elegans discussion meeting organized by TIFR-Mumbai during 10-11 Feb, 2017
19. *Anindya Ghosh Roy*: "Restoration of Functional Connectivity After Neuronal Injury" in 21st International C. elegans Meeting being held June 21-25, 2017 at UCLA.
20. *Dharmendra Puri, Anindya Ghosh Roy*: "Regulation of neuronal microtubule cytoskeleton" in 21st International C. elegans Meeting being held June 21-25, 2017 at UCLA.
21. *Ellora Sen*. Link between pentose phosphate pathway and telomerase activity in Glioblastoma. IUBMB 18th July 2016, Vancouver (Invited Talk)
22. *Ellora Sen*. SIRT6 regulates Hexokinase 2 expression and its function. IUBMB 20th July 2016, Vancouver (Invited Talk)
23. *Ellora Sen*. Unraveling the link between dysregulated metabolism and telomerase in glioma. ISNOCON, Hyderabad, April 2016
24. *Ellora Sen*. Decoding metabolic programming in glioblastoma. Indian Association of Cancer Research, New Delhi, April, 2016
25. *Ellora Sen*. Dysregulated metabolism in glioblastoma: Involvement of telomerase. NIMHANS Bengaluru, August 2016
26. *Ellora Sen*. Link between dysregulated metabolism and telomerase activity in Glioblastoma. 3rd International Meeting on Advanced Studies in Cell Signaling Network (CeSiN 2016), Kolkata, December 2016
27. *Ellora Sen*. Metabolic networks: Implications in Cancer and Inflammation. SAP-UGC, Dept. of Biochemistry, University of Delhi, March 2017
28. *Ellora Sen*. Metabolic storms: Feeding the tumor black-hole. Regional Centre for Biotechnology, Faridabad, March, 2017
29. *Ellora Sen*. Health and well being: Neurotheological perspectives. International Vedic Conference, Special Centre for Sanskrit Studies, Jawaharlal Nehru University, New Delhi, Dec 2016
30. *Ellora Sen*. Cognition of death and mortality awareness. The Nalanda Dialogues, Nava Nalanda Mahavihara, Nalanda, January 2017
31. *P. Seth* (Invited Speaker), An ill fated relationship – HIV and Brain. International Symposium on Neurodegenerative Disorders (ISDN-2017) at National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India, March 29-30, 2017.
32. *P. Seth* 5th Sarath Chandran Memorial Lecture, Novel Insights into NeuroAIDS, Sri Venkateshwara College, New Delhi, India, March 7, 2017.
33. *P. Seth* Neural Stem Cells: the amazing cells in brain, on National Science Day at Kendriya Vidyayalaya, NSG Campus, Manesar, India, February 28, 2017.
34. *P. Seth* Unique model of neural stem cells for understanding NeuroAIDS. Government Girls College, Gurgaon, India, February 13, 2017.
35. *P. Seth* Neural Stem cells as model system for

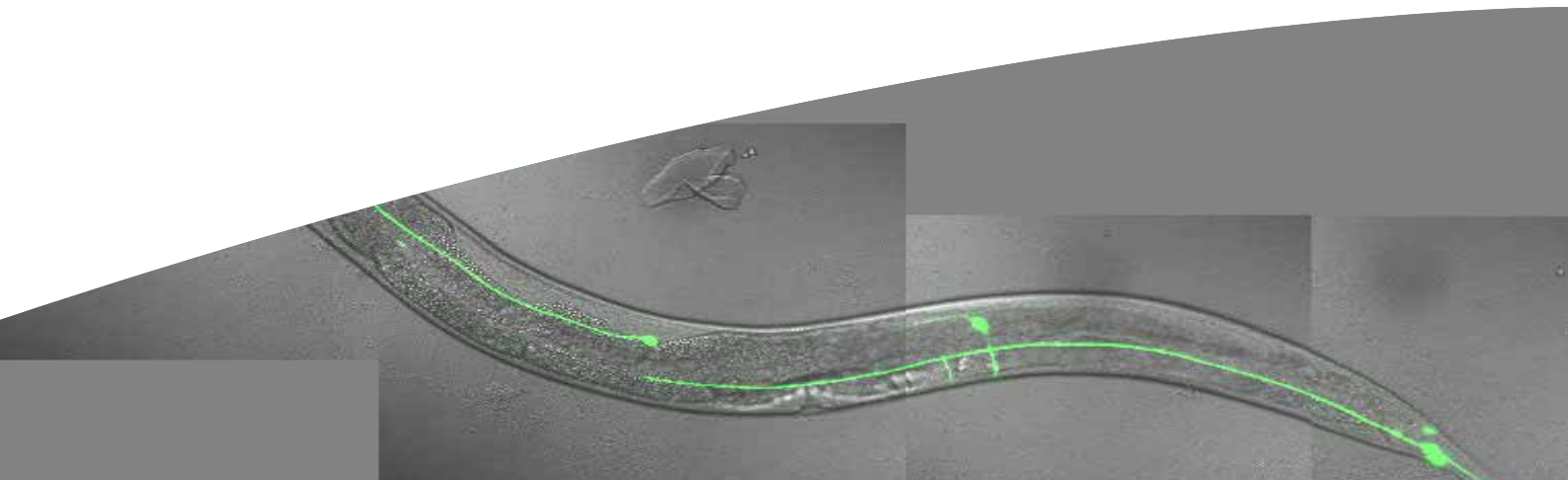
- understanding brain damage by HIV-1. Delhi Technical University, New Delhi, India, February 11, 2017.
36. *P. Seth* Understanding neuron-glia crosstalk in HIV-1 Neuropathogenesis. Brain Storming Session on DBT National Initiative-Glial Research on Health and Disease, Jiwaji University, Gwalior, India, February 2-3, 2017.
 37. *P. Seth* HIV-1 Modulates Properties of Neural Stem Cells. NeuroCON 2017, ICARE Institute of Medical Sciences and Research (IIMSR), Haldia, West Bengal, India, January 19-22, 2017.
 38. *P. Seth* Consequences of HIV-1 Infection in Human Neural Stem Cells, Indo-US symposium on Central Nervous System Viral Infections and its therapy, Doars, Chalsa Hilltop, India, November 14-17, 2016.
 39. *P. Seth* Molecular insights into HIV-1 neuropathogenesis, Department of Pathology Seminar Series, Uniformed Services University of Health Sciences, Bethesda, USA, November 1, 2016.
 40. *P. Seth* Novel Molecular pathway of ATP perturbation of ATP release in human astrocytes contributes neuronal death in HAND, 14th International Symposium of International Society of Neurovirology (ISNV) and HIV Endgame, Toronto, Canada, October 24-28, 2016.
 41. *P. Seth* HIV-1 viral protein alters properties of human neural stem cells, National University of Singapore, September 1, 2016.
 42. *P. Seth* Neuron-Glia interactions: Friends turn foe in HIV-1 induced neurodegeneration, at Asia Pacific Society of Neurochemistry (APSN 2016), Kuala Lumpur, Malaysia, during August 26-30, 2016.
 43. M. Fatima, K. Saleem and P. Seth [2016] "Novel molecular pathway of ATP release perturbed in astrocytes contributes to neuronal death in HIV-1 induced neurodegeneration" at the 34th annual meeting of Indian Academy of Neurosciences (IAN), National Brain Research Center, India, October 19th-21st, 2016.
 44. *S. Iyengar*: Cognition in Corvids – an Avian Model System. Invited lecture at the Cognitive Science workshop and NBRC-IITD workshop, January 2016.
 45. *S. Iyengar*: The Effects of Opioids on Vocalization and Vocal learning using Songbirds as a Model System. Invited lecture presented at the IBRO-APRC [Asia Pacific Regional Committee] School, NBRC "Theme: Development and Functions of Brain Circuits: From Molecules to Behaviour", March 2016.
 46. *S. Iyengar*: Mirror, Mirror on the Wall and some other aspects of Corvid Brain Structure and Cognition. Invited talk presented at IISER, Pune, July 2016.
 47. *S. Iyengar*: The Role of Mu-Opioid receptors in modulating the songs of Adult Male Zebra Finches, talk presented at the NeuroGroup Meeting, Khandala, Pune, September 2016.
 48. *S. Iyengar*: Effects of Mu-opioid Receptor Modulation on Singing in Adult Male Zebra Finches. Invited lecture presented at the XXXIV Annual Conference of Indian Academy of Neurosciences, NBRC, Manesar, October 2016.
 49. *S. Sen, P. Raghunathan, SS Kumaran and S. Iyengar*: A Three-Dimensional Digital Atlas of the Indian House Crow [Corvus splendens] Brain. Poster presented at the XXXIV Annual Conference of Indian Academy of Neurosciences, NBRC, Manesar, October 2016.
 50. *S. Sen, S. Paul, P. Raghunathan, SS Kumaran and S. Iyengar*: A Three-Dimensional Stereotaxic MRI Brain Atlas of House Crows [Corvus splendens]. Poster presented at the Annual Meeting of Society for Neuroscience, San Diego, CA, USA, November 2016.
 51. *Priyabrata Haldar and Neeraj Jain [2016]*. Reorganization of cuneate nucleus in macaque monkey following chronic partial spinal cord injuries. Neuroscience 2016, Annual Meeting of the Society for Neuroscience, USA.
 52. *Kalpna Gupta, Manika Arora, Mithlesh K. Singh and Neeraj Jain [2016]*. 'Sensory and motor changes in ageing rats'. 34th Annual Meeting of Indian Academy of Neurosciences, National Brain Research Centre, Manesar.

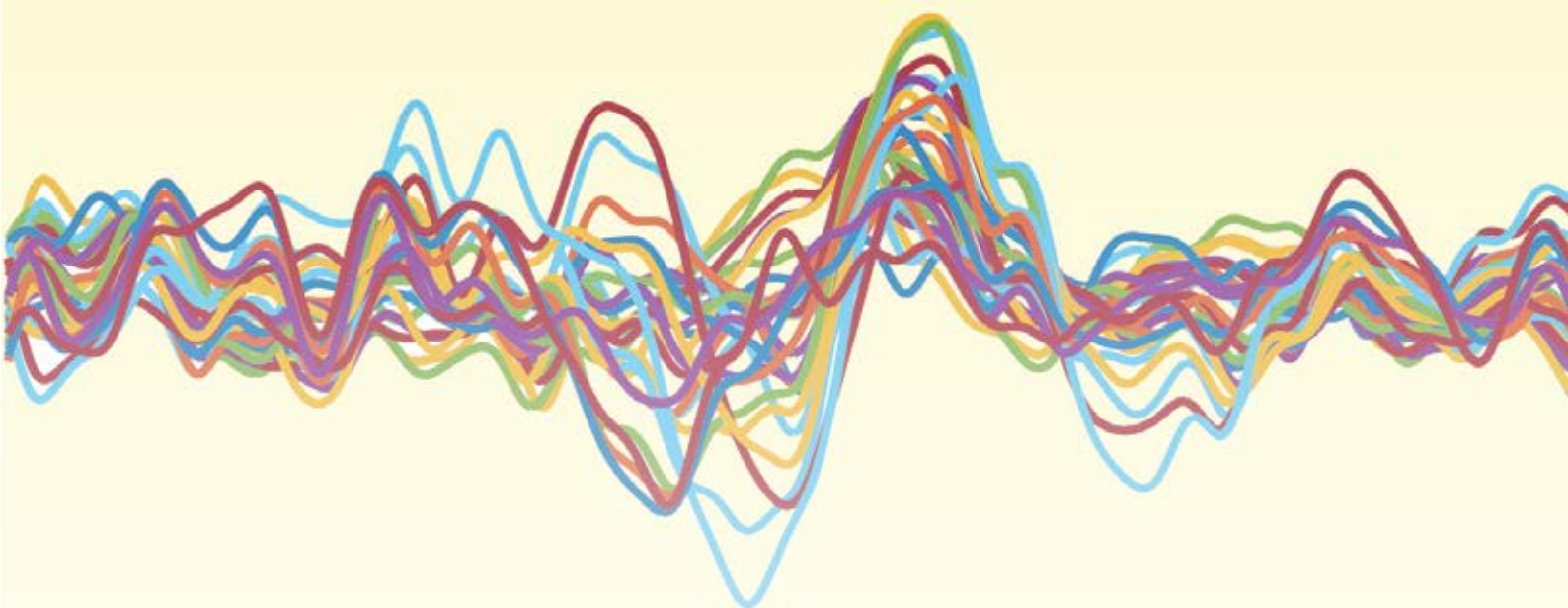
53. *Shanah Rachel John, Priyabrata Halder and Neeraj Jain (2016)*. 'Topographic representations in the mouse motor cortex is not well defined'. 34th Annual Meeting of Indian Academy of Neurosciences, National Brain Research Centre, Manesar.
54. *Prem chand and Neeraj Jain (2016)*. 'Cortico-cortical and thalamocortical connections between the hand and face regions of area 3b are unaffected following dorsal spinal cord injuries in macaque monkeys'. 39th Annual Meeting of the Japan Neuroscience Society, Pacifico Yokhama, Japan.
55. *Neeraj Jain, Leslee Lazar, Prem Chand, Radhika Rajan (2016)*. 'Neurophysiological and neuroanatomical correlates of independent use of opposable thumb in macaque monkeys'. 39th Annual Meeting of the Japan Neuroscience Society, Pacifico Yokhama, Japan.
56. *Neeraj Jain* 'How spinal cord injuries affect the brain: some mechanistic insights', at Indian Institute for Science Education and Research Mohali, March 31, 2017.
57. *Neeraj Jain* 'How spinal cord injuries affect the brain', at Seventh Symposium on Frontiers in Molecular Medicine, Jawaharlal University, New Delhi, March 23-24, 2017.
58. *Neeraj Jain* 'Spinal cord injuries and brain reorganization – what have we learnt', at Centre for Neuroscience, Indian Institute of Science, Bangalore, March 21, 2017.
59. *Neeraj Jain* 'Somatosensory information processing in the brain and effects of injuries', at a workshop on 'Brain Science and Technology: Tools and Techniques to understand human Brain', Indian Institute of Technology Delhi, December 14-18, 2016.
60. *Neeraj Jain* 'Spinal cord injuries and brain reorganisation', at Department of Neurobiology, Weizmann Institute of Science, Rehovot, Israel, December 8, 2016.
61. *Neeraj Jain* 'The Somatosensory Information Processing and Spinal Cord Injuries' at Israel – India Neuroscience Symposium, December 3-4, 2016, Eilat, Israel.
62. *Neeraj Jain* 'Somatosensory cortex is designed for opposable thumb', at the 1st NeuroGroup Meeting, September 27-28, 2018, Khandala.
63. *Neeraj Jain* 'How modular organization of the brain contributes to information processing' a Plenary Talk at the 3rd Annual Conference of Association for Cognitive Science, IIT Gandhinagar; October 3-5, 2016.
66. *Neeraj Jain* 'Brain-Computer Interface: Challenges in designing a useful motor and sensory prosthetic' at Special Session on 'Brain Computer Interface' in 8th ISSS National Conference on MEMS, Smart Materials, Structures and Systems, IIT Kanpur, September 30, 2016.
64. *Tushar Arora and Shiv K. Sharma*: Targeting amyloid aggregation using a novel peptide. Poster presentation in the 34th annual meeting of Indian Academy of Neurosciences. October 19-21, 2016, NBRC, Manesar, Haryana.
65. *Kumar, V. G., Halder, T., Jaiswal, A., Mukherjee, A., Roy, D. & Banerjee, A.* Large-scale functional brain network underlying perceptual variability during multisensory speech perception, IMRF, June 15-18, 2016, Suzhou, China
66. *Banerjee, A., Kumar, V. G., Mukherjee, A., Thakur, B.* Neurocognitive networks underlying multisensory perception. Japan Neuroscience Society Meeting 2016, Yokohama, Japan.
67. *Banerjee, A.* Multimodal correlates of Multisensory Perception. NeuroImaging Workshop 2016, INMAS-DRDO, Timarpur, Delhi
68. *Banerjee, A.* Multimodal correlates of Multisensory Perception. 3rd Bangalore Cognition Workshop 2016, IISc Bangalore.
69. *Ray, D., Hajare, N., Banerjee, A.* Dual stream hypothesis of visual processing: model comparison and exploration of functional plasticity. ACCS 2016 Meeting Gandhinagar.
70. *Talwar, S. Kumar, V. G., Banerjee, A.* Comparative Analysis of Cortical Sources Underlying P300 Complex Across Multiple Sensory Modalities. ACCS 2016 Meeting Gandhinagar.

71. *Pareek V. Tissue Mechanisms Involved in Recovery of Traumatic Brain Injury and its Validation using Diffusion Tensor Imaging (DTI), International Neuro-Trauma Workshop, All-India Institute of Medical Sciences (AIIMS), New Delhi, Aug. 2016.*
72. *Kapoor, S. Endogenous plasticity mechanisms as therapy for Stroke. Annual Meeting of Japanese Neuroscience Society, Yokohama, Japan, July 2016.*
73. *Roy, P K. Neuroinformatics in India, Council of Training, Infrastructure and Science in Neuroinformatics, University of Reading, Reading, U.K., Sept. 2016.*
74. *Rathee, R. Structural Integrity Changes of the Brain in Healthy Aging, Workshop on Imaging the Brain and Behaviour. Indian Institute of Technology - Delhi, July 2016.*
75. *Kapoor, S. A multidisciplinary systems approach to neural remodeling post ischaemic stroke injury using endogenous adult neural stem cells, Int. Conf. Cerebral Blood Flow & Metabolism: Brain & Brain PET 2017, Berlin, Jan 2017.*
76. *Nandini C Singh: 'The Rasa in the raga - characterising emotion in Indian Classical Music', Plenary lecture at Presidency College, Kolkata, India, March 2016.*
77. *Nandini C Singh: The development of language specific reading networks in biliterate bilinguals, International Conference on Language', University of Hyderabad, March 2016.*
78. *Nandini C Singh: 'Screening and assessment of dyslexia in India', Un Learn workshop, UNESCO Mahatma Gandhi Institute of Education for Peace and Sustainable Development, IIT New Delhi, April [2016].*
79. *Nandini C Singh: 'Dyslexia Assessments in Indian Languages', Dyslexia Association of Singapore, June 2016*
80. *Nandini C Singh: 'The biliterate reading brain - implications for classroom and dyslexia', National Centre of Educational Research and Training, New Delhi, November 2016.*
81. *Nandini C Singh: Literacy, Global Literacy Meet at Yale University, New Haven, Connecticut, USA, December 2016.*



Externally Funded Research Projects





Externally Funded Research Projects

LIST OF EXTRA MURAL PROJECTS AS ON DATE 31.03.2017(FOR THE FINANCIAL YEAR 2016-17)

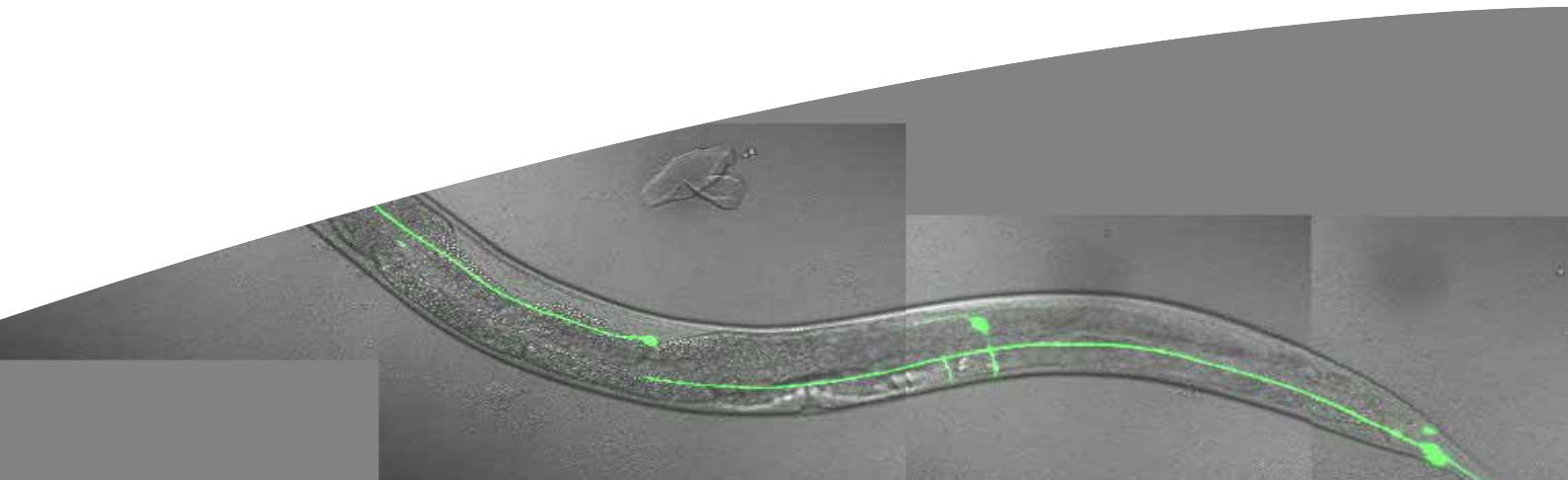
Name of P.I.	S. No.	Name of Project	Name of the Implementing Agency	Date of Sanction of Project	Original Sanctioned Cost (Rs. In Lakh)	Date of Completion
Dr Neeraj Jain	1	Mechanisms of Adult Brain Reorganization	D.B.T.	28.05.2014	35.74	27.05.2018
Dr. Anirban basu	2	Implementing Proteomic approach to understand the Etiology of Neuropathogenesis induced by Chandipura Virus infections	DBT/ Chandipura	21.08.2013	37.4	20.08.2016
	3	To Study the molecular mechanism of microbial activation and identify the therapeutic targets critical for IL-1B signaling in brain following inflammation	S.E.R.B.	20.10.2014	41.95	19.10.2017
	4	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
	5	Micro RNAs as a potential therapeutic target in Neuro tropic viral infection (Tata Innovation fellowship)	D.B.T.	01.05.2015	27.00	31.04.2018

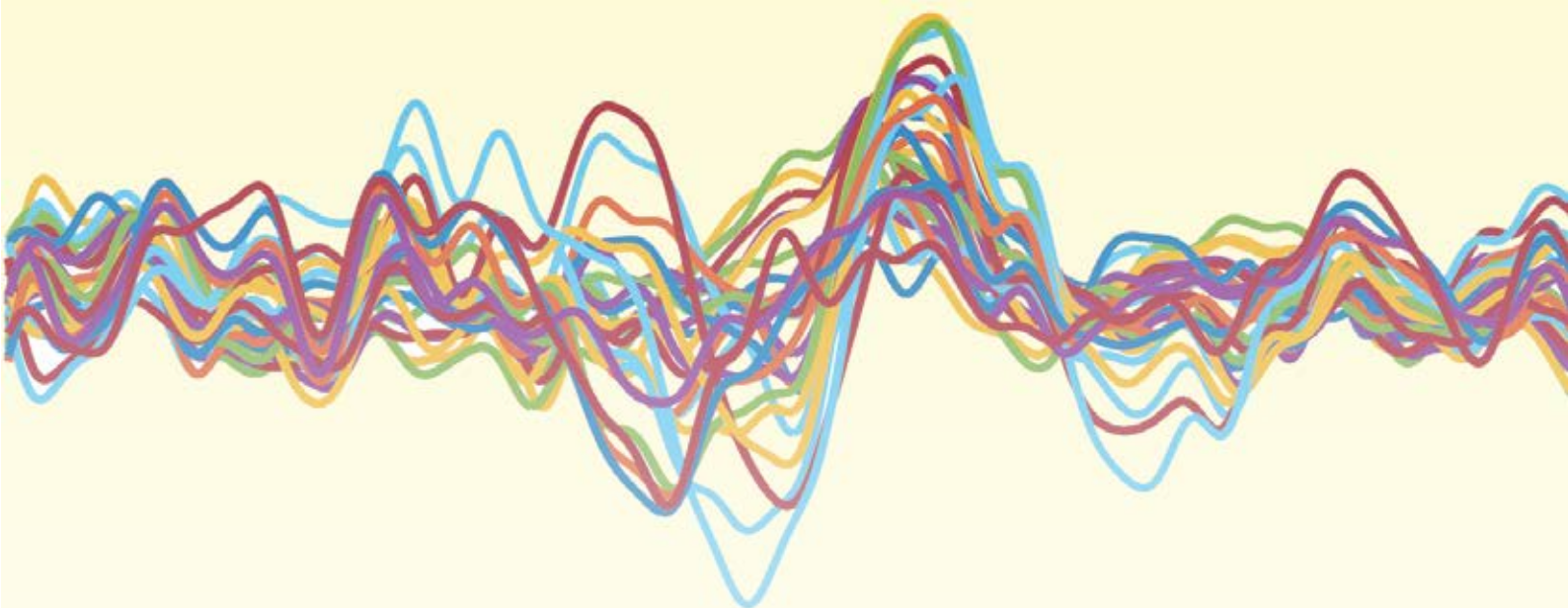
Dr. Ellora sen	6	Understanding inflammation driven regulation of macrophages function: Implications in glioblastoma progression (National Bioscience Award)	D.B.T.	25.11.2014	15.00	24.11.2017
	7	Role of Chromatin Remodelers in regulating associated with resistance to apoptosis under inflammatory and hypoxic conditions in glioma cells	D.B.T.	25.07.2013	36.75	24.01.2017(six month ext.)
	8	Inflammation regulated metabolic reprogramming Implications in tumor progression(UOE)	D.B.T.	30.03.2015	172.9	29.03.2018
Prof. Prasun ku Roy	9	India Intergration with Global Imaging System via MCGill Linkage(NKN)	NICS	06.07.2011	89.89	05.07.2017
	10	Using Stereo X-Ray image to develop a ready automated method for screening of Alzheimer type mild cognitive impairment from normal ageing in resource constrained setting (Tata Inovation Fellowship Award)	D.B.T.	04.05.2012	22.02	03.05.2017
	11	Spatiotemporal Dynamics of the Neural System (DEIT)	DEIT	01.01.2014	66.28	31.12.2017
Dr. Nandini C. Singh	12	A longitudinal 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 lyengar	13	Effects of the δ - opioid receptor system on singing and song learning in Zebra Finches	D.S.T.(SERB)	23.09.2016	3743	22.09.2019
Dr. Pravat kumar Mandal	14	Characterizing biomarkers of Alzheimer's disease :A longitudianal multii modal brain imaging study (Brain imaging)	D.B.T.	25.09.2013	120.68	24.09.2018
	15	National Programme On Perception Engg. Phase II	D.E.I.T.	20.12.2013	86.40	19.12.2017
	16	Non-invasive imaging Technology Development to aid Differential Diagnosis of Alzheimer, 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
	17	Construction of an Indian population specific brain template	C.S.I.R.	11.05.2016	26.12	10.05.2019
	18	Unravelling the causes of stroke and cognitive decline in general between population and A cross-Cultural perspective (DBT Netherland Grant)	D.B.T.	21.04.2016	73.66	20.04.2022

Dr. Nihar Ranjan Jana	19	Tata Inivation Fellow	D.B.T.	22.01.2014	18.00	21.01.2017
Dr. Sourav Banarjee	20	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
	21	Regulation of energy metabolism by miRNA-mediated control of neurogenesis	D.B.T.	21.02.2015	78.09	20.02.2018
	22	Ramalingaswamy fellowship 2011-12	D.S.T.	07.06.2012	74.50	06.06.2017
Dr. Subrata Sinha	23	Epilepsy Project(M.E.G.)	D.B.T.	11.02.2011	2776.76	10.02.2018
	24	Neuroscience education research fellowships in clinical neuroscience and Neuro-informatics & Computational neuroscience	D.B.T.	27.09.2012	620.00	26.09.2017
	25	Distributed infromation Centre (DIC)	D.B.T.	01.04.2013	72.40	31.03.2017
	26	Dementia Programme	D.B.T.	14.09.2007	37.50	31.03.2017
	27	Delcon(E- Laibrary) Project	D.B.T.	18.03.2009	2180.3	17.03.2016
Dr. Yoga	28	(D.B.T. Project)Natural Network Machenism	D.B.T.	21.01.2011	9742	23.01.2016
Dr. Arpan Banerjee	29	Neuro -Cognitive networks underlying goal Directed Behavior	D.B.T.	28.11.2013	82.00	27.11.2018
	30	How do vision guide speech perception (IYBA-2013)	D.B.T.	21.05.2014	38.81	20.05.2017
Dr. Anindya Ghosh Roy	31	Wellcome Trust/DBT Indian Alliance	D.B.T.	01.12.2013	321.93	30.11.2018
Dr. Yogita K Adlakha	32	Innovation in science pursuit for inspired Research(INSPIRE)	D.S.T.	01.07.2014	35.00	31.06.2019
Dr. Aparna Dixit	33	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	34	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	35	Post Doctoral Fellowship	SERB	08.08.2016	14.40	07.08.2018
Dr. Akansha Jalota	36	Post Doctoral Fellowship	SERB	15.11.2016	19.20	14.11.2018



Distinctions, Honors and Award





Distinctions, Honors and Award

FACULTY

Subrata Sinha

- ❖ J C Bose fellowship of the DST [2016]
- ❖ Sun Pharma Award Medical Sciences – Basic research, for 2015 (announced in 2016)

Anirban Basu

- ❖ Elected as a Fellow of the Indian National Science Academy (INSA)

Ellora Sen

- ❖ Kshanika Oration Award, Indian Council of Medical Research, 2016
- ❖ Indian Society of NeuroOncology ISNO Annual Award for outstanding work in neuro-oncology, 2016.

STUDENTS

Abhishek Verma An Integrated PhD student received the best poster presentation award in INDO-US Symposium on CNS Viral infection,

14-17th November, 2016, Sinclairs Retreat Dooars, Chalsa, West Bengal.

Chitra M.S. Singal - Awarded International Travel Grant from Society on NeuroImmune Pharmacology and Department of Biotechnology for presenting a poster in the 23rd Society on NeuroImmune Pharmacology meeting held in Philadelphia, PA from 29th March 2017 to 1st April 2017.

Pareek Vikas, Training Program Fellowship Award, International Brain Research Organization, School on Neuroinformatics & Brain Network Analysis. Petronas University of Technology, 2017.

Alam A. Team project awarded Best Presentation prize. Route 28 Workshop on Adult Neurogenesis - Frauenchiemsee, Munich, 2016.

Kapoor S, Japanese Neuroscience Conference, Travel Fellowship Award, Yokohama, 2016.

COURSE-WORK

M.Sc. 2015

Ms. Meenakshi Bhaskar M.Sc. student, has been awarded first rank upon completion of Course-Work during the year 2015-16 and a certificate was given to her on the 13th Foundation Day, the 16th December 2016.

Ms. Himali Arora M.Sc. student, has been awarded second rank upon completion of Course-Work during the year 2015-16 and a certificate was given to her on the 13th Foundation Day, the 16th December 2016.

Ph.D. 2015

Mr. Surajit Chakraborty Ph.D. student, has been awarded first rank upon completion of Course-Work during the year 2015-16 and a certificate was given to him on the 13th Foundation Day, the 16th December 2016.

Ms. Sarbani Samaddar Ph.D. student, has been awarded second

rank upon completion of Course-Work during the year 2015-16 and a certificate was given to her on the 13th Foundation Day, the 16th December 2016.

COMPREHENSIVE VIVA-VOCE

Mr. Surajit Chakraborty Ph.D. student has been awarded first rank upon completion of

Comprehensive Viva-Voce during the year 2015-16 and a certificate was given to him on the 13th Foundation Day, the 16th December 2016.

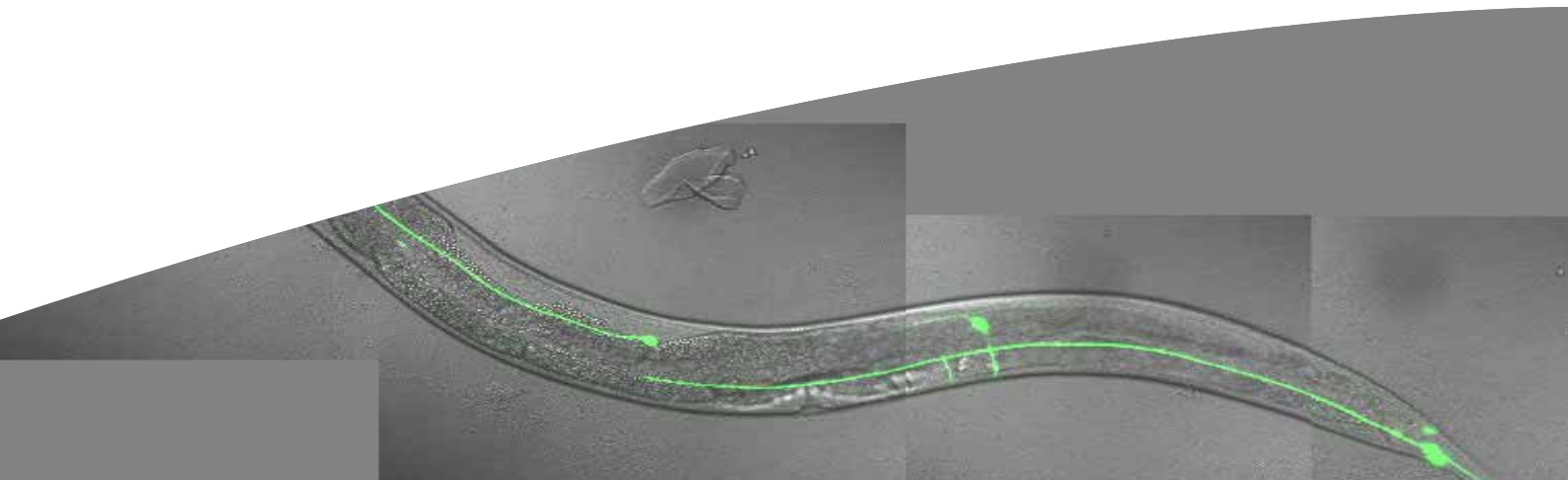
PH.D. DEGREES AWARDED

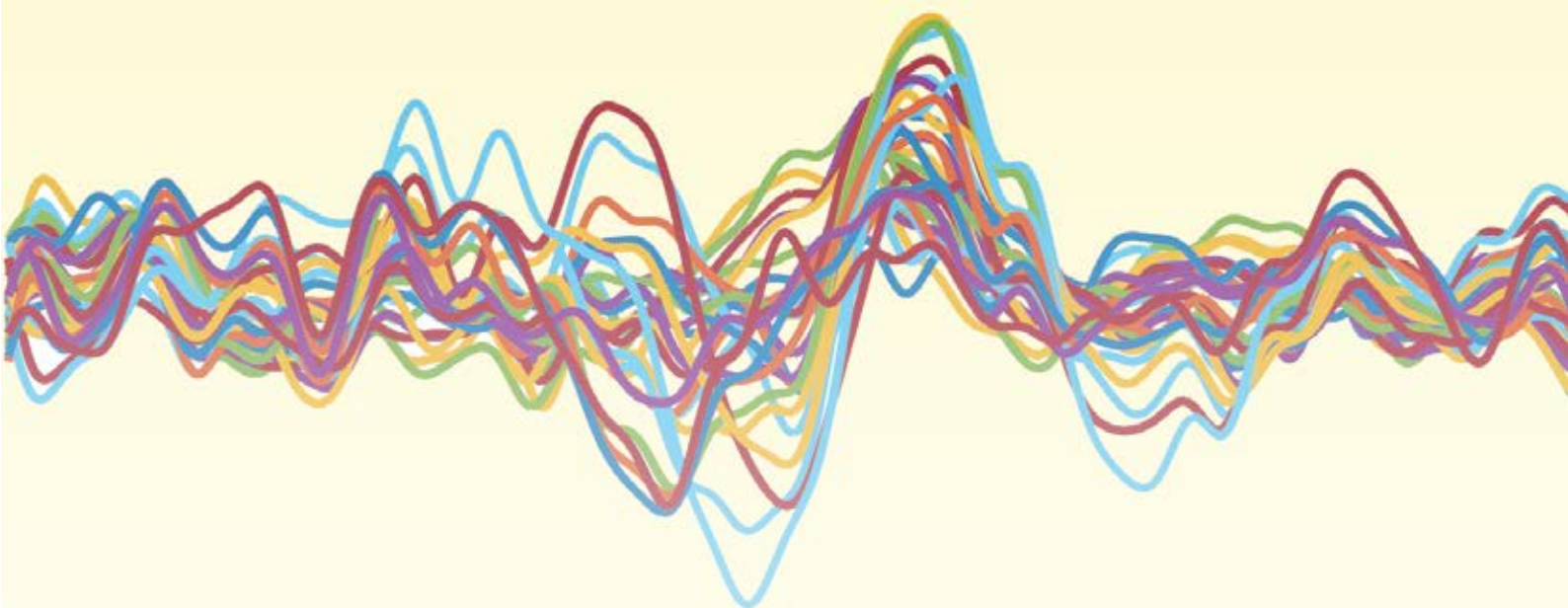
S/No	Name of the Student
1	Dr. Piyushi Gupta
2	Dr. Sourish Ghosh
3	Dr. Sarika Cherodath
4	Dr. Manju Tewari
5	Dr. Suhela Kapoor
6	Dr. Fahim Ahmad
7	Dr. Mahar Fatima
8	Dr. Kaushik Pramod Sharma
9	Dr. Deepak Poria

M.SC. DEGREES AWARDED

S/No	Name of the Student
1	Ms. Piyushi Gupta
2	Ms. Sarika Cherodath
3	Ms. Suhela Kapoor
4	Mr. Fahim Ahmad
5	Mr. Deepak Poria

Academic Programs





Academic Programs

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

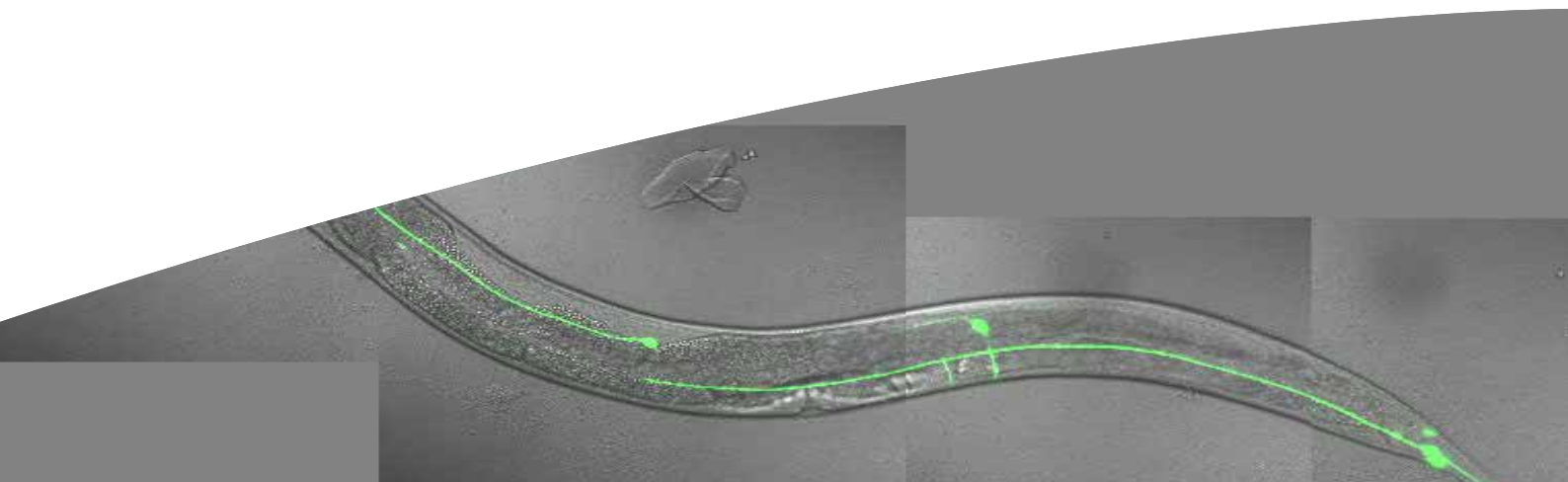
related to Neurosciences, Psychology or M.B.B.S., B.E., or B.Tech. NBRC recognizes that understanding brain functions requires a fusion of knowledge from multiple disciplines.

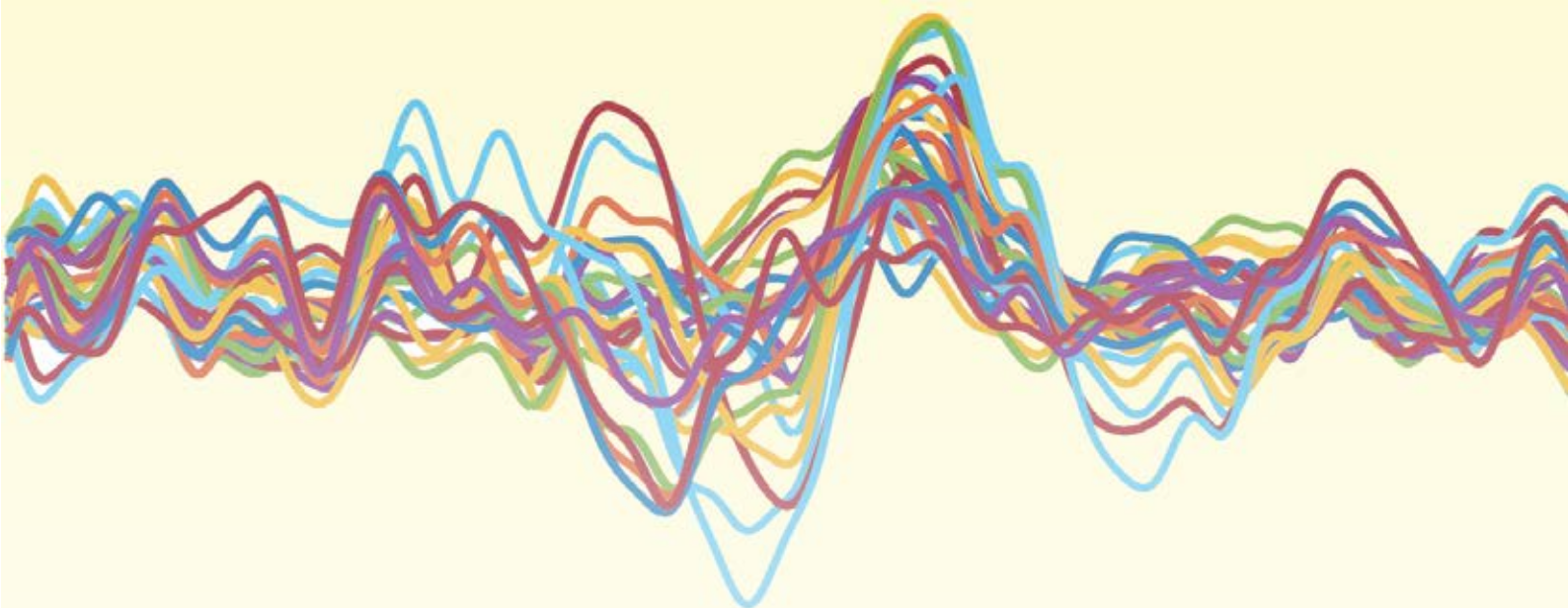
SUMMER TRAINING AND SHORT-TERM PROGRAMMES

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.



Core Facilities





Distributed Information Centre (DIC)

The Distributed Information Centre (DIC) manages the overall ICT infrastructure and communication network of the Institute. The department primarily focuses on providing Scientific Services related to Computational facility to the Scientists on one hand and promoting e-Governance activities of the institute on other hand. It is also funded with a DIC Centre under the Biotechnology Information System Network 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:

CAMPUS CONVERGED NETWORK

(NBRC-IntraNet) The campus converged network consists of campus wide Local Area Network running on 10Gbps fiber optic backbone with redundant paths over manageable switching fabric. The redundancy and robustness is built in the network architecture itself. The core LAN network is further integrated with wireless access points installed across the campus and managed through central wireless controller. The network is further 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 further integrated 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 –

- a. Multi site neuro-imaging data repository project (Model NKN project PI : Prof. P K Roy)
- b. NBRC-AIIMS data pipeline for MEG as part of collaborative Centre of Excellence in Epilepsy project funded by DBT.

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 active-passive 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.

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.

OTHER FACILITIES & SERVICES

- a. *Central Documentation Facility:* A additional central facility for users with up to 12 user terminals with facility for printing, scanning, poster-printing etc. has been created in the DIC facility which is operational 24x7 with CCTV monitoring.
- b. *Upgradation of datacenter* The capacity of the existing datacenter facility has been increased and it will now fulfill the expansion requirements for addition of new server racks etc.

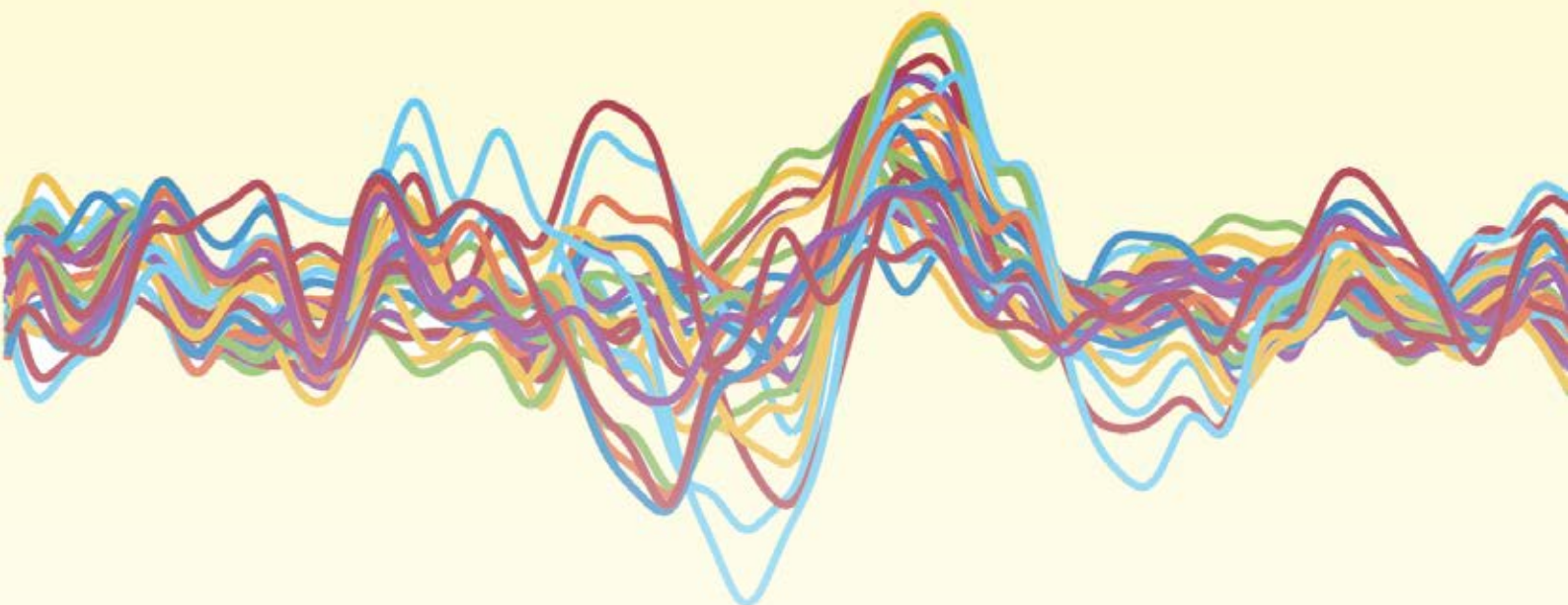
- c. *ICT Support & Service:* The computing facility also provides support and manages maintenance activities for the entire computing infrastructure of the institute which also includes user endpoints like computers, peripherals, software's etc. An online support ticketing system with automated workflow management is functional for support activities.

- d. *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.

- e. *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.

PLANNED FUTURE EXPANSIONS

- a. An Enhanced storage server facility with Disaster Recover storage solution has been proposed subject to necessary administrative and financial approval from the competent authority.
- b. Integrated Multi-Media Digital Classrooms with facility for webcasting etc. has also been proposed while upgrading the existing Video-Conferencing Facility in near future.



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 requirements 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 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 $22 \pm 2^\circ \text{C}$, 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 the 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. This includes 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) 85Dbo Tg(PSEN1) 85Dbo (Alzheimer's disease model)
- ❖ UBC-GFP (Green fluorescent protein)
- ❖ B6CBA-Tg (Hdaxon1) 62Gpb/3J (Huntington disease model)
- ❖ B6.Cg-Mapttm1 (EGFP)KltTg (MAPT) 8cPdav/J (Alzheimer's disease model)
- ❖ B6.129P2-Gsk3btm1Dgen/J (Alzheimer's disease model)
- ❖ B6;129P2Pvalb <tm1(cre)Arbr>/J
- ❖ B6.CgGt (ROSA) 26Sor <tm9(CAGtdTomato)
- ❖ B6.CgTg (Scnn1acre)3Aibs/J
- ❖ STOCK Gad2<tm2(cre)Zjh>/J
- ❖ B6.CgTg(Camk2a-cre)T29-1Stl/j
- ❖ B6.129-Rp122<tm1.1Psam>/j
- ❖ STOCK Tg(Thy1-EGFP)Mjrs/J
- ❖ B6.Cg-Tg(Thy1-YFP)16Jrs/J
- ❖ B6.Cg-Tg(Thy1-YFP)HJrs/J
- ❖ B6;129S6-Tg(Camk2a-cre/ERT2)1Aibs/J
- ❖ STOCK Sst^{tm2.1(cre)Zjh}/J
- ❖ B6.Cg-Gt(ROSA)26Sor^{tm6(CAG-ZsGreen1)Hze}/J
- ❖ B6;129X1-Gt (ROSA) 26Sor<tm(EYFP)Cos>/j
- ❖ C57Bl6-Tg(Nes-cre/ERT2)Keise/j

KNOCK OUT MICE

- ❖ UBE3A null mice (Angelman syndrome model)

MUTANT MICE

- ❖ CBA/J mice (Retinal degeneration model)

RAT STRAINS

- ❖ Long Evans
- ❖ Sprague Dawley
- ❖ Wistar

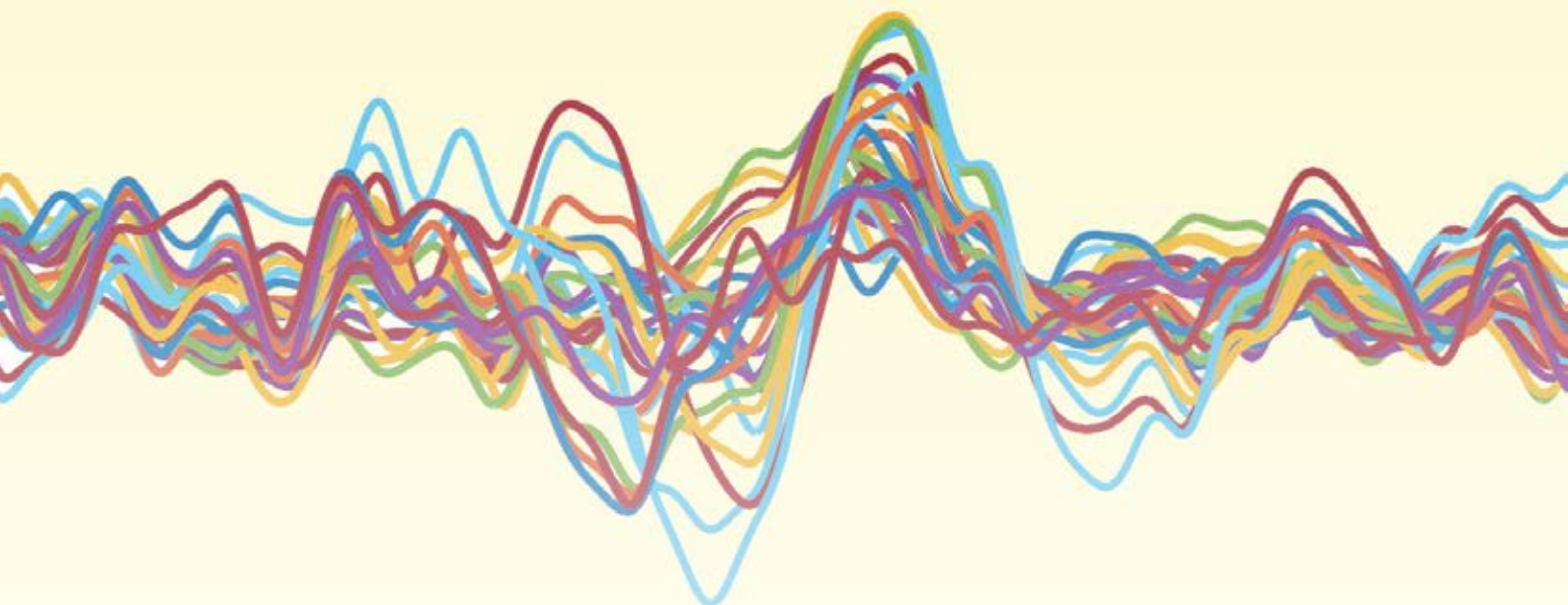
NON-HUMAN PRIMATES

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

BIRDS

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

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 1171 online journals through the DBT e-Library Consortium (DeLCON), 3 specialized journals, and 122 freely accessible online journals. It also maintains digital archives and news clips about the Centre and subscribes to Newspapers and News Letters. The collection of the NBRC Library is growing day-by-day along with new developments in research and knowledge in the field of Neuroscience and related areas.

To provide optimum service to all users, the NBRC library is currently digitizing its list of collections using the LSEASE software, to which all users will have full access. A barcode technology has also been installed for accurate and speedy circulation and the management of all library documents. The new software will also help in efficient library operations viz. administration, acquisition, circulation, serial control, cataloguing and information retrieval.

The Library has set up 22

Computers with Internet facility to provide services for use of researchers and students in the NBRC Common room and has been providing electronic access to the subscribed journals through the campus portal.

The NBRC Library also provides Inter Library Loan Services to NBRC's 48 networked centres all over India. Researchers at different centres send their requirement for research material or journal articles through email to NBRC Library library@nbrc.ac.in or to the Librarian Dr. D. D. Lal, ddlal@nbrc.ac.in which are then downloaded and sent to them free of cost. The library entertains an average of approximately 450 requests for articles and this number is increasing every year.

The NBRC Library regularly evaluates its information services to ensure that the Institution's requirements are met. It promotes resource sharing and cooperation activities among libraries by providing an efficient and reliable means of

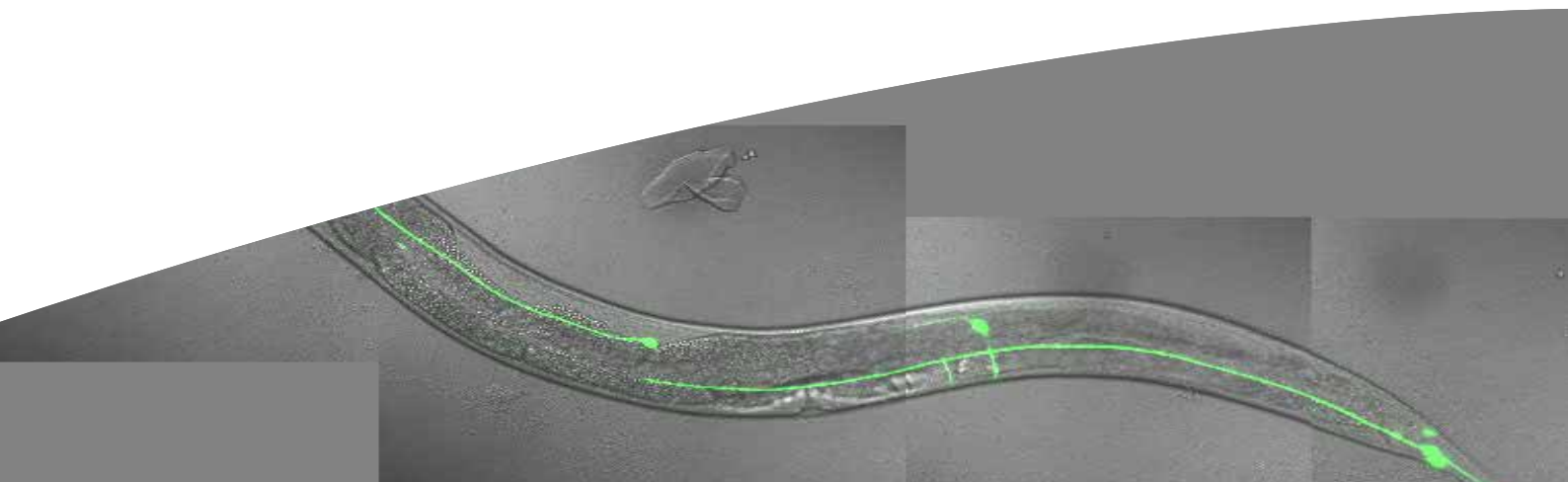
resource sharing, that is, the inter library loan for the maximum use of resources, by providing copies of documents which are not available to researchers at centres outside the institute.

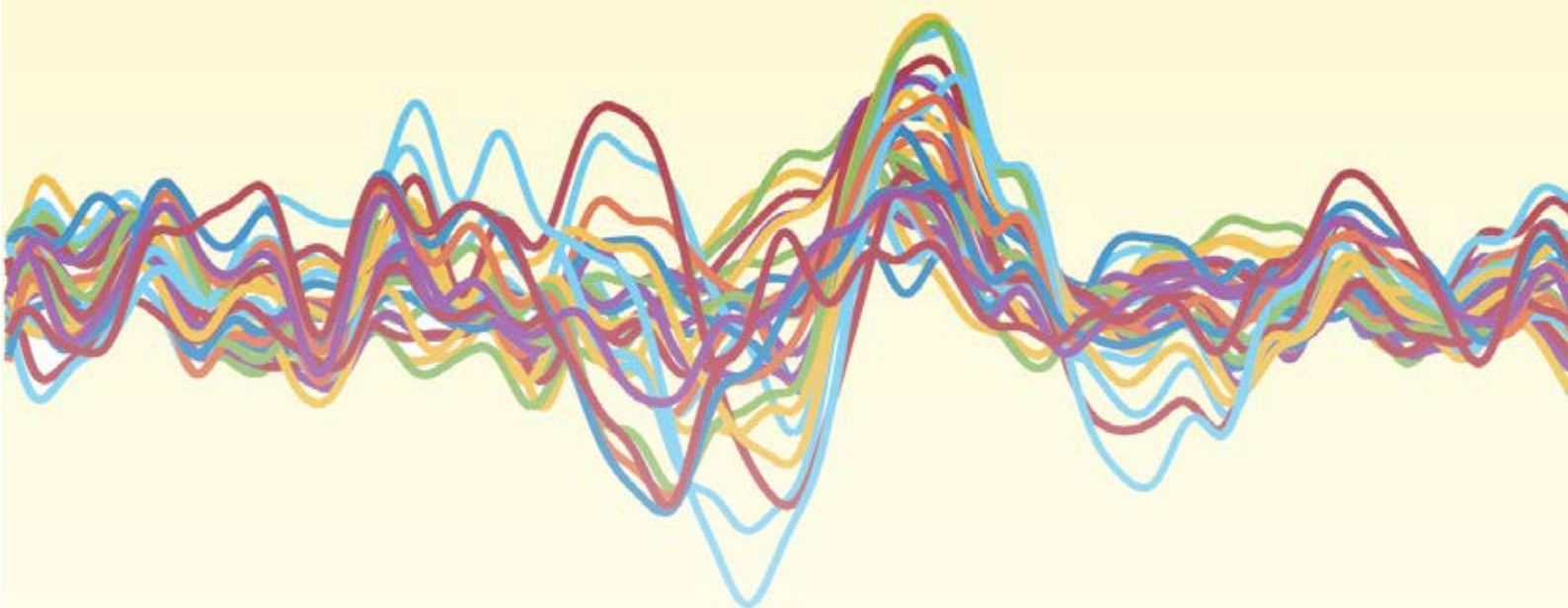
MAIN ACTIVITIES OF NBRC LIBRARY

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



DBT's Electronic Library Consortium (DeLCON)





DBT's Electronic Library Consortium (DeLCON)

DeLCON CONSORTIUM: AN 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 963 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) – Bhubaneswar
- ❖ 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
- ❖ Gauhati 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 (NIBMG), 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), Bhubaneswar
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

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. Gauhati 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/> → 17
- ❖ 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> → 36
- ❖ Oxford University Press (OUP) → <http://www.oxfordjournals.org> → 22
- ❖ Springer India → <http://www.springerlink.com> → 339

- ❖ 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> → 84
- ❖ Elsevier Science (ScienceDirect) → <http://www.sciencedirect.com> à 432
- ❖ American Society of Plant Biologist → <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 covers 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.

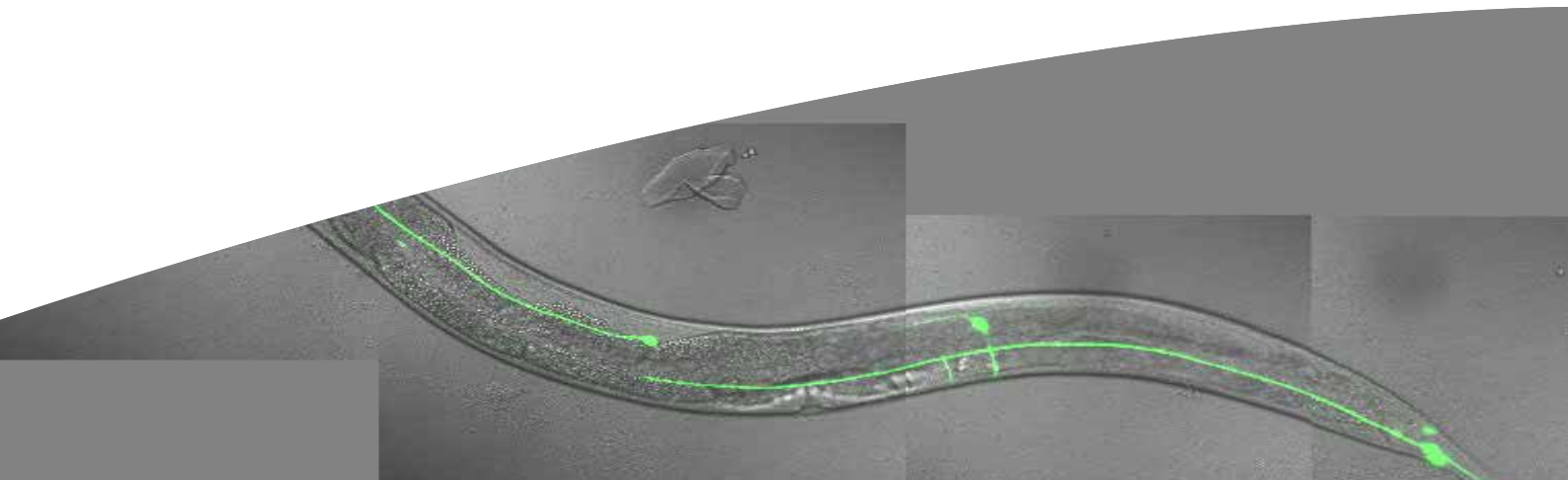
NODAL CENTRE & HEAD QUARTER OF DeLCON CONSORTIUM & ITS ACTIVITIES

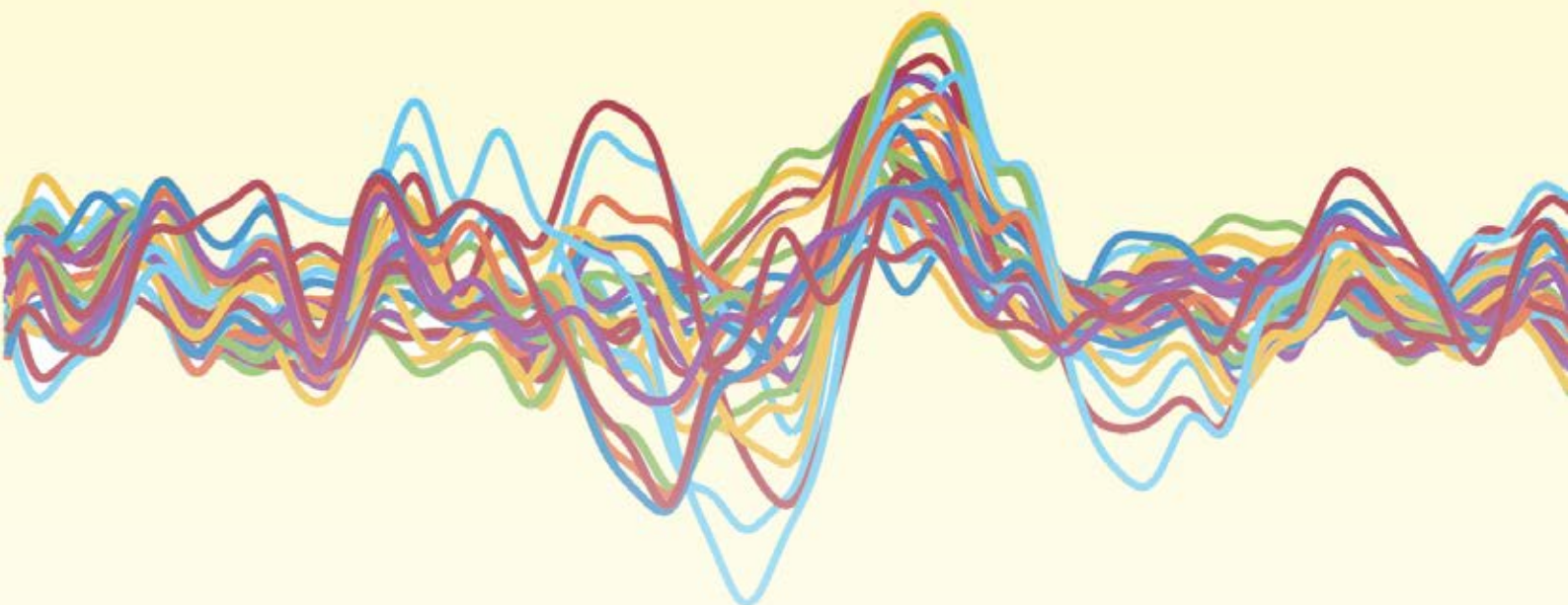
The consortium headquarter functions under a National Steering

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

National Neuroimaging facility, sponsored by the Department of Biotechnology, Govt. of India, came into existence in the year of 2006. The main purpose this National Facility to facilitate/support cutting edge brain imaging research. The facility is equipped with four state-of-the-art equipments such as,

1. 3 tesla Magnetic Resonance Imaging (MRI) Scanner
2. Electroencephalography (EEG)
3. Evoked Response Potential Recording (ERP)

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. There are various imaging modalities, which 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 correlates functional (haemodynamics) activity with images of brain activation

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 for performing structural, metabolic (multinuclear, e.g. proton and phosphorous) and functional MRI. 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)

This is a test that measures and records the electrical activity of the brain. Special sensors are attached to the head and accessed by wires to a computer. The computer records brain's electrical activity on the screen or on paper as wavy lines. Certain conditions, such as epilepsy, dementia, consciousness and narcolepsy (sleeping disorder) can be studied by EEG.

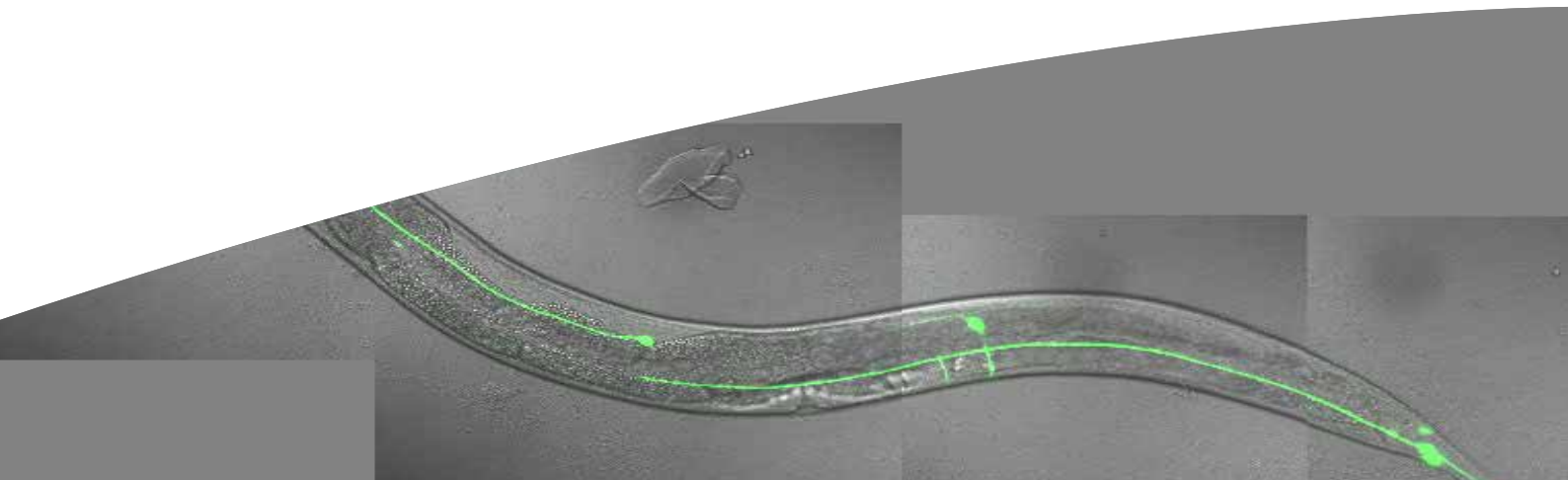
EVOKED RESPONSE POTENTIAL RECORDING (ERP)

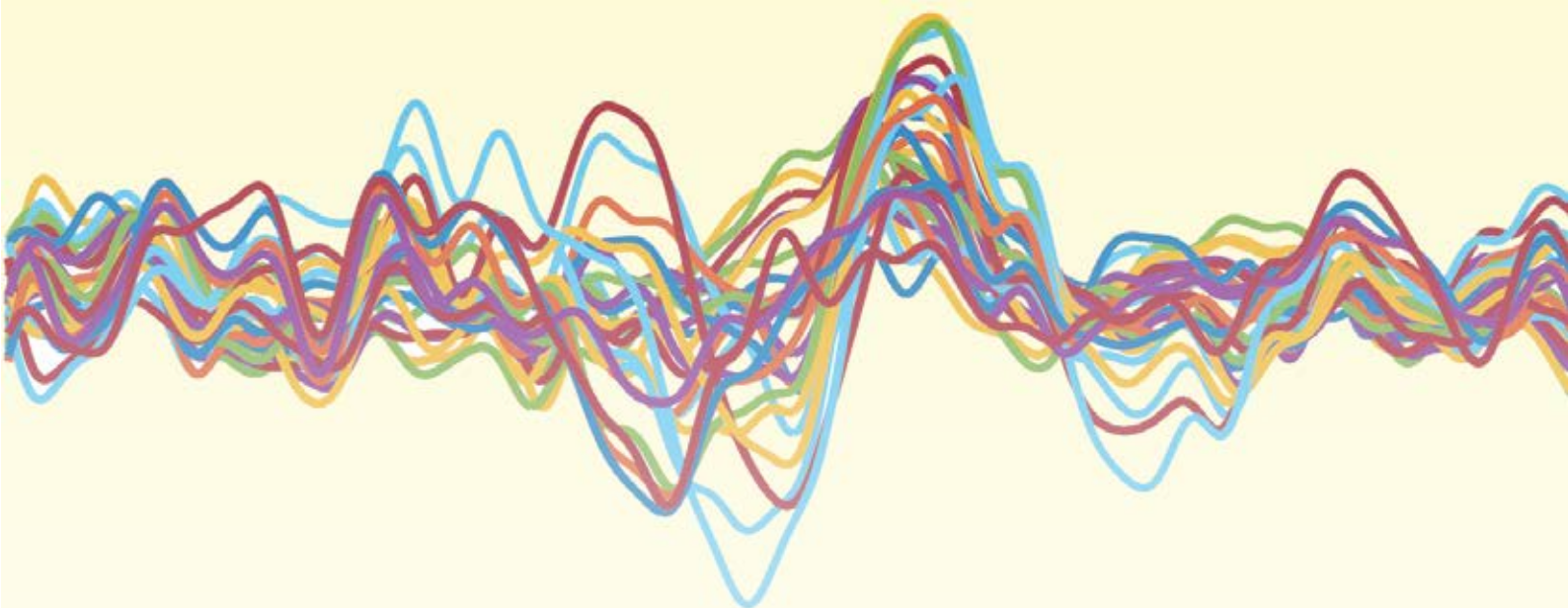
EPS is an electrical potential recorded from the nervous system of a human or other animal following presentation of a stimulus. Evoked potential amplitudes tend to be low, ranging from less than a microvolt to several microvolts.

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.



Translational Research: Clinical Unit





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 Assistant Professor, Neurology: Dr Rajnish Kumar

Consultant Clinical Assistant Professor, Neurology: Dr Amit Arora

Clinical Psychologist: Priyanka Kaushik

Clinic Assistant: Hanuman Singh and Pawan Kumar

Translational research aims to connect basic research to patient care bidirectionally for mutual benefit: "From the Bench lab to the Bedside patient and back to the Bench". The Clinical Research Unit of NBRC covers 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 out-patients facility is busy, and on some days attendance can exceed 70 to 80 patients. The follow up by the patients is about 75%. Male to female ratio is almost equal. Paediatric group patient attendance is mainly for management of Epileptic Seizure and disorders of the Mentally Challenged. There are also Elderly or Geriatric patients attending, and Movement Disorders are an important cause of attendance.

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 so desires.

Outpatient 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

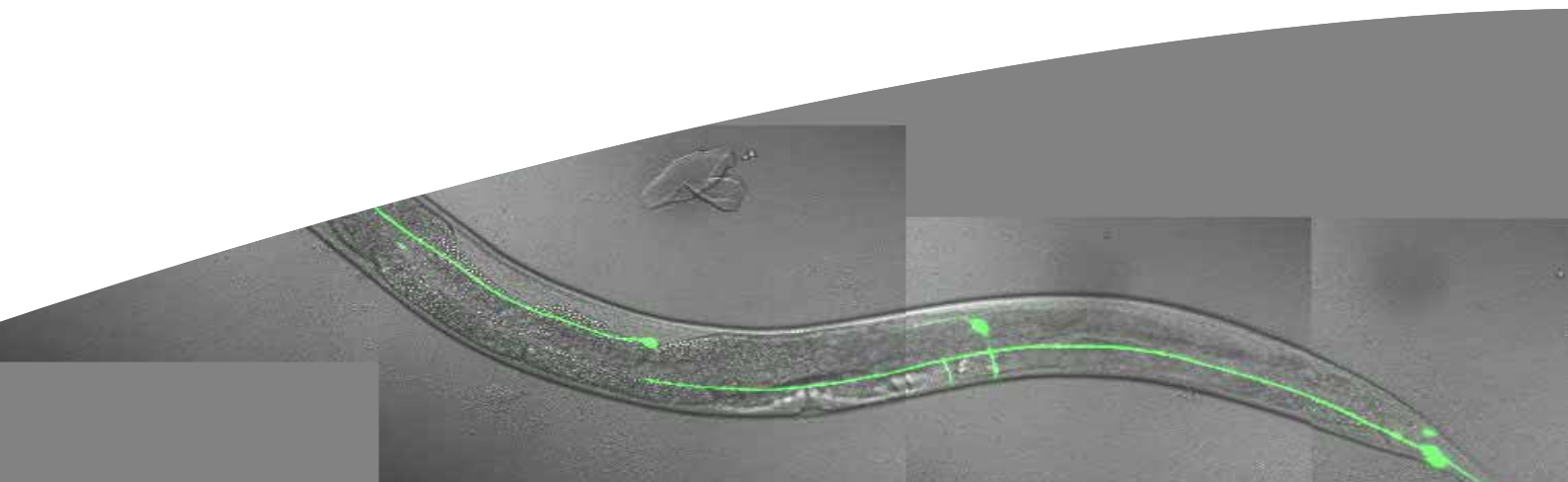
Neurology case sheet has been formulated and formatted by Distributed Information Centre of NBRC. We are undertaking to prospectively enter all the medical data of new patients, to create computer database with relevant patient data along with any planned imaging/molecular/neurophysiological studies 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.

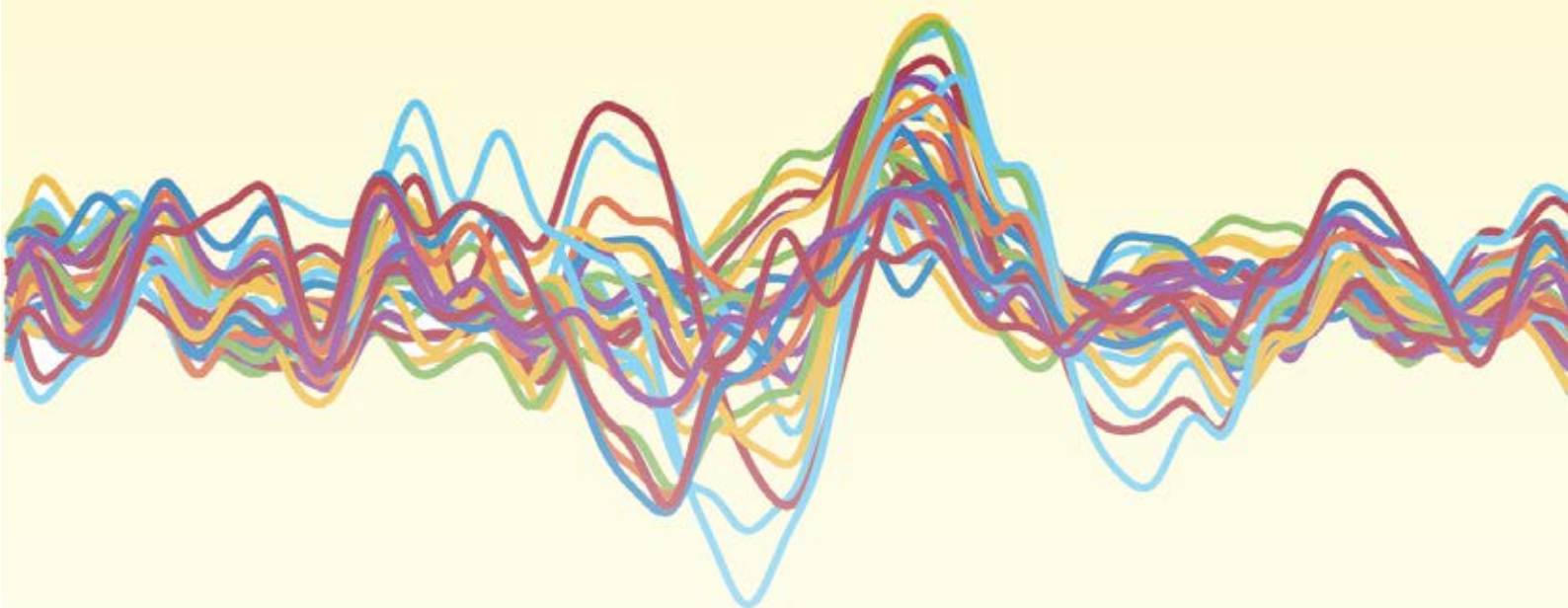
For proper functioning and further clinical support, the NBRC Unit at

the Hospital receives the fullest cooperation of the Ministry of Health - Government of Haryana, and the Deputy Commissioner - Gurgaon, as well as from the Chief Medical Officer & Civil Surgeon as well as the Principal Medical Officer of the Hospital.

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.

Centre of Excellence





Centre of Excellence (CoE) for Epilepsy Research

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

SCIENTIFIC FACULTY

Prof. P Sarat Chandra, AIIMS
Prof. Manjari Tripathi, AIIMS
Prof. Subrata Sinha, NBRC
Dr. Jyotirmoy Banerjee, NBRC
Dr. Aparna Dixit, NBRC

MEG TECHNOLOGISTS

Mr. V. Vibhin
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.

ICTAL-MEG SOURCE LOCALIZATION FOR DELINEATING THE ICTAL-ONSET ZONE (MEG FACILITY)

Ictal-magnetoencephalography (ictal-MEG) source localization (SL) added information towards delineating the ictal-onset zone (IOZ), and helped final decision

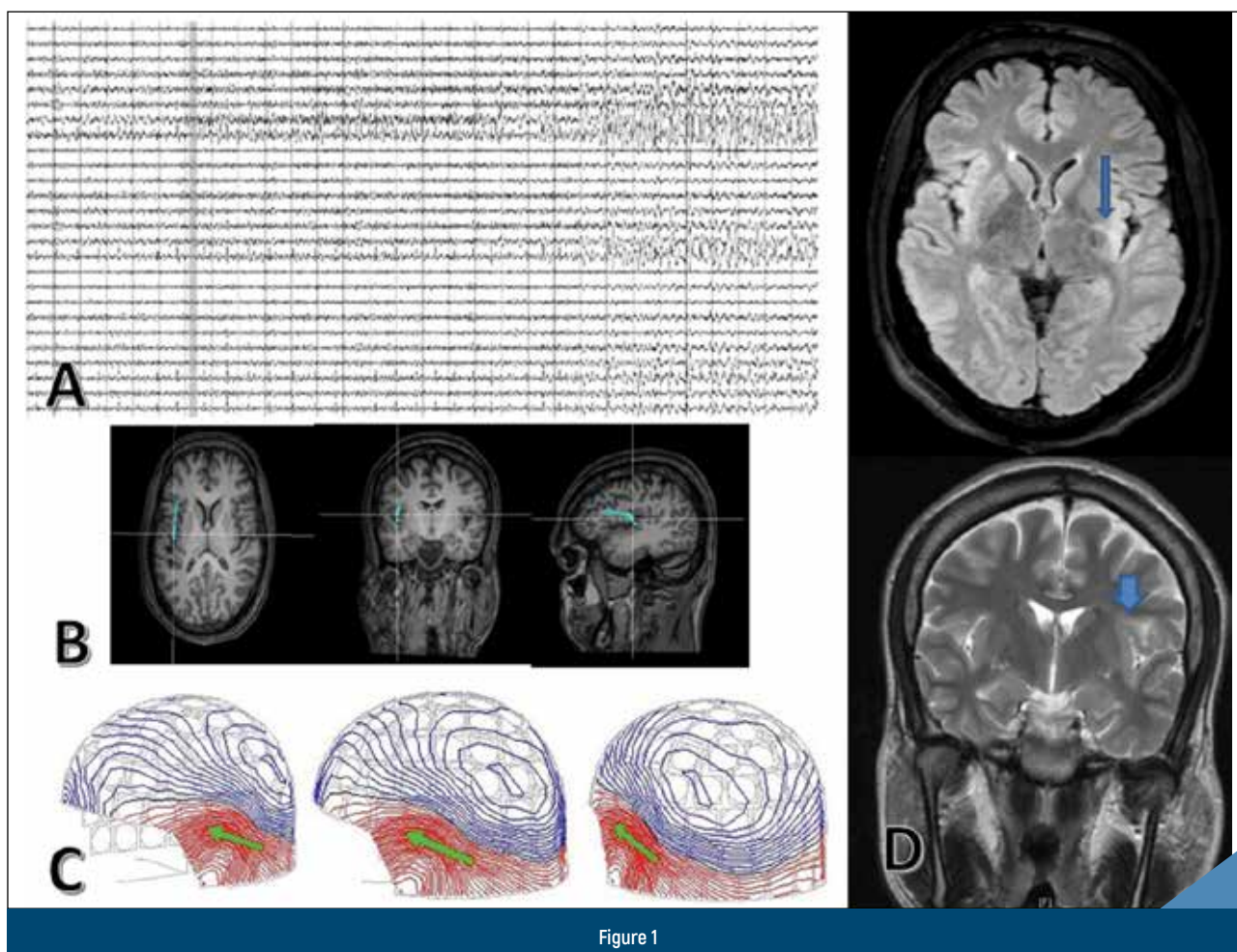
making in epilepsy-surgery. To this end definite focal clusters on ictal-MEG data was analysed and single equivalent current dipole (ECD model) along with SL was performed. Clinical history, long-term video-EEG (VEEG) monitoring, epilepsy-protocol MRI, FDG-PET, ictal-SPECT and interictal-MEG were discussed 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 ictal MEG data was statistically significant ($p = 0.0044$); but the difference in those cleared for phase II monitoring was not ($p = 1.00$) as shown in figure 1. Ictal MEG influenced decisions on possibility of surgery in nine and converted decisions of phase II monitoring in eleven patients to electrocorticography-guided lesionectomy. Delineation of IOZ by ictal-MEG helped convert DRE patients unsuitable for surgery or planned for phase II monitoring

into candidates suitable for surgery. We found that even ECoG-guided resections resulted in favourable outcomes in those who were operated.

PUBLICATION

Ramanujam B, Bharti K, Viswanathan V, Garg A, Tripathi M, Bal C, Chandra PS, Tripathi M. Can ictal-MEG obviate the need for phase II monitoring in people with drug-refractory epilepsy? A prospective observational study. *Seizure*. (2016) 31:45:17-23.

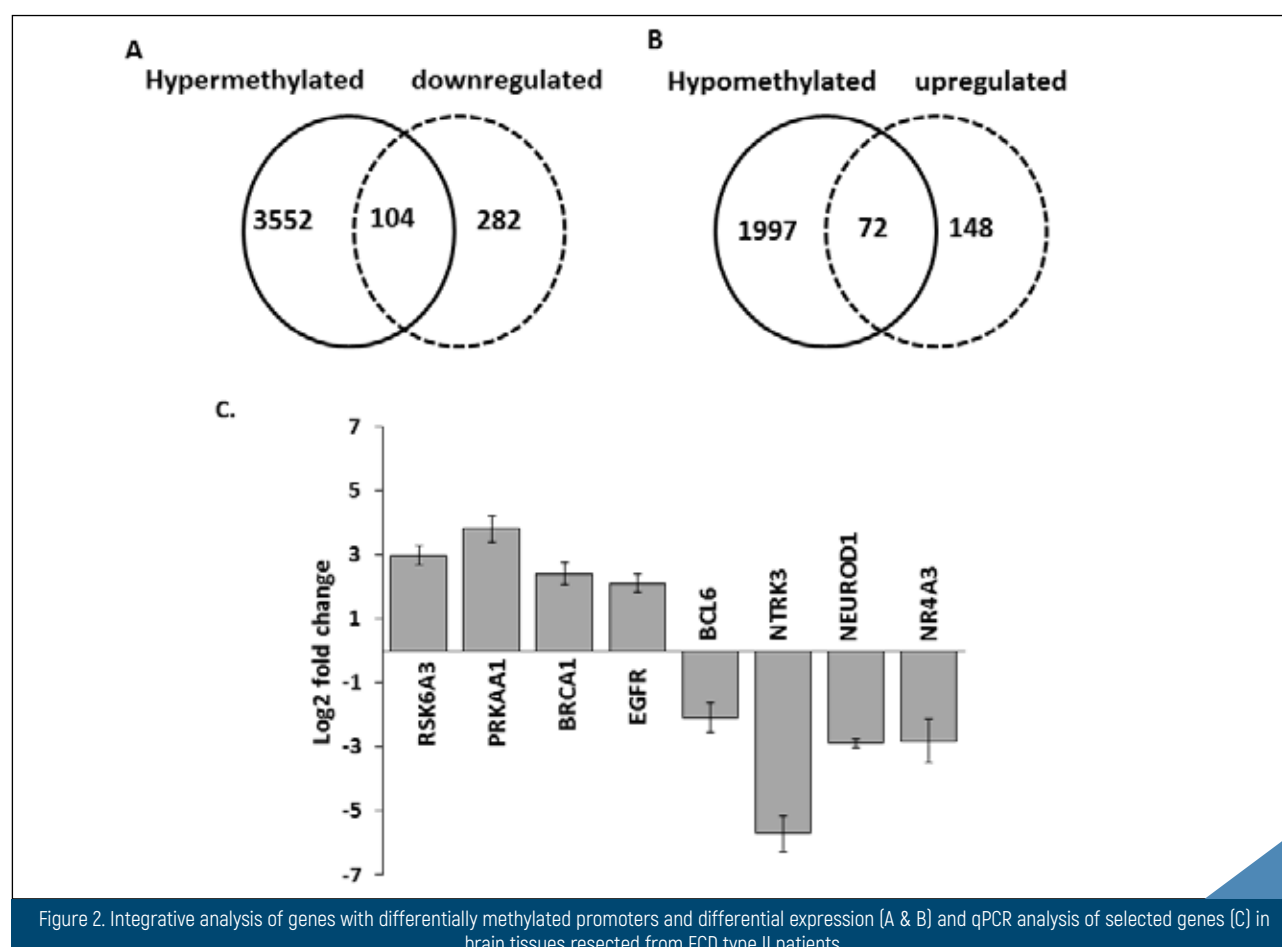


Integrated genome-wide DNA methylation and RNAseq analysis of resected brain tissues identifies aberrant signalling pathways in patients with Focal Cortical Dysplasia (Aparna Dixit)

Focal Cortical Dysplasia (FCD) is one of the most common pathologies of drug resistant epilepsy (DRE). The pharmacological targets are often inappropriate as the molecular mechanisms underlying FCD remain unclear. Implications of epigenetically modulated aberrant gene expression in disease progression are reported in DREs other than FCD. This

study investigates the role of epigenetically deregulated genes potentially involved in the development/ progression of FCD. We performed Genome scale CpG-DNA methylation profiling by Methylated DNA immunoprecipitation microarray (MeDIP-chip) and RNA sequencing using standard protocols on Illumina HiSeq 2500 platform on cortical tissues resected from FCD type II patients undergoing surgery. Differentially methylated genes were analysed using gene spring software GX version 13.0. and differential gene expression (DGE) was performed using

cuffdiff (version = 2.2.1). Integrative analysis of DNA methylation and RNAseq data was carried out using gene spring software GX version 13.0. Validation of both MeDIP and RNAseq experiments was performed using quantitative PCR on autopsy controls (n=10) and FCD type II patients (n=10). A total of 19088 genes showed altered DNA methylation in all the CpG islands, 5725 genes with altered CpG methylation in the promoter regions out of which 176 genes (Figure 2) were showing inverse correlation with the gene expression patterns.



Many of these belong to a cohesive network of physically interacting proteins linked to several cellular functions. Pathway analysis revealed significant enrichment of receptor tyrosine kinase (RTK) EGFR, PDGFR, NTRK3 and mTOR signaling pathways (Figure 3). We report for the first time,

integrated analysis of genomic methylation signature and differential gene expression patterns of tissues resected from FCD type II patients undergoing surgery. We have identified epigenetically modified canonical pathways and candidate genes with potential impact on the pathogenic

mechanisms of epileptogenesis in FCD type II patients.

Differential modulation of breast cancer resistance protein and Major Vault protein in patients with Mesial Temporal Lobe Epilepsy & Focal Cortical Dysplasia (Aparna Dixit).

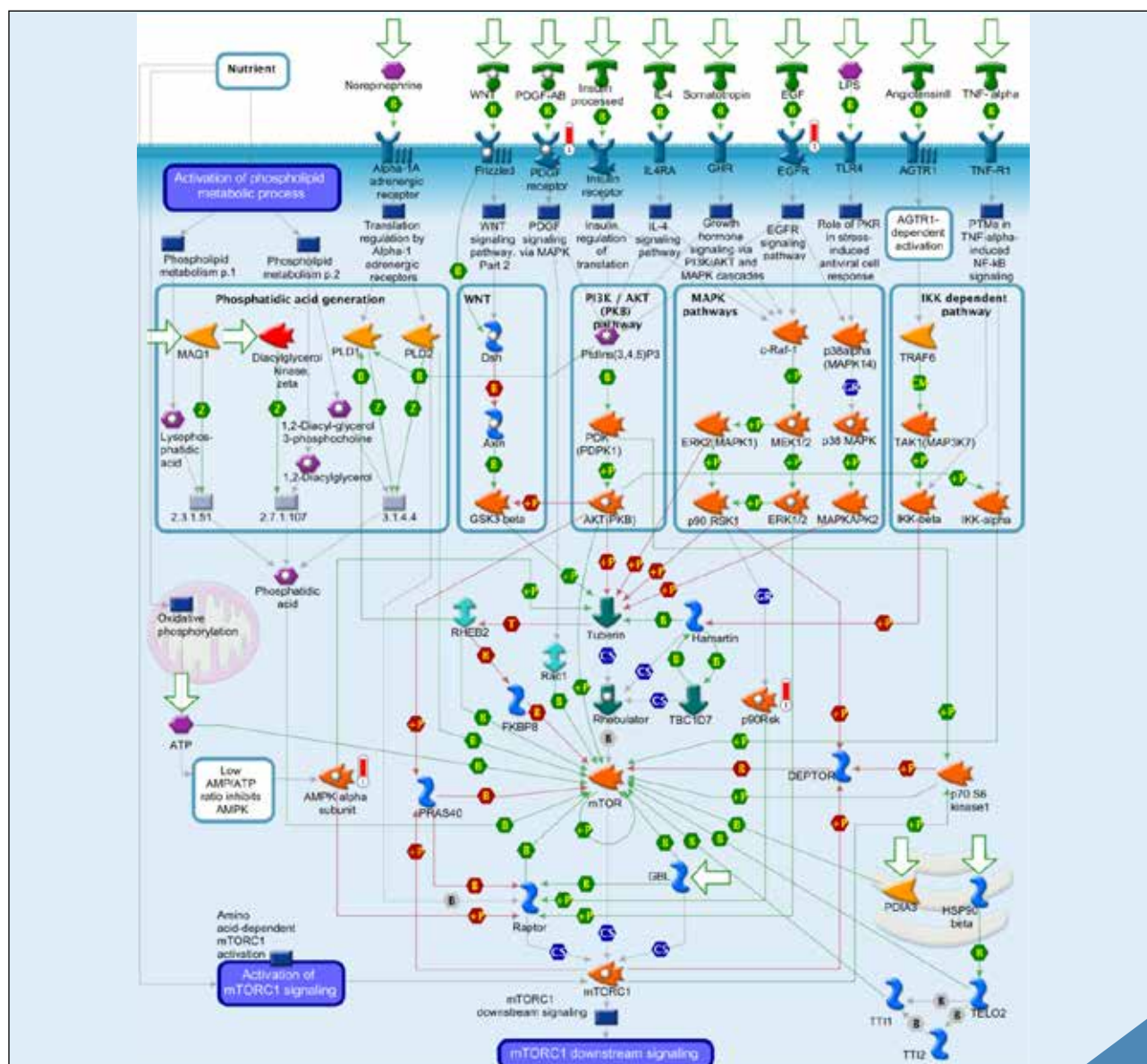


Figure 3. Canonical pathway analysis in MetaCore tool identified EGFR, PDGFR and mTOR signaling as the top 3 canonical pathways to be modulated in FCD type II patients. Red thermometers show an object that is upregulated. The big arrows indicate the "pathway start". GR: group relation; CS: complex subunit; B: Boxes on lines denote the type of regulation where P is phosphorylation, B is binding and Z is catalysis.

Candidate gene specific studies have shown modulation of resistance to drugs by various multidrug resistance proteins in DRE. However, the resistance to drugs in DRE could be more complex and multifactorial involving molecules involved in different pharmacokinetic processes. In this study, we have analysed the gene expression levels of three drug resistance proteins and one drug metabolising enzyme in the two most common DRE pathologies, mesial temporal lobe epilepsy (MTLE) and focal cortical dysplasia (FCD). Brain tissues resected from MTLE (n=16) and FCD type I

and II (n=12) patients undergone surgery were analysed for mRNA levels of multidrug resistance-associated protein 1 (MRP1), major vault protein (MVP), breast cancer resistance protein (BCRP), and one drug metabolising enzyme UGT1A4 as compared to non-epileptic controls which includes tissues resected from tumor periphery (n=4) and autopsy tissues (n=4) by quantitative PCR. The results showed that the relative normal expression of MVP and BCRP were significantly higher in both the pathologies with respect to the non-epileptic autopsy (H/F) controls, whereas MRP1 and

UGT1A4 were unaltered (Fig. 4A & B), MTLE (n=16), FCD (n=12), H (n=4), F (n=4), TP (n=6). To validate the up regulation observed in MVP and BCRP, qPCR was performed using tumor periphery control tissues. Relative normal expression of MVP and BCRP was significantly higher in both the pathologies even with respect to the tumor periphery controls. Relative normal expression of BCRP was significantly higher in MTLE with respect to FCD whereas relative expression of MVP was significantly higher in FCD with respect to MTLE (Fig. 4D) [Dixit et al., 2016].

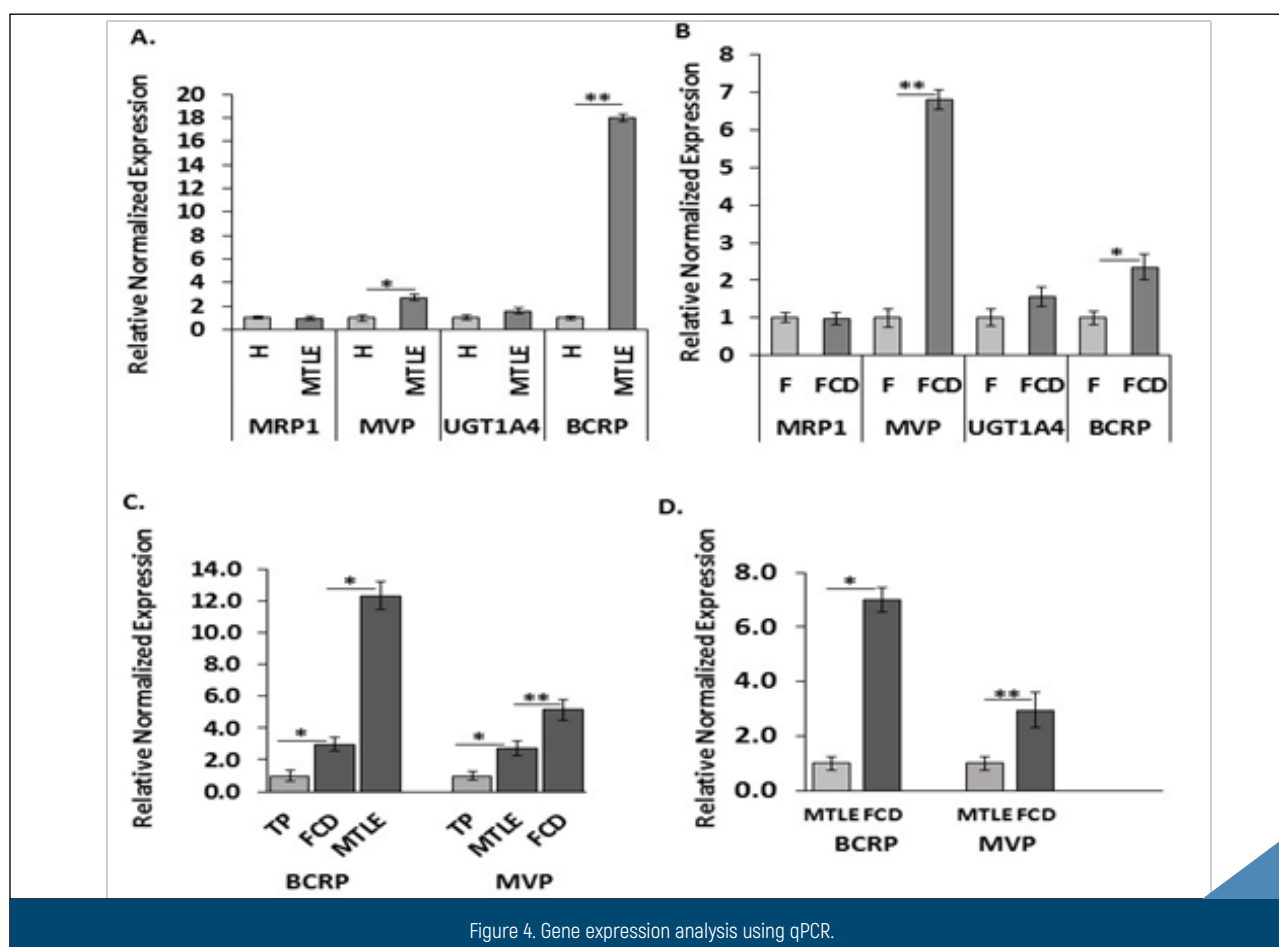


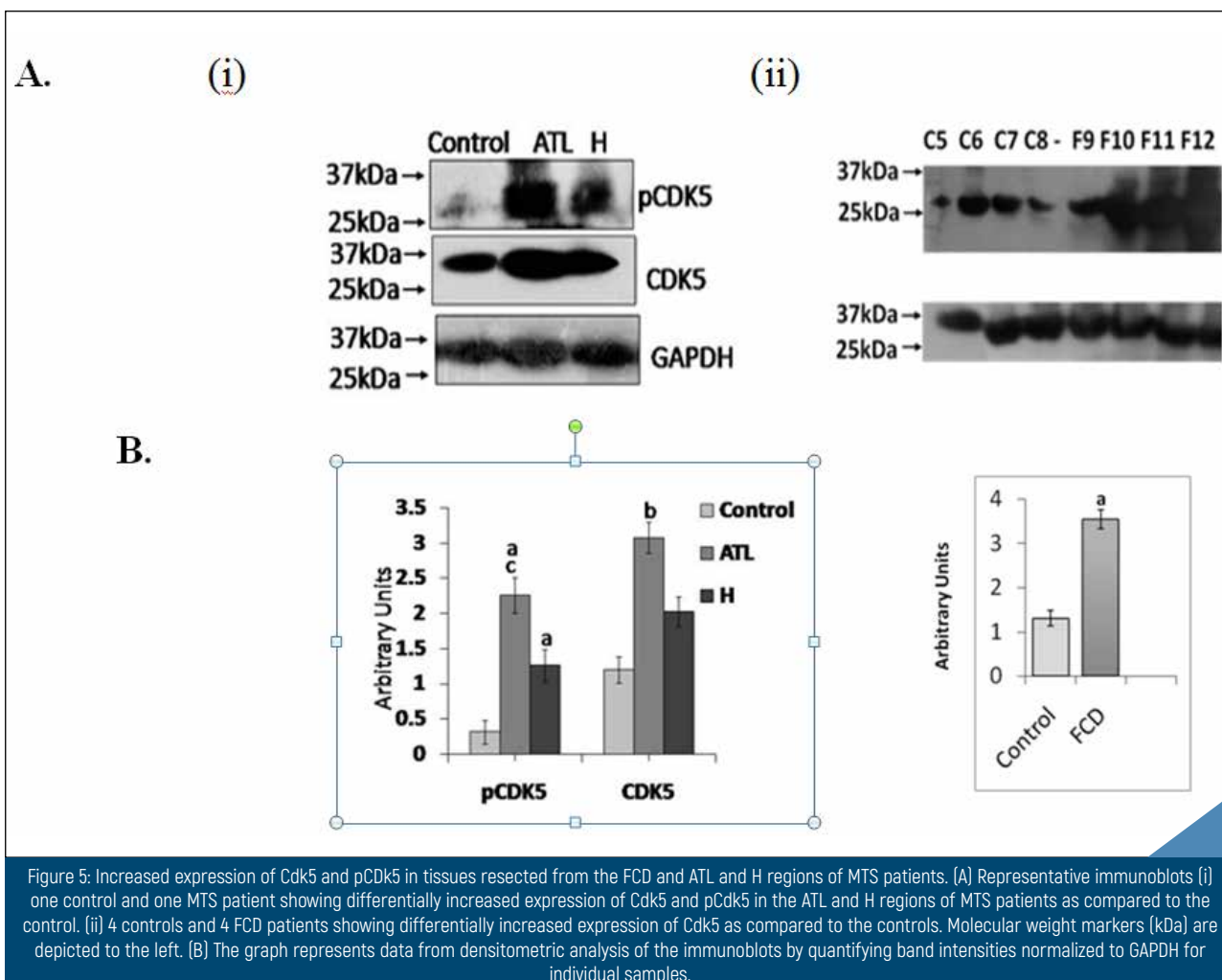
Figure 4. Gene expression analysis using qPCR.

We propose that upregulation of BCRP and MVP is associated with MTLE and FCD and these molecules not only may have the potential to predict MDR phenotypes but may also have therapeutic potential as adjunct treatment in these pathologies.

Upregulation of Cdk5 in both MTLE and FCD patients and differentially alteration of Cdk5 and pCdk5 in the hippocampal and ATL regions of MTLE patients (Aparna Dixit)

Both Cdk5 and pCdk5 levels were differentially increased in the ATL ($p < 0.01$) and hippocampal regions ($p < 0.05$) as compared to control in MTLE patients. pCdk5 was significantly higher in ATL as compared to hippocampal regions ($p < 0.01$), Figure 5A(i) & B(i)). In another study in our lab we have shown differences in hyperexcitability in the ATL and hippocampal regions. Our data suggests that Cdk5 might be contributing differentially in the

ATL and the Hippocampal regions. We also observed significant upregulation of Cdk5 levels in cortical tissues resected from FCD patients, Figure 5A(ii) & B(ii). As Cdk5 is a multifunctional enzyme with large number of substrates, so its downstream signaling might be differentially regulated in the two regions in MTLE patients and in FCD patients and might be contributing differentially in these two most common DRE pathologies.



PUBLICATIONS

Aparna Banerjee Dixit, Devina Sharma, Arpna Srivasatava, Jyotirmoy Banerjee, Manjari Tripathi, Deepak Prakash & P Sarat Chandra. [2017]. Upregulation of BCRP and MVP in Drugresistant epilepsy. *Seizure-European Journal of Epilepsy*, 47:9-12.

Aparna Banerjee Dixit, Jyotirmoy Banerjee, P Sarat Chandra & Manjari Tripathi. [2017]. Advances in Epilepsy Research in India. *Neurology India* 65(Supplement):S83-S92.

Aparna Banerjee Dixit, Jyotirmoy Banerjee, Manjari Tripathi, Chitra Sarkar, Sarat Chandra. [2017]. Synaptic roles of Cyclin dependent Kinase 5 and its implications in epilepsy. *Indian J Med Res* 145, 179-188.

PRESENTATIONS

Invited lecture at XXXIV Annual Conference of Indian Academy of Neurosciences, National Brain Research Centre, Manesar on 19th to 21st October, 2016.

Facilitated "DBT-NBRC-AIIMS Epilepsy Surgery & Epilepsy Neurobiology Workshop" held at All India Institute of Medical Sciences, New Delhi on 1st to 3rd September, 2016.

FUNDING

Principal investigator: "Bio-CARe" Women Scientist Scheme (RGO) BT/AB/08/01/2008 (III) Grant entitled "Deciphering the role of the multifaceted kinase CDK5 in intractable epilepsy." Since October 2014, funded by Department of Biotechnology, India.

Co-investigator: "Centre of Excellence in Epilepsy" a collaborative project between NBRC & AIIMS, funded by Department of Biotechnology, India, since July 2014.

Altered synaptic transmission associated with drug-resistant epilepsy (DRE): A comparison between cortical dysplasia (CD) and non-CD pathology. (Jyotirmoy Banerjee)

Cortical dysplasia (CD) is the commonest subtype of drug-resistant epilepsy (DRE) in pediatric population. There are considerable amount of evidences that suggest that modulation of GABA_A receptor-mediated inhibitory synaptic transmission plays a key role in epileptogenesis in case of focal cortical dysplasia. Spontaneous pacemaker GABA receptor-mediated synaptic activity has been shown in immature pyramidal neurons in the resected specimen obtained from epileptic foci of paediatric CD patients. It has been demonstrated that the ratio of GABAergic to glutamatergic activity is higher in cases with CD compared to non-CD cases. In paediatric CD tonic GABAergic synaptic transmission is abnormally higher. This increase in GABA_A receptor activity has been attributed to the fact that GABA might be acting as excitatory neurotransmitter possibly due to an immature neuronal network. Spontaneous, rhythmic GABAergic synaptic activity has been reported in immature pyramidal neurons of CD tissues which leads to network synchronization. Dysmaturity in

tissues obtained from paediatric patients with CD is a well-known phenomenon. Studies suggest that the enhanced GABAergic transmission is present in the pyramidal neurons of tissue obtained from the primary focus and only limited to paediatric patients with cortical dysplasia. There are no reports where the GABAergic activity in the epileptic foci of paediatric patients with CD is compared to that in case of adult patients. Moreover, it is possible that the altered inhibitory synaptic transmission in patients with CD may not be restricted only to the epileptic foci but may occur in regions remote of the foci. Even though few studies have investigated the inhibitory transmission in regions remote of the primary focus, but there are no data to quantify GABAergic activity in the two regions.

Multimodal imaging including MEG and ECoG helped in targeted resection of brain specimens from the epileptogenic zone. The resected samples were graded as maximally (MAX) and minimally (MIN) abnormal regions. Combination of ECoG, MRI and PET score was used to distinguish between MIN and MAX regions. We assessed the change in GABA_A receptor-mediated spontaneous synaptic transmission in pyramidal neurons in brain specimens obtained from both paediatric and adult patients with CD. To this end, the frequency and amplitude of spontaneous inhibitory postsynaptic currents (IPSCs) recorded from pyramidal neurons in tissues obtained from

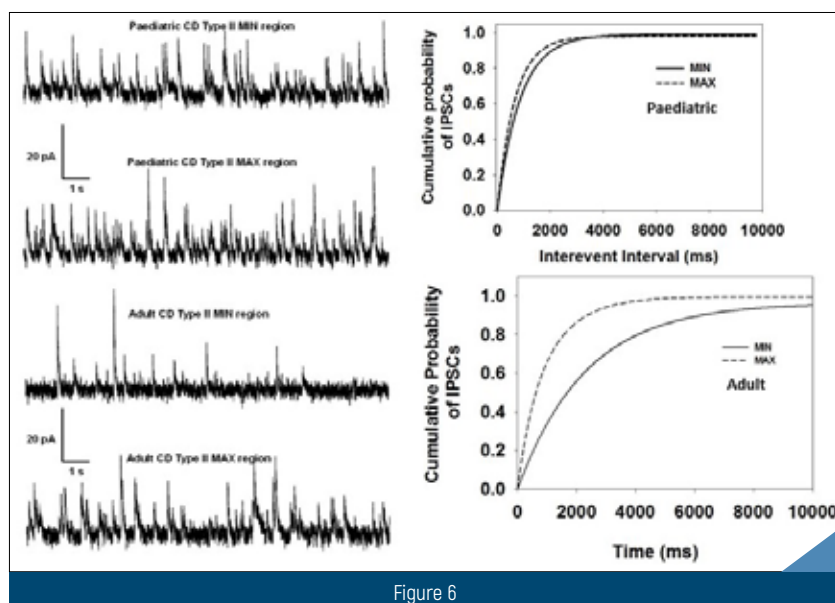


Figure 6

the MAX region of epileptic foci were compared to those recorded from pyramidal neurons in MIN region under specific experimental conditions. We observed that in paediatric cases the frequency of spontaneous IPSCs recorded from pyramidal neurons in the sample obtained from MAX area is higher compared to that in case of non-epileptic control specimens (Figure 6). This finding is in agreement with the concept that paediatric CD patients possess immature cerebral cortex and thereby having an increased GABAergic transmission. The frequency of IPSCs in samples obtained from MIN area were comparable to that in MAX area of paediatric patients. However, when similar experiments were performed on adult patients with CD we observed a significantly higher frequency of IPSCs in samples from the MAX region compared to that in the MIN region (Figure 6).

An index ratio was obtained by dividing the average frequency of GABAergic events by that of glutamatergic events in subset of neurons where the GABAergic and glutamatergic synaptic activities could be recorded in the same cell. The average GABA-glutamate ratio in MIN region was lower than in MAX region in case of adult patients (Figure 7). The

ratio of GABAergic/Glutamatergic events were comparable in the MIN and the MAX region of resected samples obtained from the paediatric patients (Figure 7). We observed that the ratio of GABAergic/glutamatergic activity in both MIN and MAX region of paediatric patients were higher compared to the ratio in non-epileptic control. This data further confirmed that compared to glutamatergic activity, the GABAergic synaptic transmission is higher in the MAX region relative to the MIN region of adult patients, whereas in paediatric cases the GABAergic activity was uniformly higher in both MIN and MAX regions. These findings provide the first direct evidence that in adult patients with CD excessive inhibitory activity is confined to the MAX region of epileptic foci, but in paediatric patients it is also present in the regions beyond the MAX area suggesting more diffused epileptiform activity in paediatric patients.

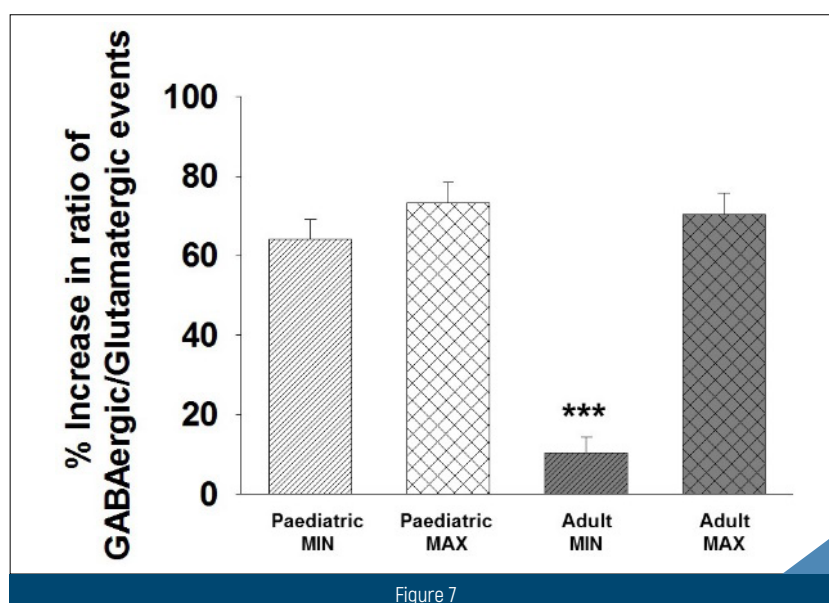


Figure 7

The most common form of non-CD pathology is mesial temporal lobe epilepsy- hippocampal sclerosis (MTLE-HS), where the mesial temporal lobe structures (including hippocampus, amygdala and other entero-rhinal structures) are involved in seizure generation through networks that involve these regions. The surgical procedures used for the treatment of HS include standard anterior temporal lobectomy, combined with amygdalo-hippocampectomy and selective amygdalo-hippocampectomy. The underlying cellular mechanisms responsible for generation of resting state networks in HS is poorly understood. We have recently utilized cellular and molecular strategies to determine the configuration of the glutamatergic networks under resting state, particularly to ascertain whether there is a single hippocampal related network or whether there are other independent networks in the extra-hippocampal regions that may contribute toward seizure

generation. Whole cell patch-clamp technique was used to record spontaneous EPSCs from pyramidal neurons in resected samples under resting conditions from the hippocampal and anterior temporal lobe (ATL) obtained from patients with HS. Frequency and amplitude of spontaneous EPSCs was higher in both the samples compared to non-seizure controls. The magnitude of contribution of the action potential-dependent excitatory activity to hyper excitability in ATL samples was higher than that in the case of the hippocampal samples. This is the first direct evidence at cellular level that two resting-state networks are present in patients with HS, one emanating from the hippocampus and the other from ATL (Banerjee et al., 2017). Index ratios were obtained by dividing the average frequency and the mean peak amplitudes of glutamatergic events by that of GABAergic events in a subset of neurons where the glutamatergic and GABAergic synaptic activities could be recorded in the same

cell. The ratio of frequency and peak amplitude of glutamatergic/GABAergic events were significantly higher in the hippocampal and the ATL samples obtained from the HS patients compared to the ratio in non-seizure controls as shown in figure 8. The average glutamatergic-GABAergic event frequency ratio in the hippocampal sample was lower than the ATL sample in these patients. The index ratio of glutamatergic-GABAergic event peak amplitude was also lower in the hippocampal samples compared to that in the ATL samples obtained from patients with HS. This indicated that the reinforced glutamatergic synaptic connectivity to form a network in the hippocampus was different from that in the ATL in patients with HS. Thus, an anterior temporal lobectomy along with amygdalo-hippocampectomy is likely to have a better outcome than selective amygdalo-hippocampectomy, which spares the anterior temporal lobe.

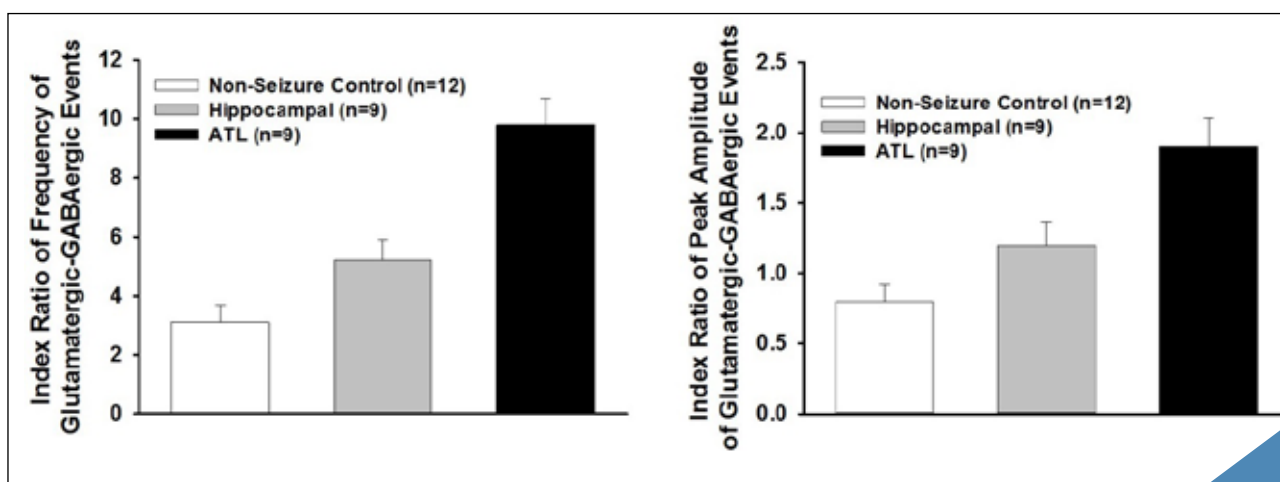


Figure 8

Our findings suggested that the pattern alteration in synaptic transmission associated with CD cases was different from non-CD pathology. Thus tailored surgical procedures needs to be developed for the treatment of patients with CD and non-CD pathologies.

PUBLICATION

1. **Banerjee J**, Dixit AB, Srivastava A, Ramanujam B, Kakkar A, , Sarkar C, Tripathi M & Chandra PS (2017). Altered glutamatergic tone reveals two distinct resting state networks at the cellular level in hippocampal sclerosis. *Scientific Reports* (Nature), 7:319

PRESENTATIONS

1. Scientific presentation at the "brainstorming session on

R&D road map for Epilepsy" conducted by Principal Scientific Adviser to Govt. of India, at Vigyan Bhavan, New Delhi on 8th March, 2017.

2. Scientific talk at Glial cell brainstorming session at School of Neuroscience, Jiwaji University, Gwalior from 2nd to 3rd February, 2017 on the topic "Role of astrocyte-derived kynurenic acid, a tryptophan metabolite, in drug-resistant epilepsy (DRE)".
3. Traditional poster presentation at the 46th Annual meeting of Society for Neuroscience (SfN), USA at San Diego, CA, USA from 12th to 16th November, 2016.
4. Invited lecture at XXXIV Annual

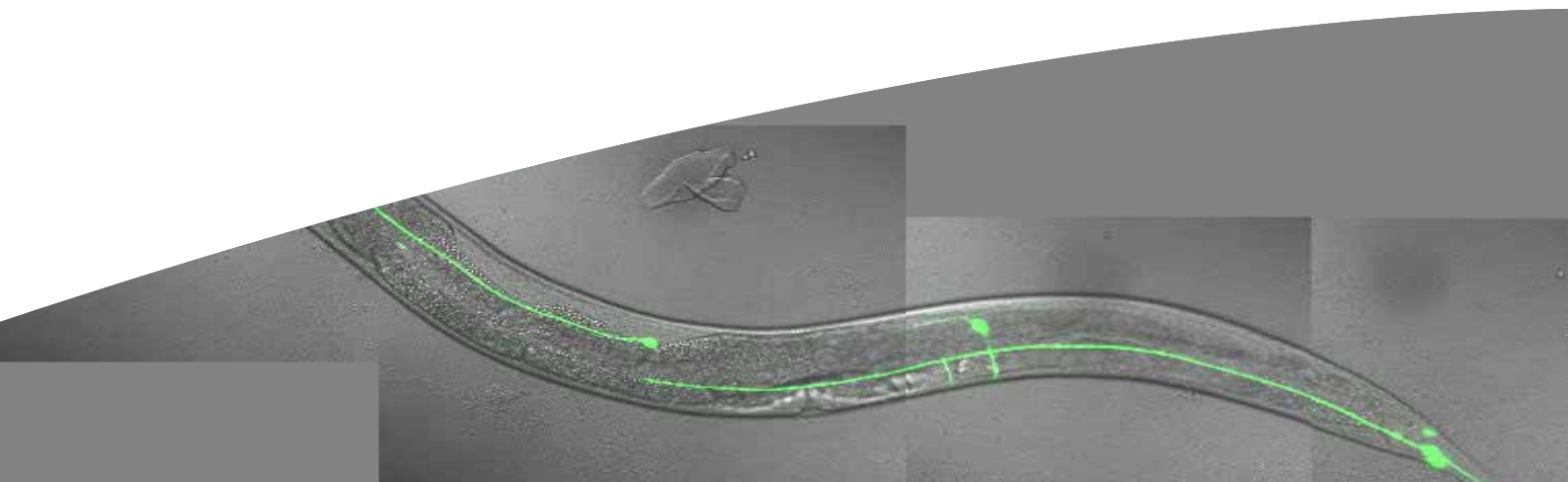
Conference of Indian Academy of Neurosciences, National Brain Research Centre, Manesar on 19th to 21st October, 2016.

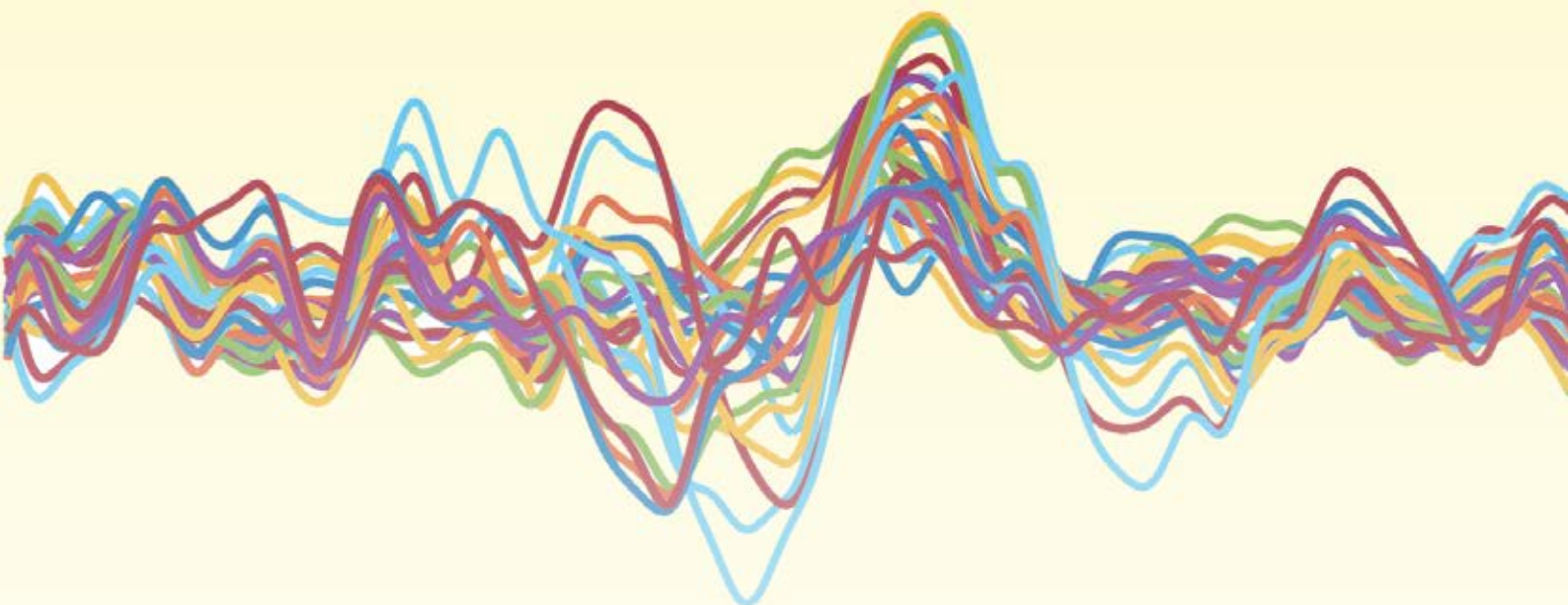
5. Facilitated "DBT-NBRC-AIIMS Epilepsy Surgery & Epilepsy Neurobiology Workshop" held at All India Institute of Medical Sciences, New Delhi on 1st to 3rd September, 2016.

FUNDING

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

Lectures, Meeting and Workshops





Lectures, Meeting and Workshops

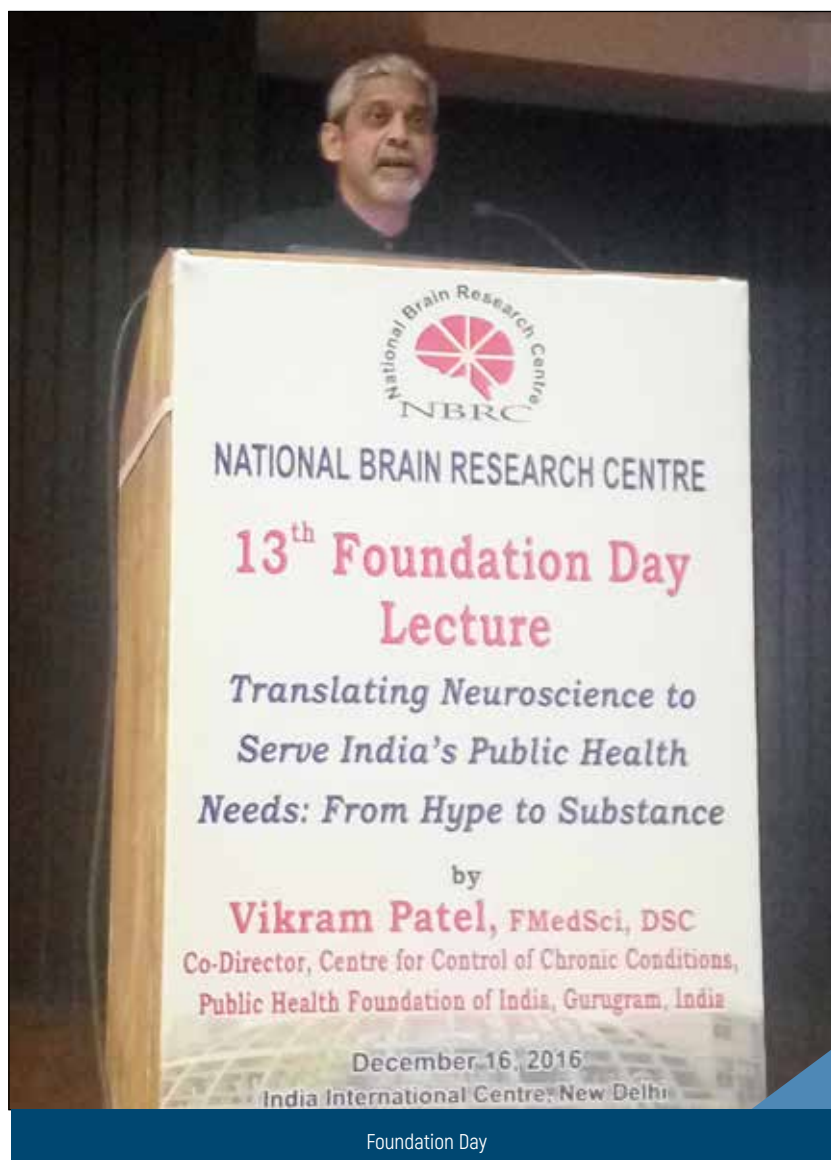
INVITED SPEAKERS AT NBRC

Sr. No.	Name of the Speaker	Title of the Lecture	Date
1	Dr. Santasabuj Das M.D. Scientist E, National Institute of Cholera and Enteric Diseases (ICMR) Kolkata	Dietary short-chain fatty acids in the regulation of intestinal immune response	May 26, 2016
2	Shri Avijit Dutta, Scientist F and Shri Prabir Mitra, Scientist F, National Informatics Centre	Knowledge Ubiquity with ICT	June 24, 2016
3	Prof Shilpa Buch University of Nebraska, Omaha	HIV and Drug abuse go hand in HAND: blaming the messenger	July 15, 2016
4	Dr. Santosh Kumar University of Nebraska, Omaha	HIV AND DRUGS OF ABUSE (ALCOHOL): ROLE OF CYTOCHROME P450	July 20, 2016
5	Dr. Arvind Kumar The Royal Institute of Technology, Stockholm	INHIBITORY NETWORK DYNAMICS UNDERLYING DECISION-MAKING & FEAR-GENERALIZATION	July 21, 2016
6	Dr Sudip Nag Indian Institute of Technology Kharagpur	Implantable Bioelectronics and Neural Prostheses	August 19, 2016
7	Dr Suresh Krishna Scientist, Cognitive Neuroscience Laboratory, German Primate Center, Goettingen, Germany	Topics in Visual Attention, Eye-movements and Auditory Processing	September 20, 2016
8	Dr. Alok Sarin Consultant Psychiatrist, Sitaram Bhartia Institute of Science and Research, New Delhi complexities of choice in severe mental illness	The Nature of Choice: Addressing the	September 23, 2016

9	Prof. Ted Abel University of Pennsylvania	Male-specific deficits in mouse models of	October 13, 2016
10	Dr Sulagna Das, Dept. of Anatomy and Structural Biology, Dept. of Neuroscience, Albert Einstein College of Medicine, New York	Visualizing cell polarization and mRNA dynamics at the single molecule level	December 5, 2016
11	Dr. Dhananjay Huilgol Cold Spring Harbor Laboratory (CSHL) Cold Spring Harbor New York	Developmental mechanisms of projection neurons in the forebrain	January 16, 2017
12	Prof. Ragini Verma University of Pennsylvania	Multimodal Patho-connectomics: Google Maps of the brain, linking connectivity and pathology	January 24, 2017
13	Prof. Pradip Kumar Mohanty Saha Institute of Nuclear Physics, Kolkata	Biological networks : disease and complexity	February 17, 2017
14	Dr Soumen Pal Molecular Imaging Branch National Institute of Mental Health Bethesda	Novel Applications of Adenosine A1 receptor Positron Emission Tomography Imaging (PET imaging)	February 27, 2017
15	Prof. B. S. Shankaranarayana Rao National Institute of Mental Health and Neuro Sciences (NIMHANS) Bengaluru Psychiatric Disorders	The Ever Changing Brain and New Challenges in Treating Neurological and	March 21, 2017

NBRC FOUNDATION DAY LECTURE

The NBRC Foundation Day was celebrated on the 16 of December to mark the anniversary of dedication of the National Brain Research Centre to the nation by the then President of India, His Excellency, Dr A. P. J. Abdul Kalam. As part of the our Foundation day celebrations Dr. Vikram Patel, Co-Director, Centre for control of chronic conditions, Public Health Foundation of India, Gurugram, India, gave a public lecture, on 16 December 2016, entitled "Translating Neuroscience to serve India's public health needs: from hype to substance". Dr Patel's lecture emphasized the enormity and burden of mental disorders in our country and the crucial role of neuroscience research to tackle these diseases.



PROF. B. RAMAMURTHI MEMORIAL LECTURE

Prof. B. Ramamurthi lecture series were initiated in 2006 to commemorate Professor Ramamurthi's significant role in setting up the National Brain Research Centre. On this occasion Prof Subrata Sinha, Director, NBRC enlightened us about Prof. Ramamurthi's vast contributions to neuroscience in India and his efforts in establishing a centre devoted to neuroscience research.

The 12th Prof. B Ramamurthi Memorial Lecture was delivered on May 12th 2017 by Dr Soumya Swaminathan, Director General, Indian Council Medical Research (ICMR). Dr Swaminathan's lecture entitled "Recent Advance in TB Diagnosis and Management" in addition to emphasizing the importance of early diagnosis and treatment also highlighted national as well as global efforts to tackle Multidrug Resistant Tuberculosis.



Prof. B. Ramamurthi Memorial Lecture

ADVANCES IN NEUROIMAGING AND APPLICATIONS IN COGNITIVE DISORDERS (ANACOD) 2016 MAY 3rd TO 4th, 2016

A conference on Advances in neuroimaging and applications in cognitive disorders 2016 was organized by National Brain Research Centre during 3rd – 4th May 2016. The conference brought together a unique intermix of eminent scholars and students in the fields of systems and

computational neurosciences, medical sciences, and behavioral sciences. The focus of the conference was on neuroimaging advancements and its diagnostic and therapeutic applications in cognitive disorders. Recent research in the key areas of metabolic mapping, diffusion

tensor imaging, functional networks, and neurocognition was discussed. This conference provided an opportunity for researchers working in the field of clinical neuroimaging to present their work, get valuable feedback, and foster cross-disciplinary exchange of research ideas.

A BRIEF REPORT ON IAN 2016 – “MOLECULES TO MIND”

The 34th Annual Meeting of Indian Academy of Neurosciences brought together leaders in the field of neuroscience for a comprehensive overview of this rapidly expanding area of research and development in India. The conference was held at National Brain Research Centre (NBRC), Manesar, Gurgaon from October 19 to 21, 2016.

A pre-conference workshop on ‘*Science communication and career*’ was scheduled on 18th of October. This enabled

the attendees (80 students delegates) to understand the do’s and don’ts in scientific documentation and get the flavour of scientific writing.

This conference was based on the theme “*Molecules to Mind*” where the neuroscientists deliberated upon recent advances in understanding of healthy and diseased brain and shared their findings in form of scientific talks, posters and panel discussion. The highlight of the meeting were 5 plenary talks, 11, Invited talks, 11

symposia, platform presentations, short talks, Special evening lectures and two poster sessions on Oct 19 and 20th, where more than 150 posters were presented.

This was the largest gathering of neuroscientists in India and was attended by more than 400 participants from USA, Japan, Singapore, Sri Lanka, Italy and India. Additional information available on the conference website – <http://www.nbrc.ac.in/ian2016/index.php>



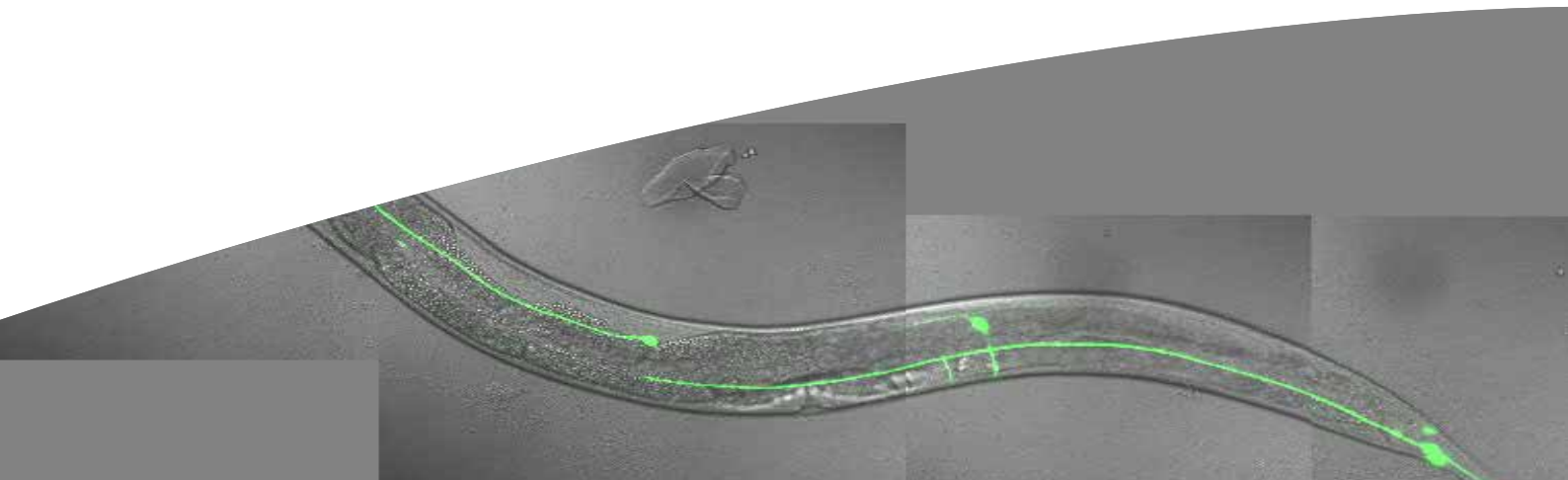
Interactive Poster Presentations (total 150 posters were presented on two days) were well attended by delegates.

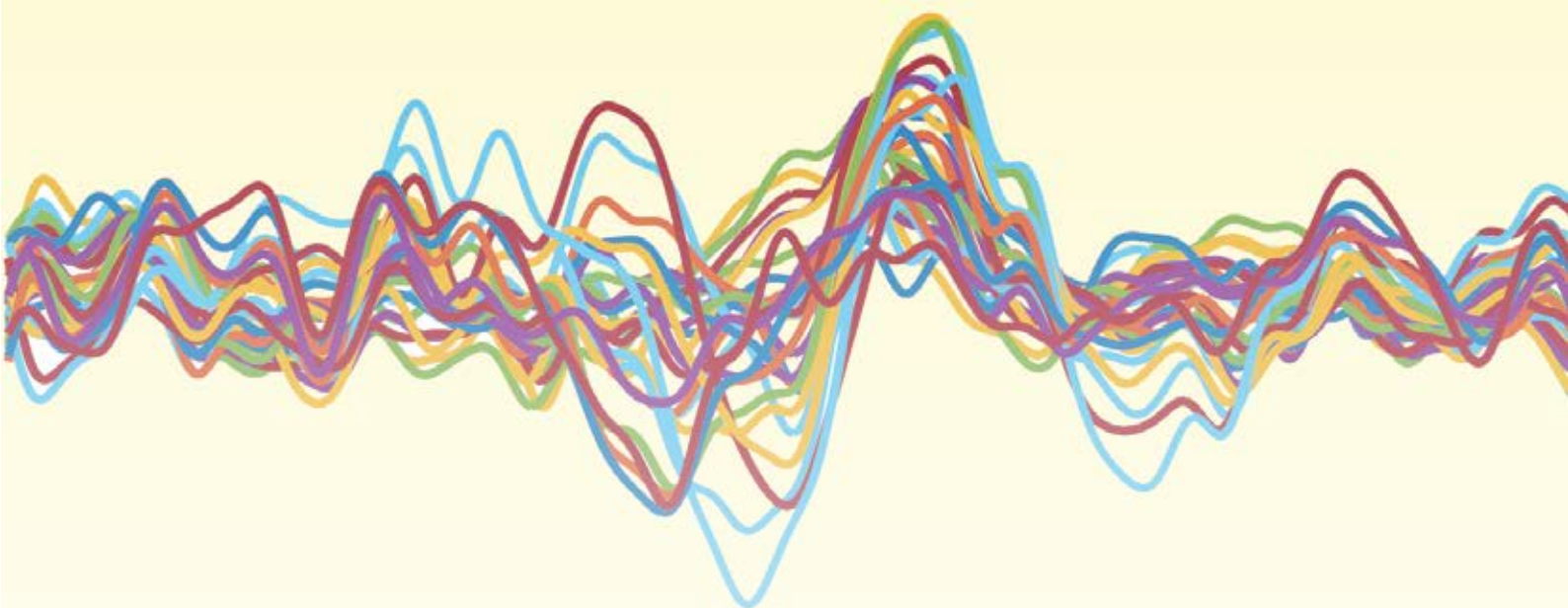


Group Photograph of IAN 2016 delegates



General & Academic Administration





General & Academic Administration – A Profile

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

1. General Administration is headed by the Chief Administrative Officer, who is responsible for overall Management of Establishment, Personnel & Administration Wing, Stores & Purchase Wing, Import & Project Cell, Finance & Accounts Wing, Estate Management & Engineering Maintenance Wing – Civil, Electrical & Mechanical. The officer is also responsible for the administration of DIC.
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 occasions 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 2016' 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 23rd September, 2016, a special guest lecture by Dr. Alok Sarin, Consultant Psychiatrist, Sitaram Bhartia Institute of Science and Research, New Delhi 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 13th Foundation Day of NBRC was held on 16th day of December, 2016. 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. Students from Presidency College, Kolkata exhibited the

models on Crude Brain Map and Magnetic Target Therapy at NBRC. On this august occasion, Prof. Vikram Patel, Co-Director, Centre for Chronic Conditions and Injuries, Public Health Foundation of India delivered a lecture to the students and scientific community at India International Centre, New Delhi.

IMPLEMENTATION OF OFFICIAL LANGUAGE

NBRC Administration has given due importance for the implementation of Hindi as the Official Language at this centre and has made full efforts to implement the use of Official Language in all the administrative jobs such as internal official meetings, interviews, debates, general applications etc. During this year on the occasion of celebration of HINDI DIWAS on 14th September, 2016, lecture competition and other on the spot competitions were organized.

Students and staff participated in these competitions held at Auditorium of NBRC. The winners were distributed the prize money.

RTI ACT

The provisions of RTI Act are being followed at NBRC in letter and spirit. All RTI applications received during 2016-17 seeking information on various matters concerning NBRC were disposed of 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 on them which ensure fair participation and protection of women's interest.

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.

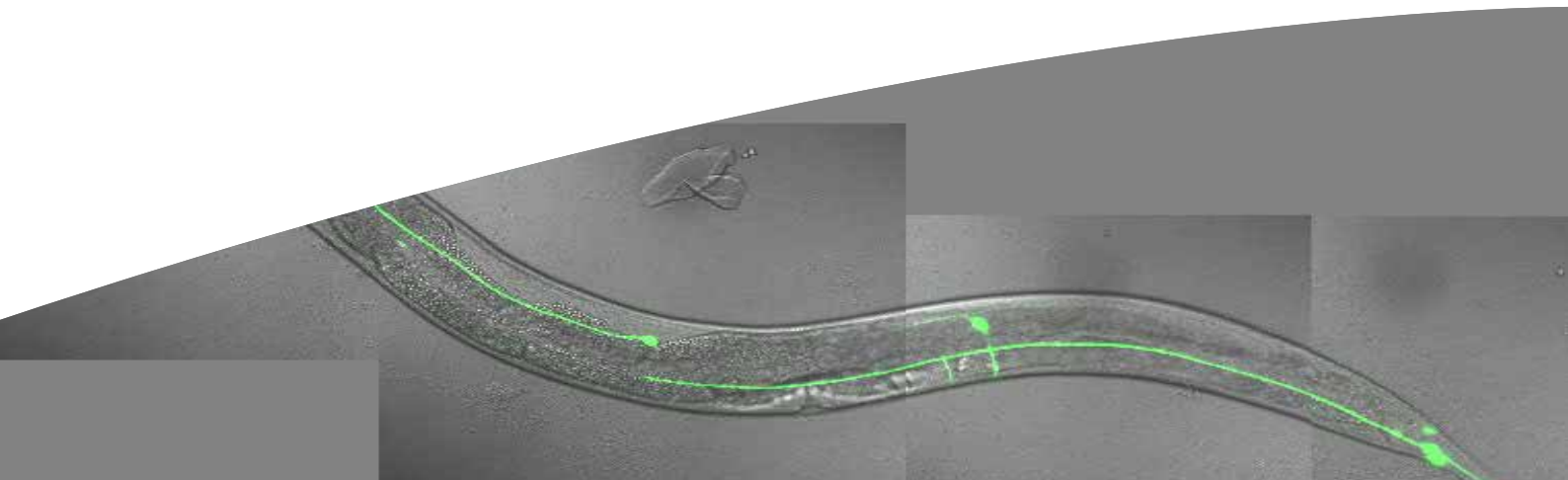
RESERVATIONS AND CONCESSIONS IN EMPLOYMENT & ADMISSIONS OF STUDENTS

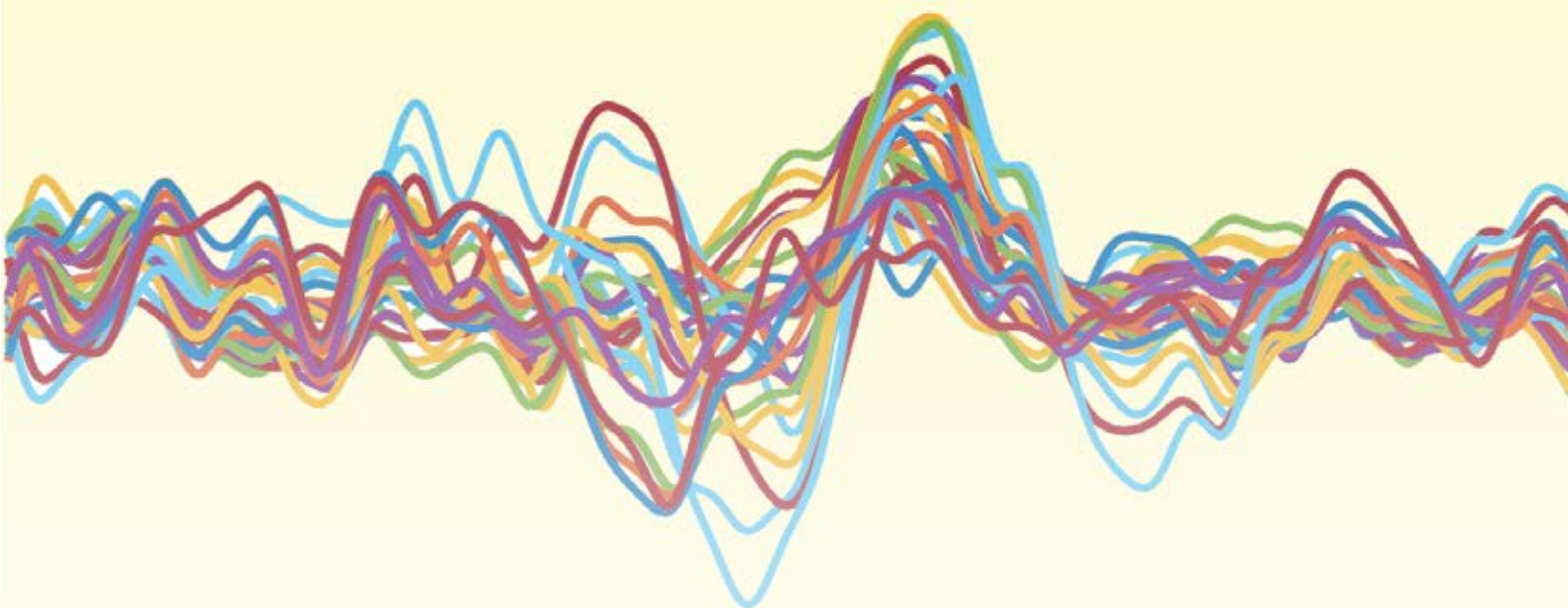
NBRC follows reservations & concessions as per the rules of Government of India in employment, and in the matter of students' admissions, the provision of exemption as provided in Gazette Notification No. 5 dated 4th January, 2007 is implemented.

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)
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Amritsar

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Prof. Neeraj Jain (Faculty)
Prof. Nihar Ranjan Jana (Faculty)
Prof. Pravat Kumar Mandal (Faculty)
Prof. Pankaj Seth (Faculty)
Prof. Shiv Kumar Sharma (Faculty)
Prof. Nandini C. Singh (on deputation to UNESCO)
(Faculty)
Prof. Soumya Iyengar (Faculty)

Prof. Anirban Basu (Faculty)
Dr. Ellora Sen (Faculty)
Dr. Ranjit Kumar Giri (Faculty)
Dr. Yoganarasimha Doreswamy (Faculty)
Dr. Sourav Banerjee (Faculty)
Dr. Arpan Banerjee (Faculty)
Dr. Anindya Roy Ghosh (Faculty)
Mr. Mahender Kumar Singh (Information Scientist)
Prof. Partha Raghunathan (Consultant)
Dr. Rema Velayudhan (Consultant)

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Dr. Yogita Kapil Adlakha

Ph.D. Students

Mr. Kaushik Pramod Sharma (Till 13/06/2016 A.N.)
Mr. Apoorv Sharma
Ms. Manju Tewari (Till 22/08/2016 A.N.)
Ms. Avantika Mathur
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
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. Debajit Bagchi (Till 21/02/2016 A.N.)
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
Mr. Varun Chaturvedi (Till 13/05/2016 A.N.)
Ms. Arshila Ashraf P.K (Till 06/03/2017 A.N.)
Ms. Bindu
Mr. Shiladitya Laskar
Mr. Sibaram Behera
Mr. Sonam Kumar
Ms. Swagata Dey (Till 09/01/2017 A.N.)
Ms. Tripti Joshi
Ms. Vandana (Till 26/08/2016 A.N.)

Integrated Ph.D.

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
Mr. Vipendra Kumar
Ms. Atrayee Basu
Ms. Priyanka
Mr. Gourav Sharma
Ms. Harjot Kaur
Mr. Pruthvi S. G
Ms. Shelly Pal
Mr. Shubham Krishna

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Ms. Himali Arora
Ms. Meenakshi Bhaskar
Mr. Neeraj Kumar
Ms. Sanskriti
Mr. Utsav Mukherjee
Mr. Anagh Pathak
Ms. Kasturi Biswas
Ms. Kirti
Ms. Ritu Moni Borah
Ms. Sreyashi Chandra
Ms. Tapasya Pal
Ms. Varsha Ramakrishna
Ms. Vini Tiwari

Project Assistants

Ms. Prerna Srivastava (Till 06/04/2016 A.N.)
Ms. Kalpana Gupta
Ms. Shanah Rachel John
Mr. Bathini Praveen (Till 24/08/2016 A.N.)

Mr. Alok Nath Mohapatra
Mr. Giri Raj Kishore Sharma
Ms. Noopur Singh (Till 30/09/2016 A.N.)
Ms. Srujana Raili (Till 24/06/2016 A.N.)
Ms. Rishu (Till 12/11/2016 A.N.)
Ms. Tanya Singh
Mr. Jacob Antony Alappatt
Ms. Pankajam T
Ms. Kanza Saleem
Ms. Mena Fatma
Ms. Rohini Roy
Ms. Hajare Nilambari Anil
Ms. Kshipra Gurunandan (Till 29/07/2016 A.N.)
Mr. Shrey Dutta
Ms. Deborah Daphne P
Ms. Monika
Mr. Archith Rajan
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(Till 03/10/2016 A.N.)

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Dr. Chetan Kumar Yadav, Research Associate-3
Dr. Md. Aftab Alam, Research Associate-3
(Till 02/02/2017 A.N.)
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Mr. Saurabh Srivastav, Research Associate-1
(Till 01/04/2016 A.N.)
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(Till 14/02/2017 A.N.)
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SERB-National Post Doctoral Fellowship

Dr. Akansha Jalota
Dr. Suvadip Mallick

Dr. Amit Naskar

Dr. Poonam

Research Fellows

Dr. Fahim Ahmad

(From 01/09/2016 Till 31/03/2017 A.N.)

Dr. Sourish Ghosh

(From 23/02/2016 Till 30/09/2016 A.N.)

Dr. Mahar Fatima

(From 29/09/2016 Till 19/04/2017 A.N.)

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Mr. Rajiv Ramaswamy, Senior Research Fellow (Project)

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Mr. Kamal Bharti, Technologist (MEG Project)

Mr. Vibhin V., Technologist (MEG Project)

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Mr. Manjit, Lab Attendant (MEG Project)

Mr. Rakesh Yadav, Nursing Orderly (MEG Project)

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Mr. Gaurav Singh, Technician (MEG Project)

Mr. Vivek Singh, Technician (MEG Project)

Mr. Om Prakash Jakhar, Nurse (MEG Project)

Mr. Tony C. Paikada, Nurse (MEG Project)

Ms. Mini Mohan, Nurse (MEG Project)

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Ms. Yamini Yadav, Research Manager (Project)
(Till 03/03/2017 A.N.)

Dr. Siya Sherif, Senior R&D Engineer (Project)

Mr. Budhaditya Basu, Junior Research Fellow (Project)

Ms. Ananya Ghosh, Junior Research Fellow (Project)

Ms. Ankita Sharma, Junior R&D Engineer (Project)

Ms. Deepika Shukla, R&D Engineer-1 (Project)

Mr. Krishan Sharma, Technician A (Project)

Mr. Dixit Sharma, Junior Research Fellow (Project)

Ms. Teesta Naskar, ICMR-SRF (Project)

Ms. Sriparna Mukherjee, DST-INSPIRE Fellow Junior
Research Fellow (Project)

TECHNICAL STAFF

Mr. Rajbir Singh
Mr. Sanjeev Kumar Choudhary
Dr. D.D. Lal
Mr. Jitender Ahlawat
Mr. Arvind Singh Pundir
Dr. Inderjeet Yadav
Mr. Kedar Singh Bajetha
Ms. Seepika
Mr. Sachin Kumar
Mr. Amit Kumar Gaurav
Ms. Tarnnum Mansoori
Mr. Kanhaiya Lal Kumawat
Mr. Shankar Datt Joshi
Mr. Sumit Kumar Sinha Mahapatra

Mr. D. Narender
Mr. Sanjay Kumar
Mr. Mithlesh Kumar Singh
Mr. Ankit Sharma
Mr. Yunish Khan
Mr. Durga Lal Meena
Md. Irshad Alam
Mr. Manish Kumar
Mr. P. Manish
Mr. Dil Bahadur Karki
Mr. Rammehar
Mr. Hari Shankar
Mr. Mahendra Singh
Mr. Sanjay Kumar Singh

ADMINISTRATIVE STAFF

Mr. Tanmoy Bhattacharyya
Mr. Santosh Kumar Choudhary
Mrs. Pooja Gosain
Mr. Ravinder Pal
Mr. Suraj Bhan
Mr. Rakesh Kumar Yadav
Mr. Himanshu Mal
Mr. Ajay Kumar Dehariya
Mr. Parmander Singh Rawat
Mr. Jitendra Kumar Meena
Mr. Kailash Chandra Khuntia
Mr. Bhupender Pal Sharma
Mr. Satish Kumar
Mr. Surender Kumar

Consultant

Mr. Suman Kumar

DIC Project Staff

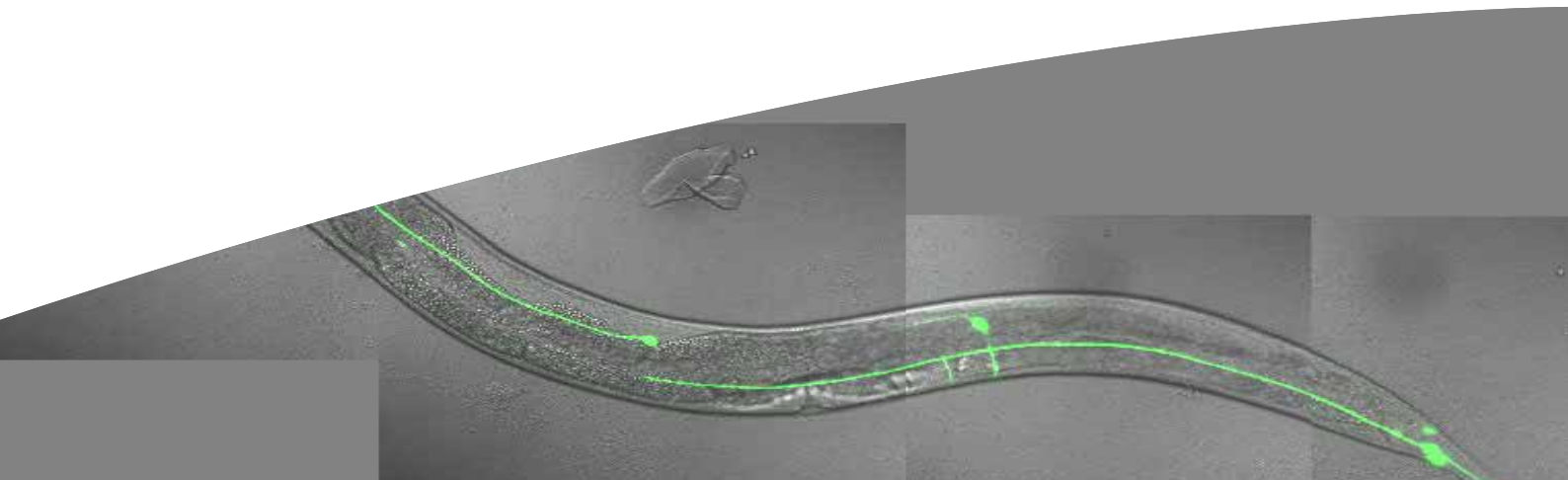
Mr. Sanjay Kumar Gupta
Ms. Reema Saxena
Ms. Sunita Yadav
Mr. Amit Kumar
Mr. R. Ganesh Gurumoorthy

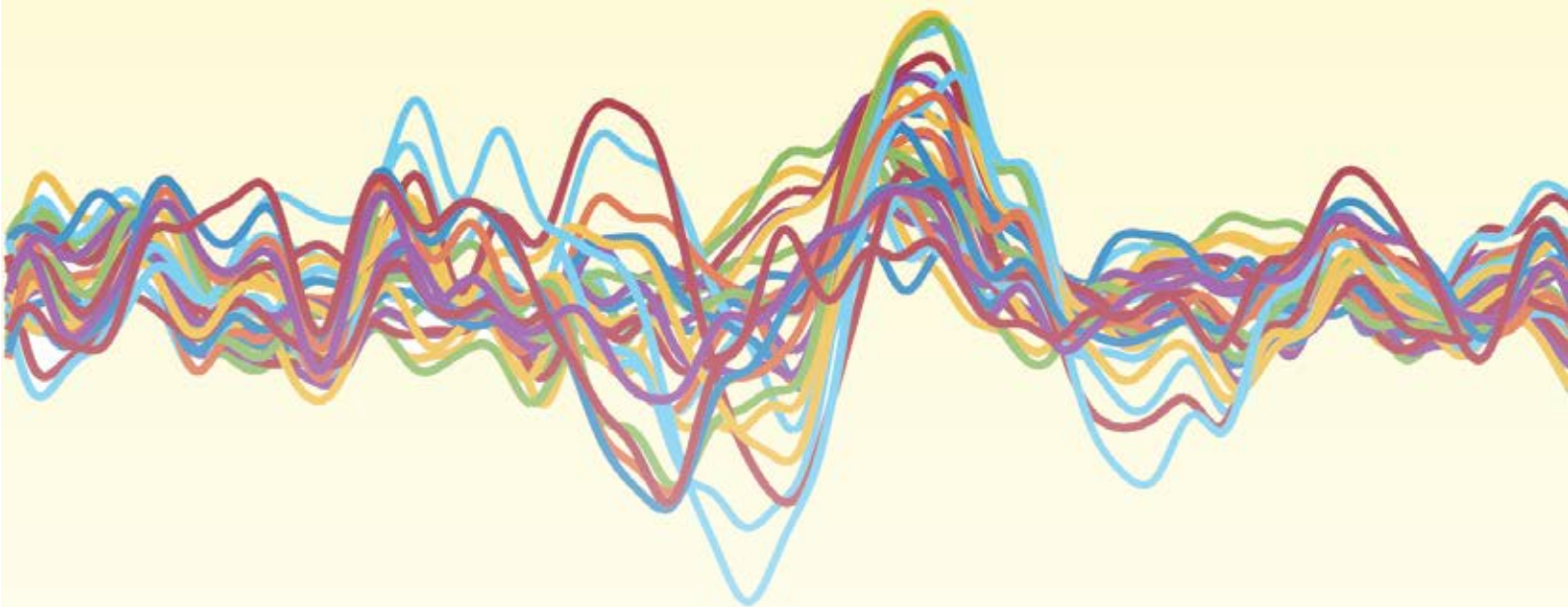
NBRC Contract Staff

Dr. Karan Singh
Mr. Hanish Kumar Sauda
Mr. Mukesh Chauhan
Ms. Sonam Saini
Ms. Nisha Devi



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, 2017, 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 completeness of the accounting records, relevant to the preparation and presentation of the financial statements that give a true and fair view and are free from material misstatement, whether due to fraud 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 perform the audit to obtain reasonable assurance about whether the financial the financial statement are free from material misstatement. An audit involves performing

procedure to obtain audit-evidence about the amounts and the disclosures in the financial statements. The procedures selected depend on the auditor's judgement, 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.

D) Opinion

Subject to clauses [4], [7], [9], [11], [12], [14], [15] & [16] of Notes to Accounts (Schedule-17) forming part of financial statements for current year, the impact whereof on results of operations 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, 2017;
- (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

[CA. Kapil Mittal]

B. Com (H), F. C. A, D. I. S. A. (ICAI), A. I. I. S. L. A.

PARTNER

M. No.-503378

Place: New Delhi

Date: November 23, 2017

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGAON, HARYANA

BALANCE SHEET AS AT March 31, 2017

	Schedule	Current Year	Previous Year
CORPUS / CAPITAL FUND AND LIABILITIES		Amount in (₹)	
Corpus/Capital Fund	1	1,093,502,000.00	1,068,502,000.00
Reserve and Surplus	2	[215,139,232.61]	[204,178,468.93]
Earmarked/Endowment Funds	3	897,493,189.08	588,095,148.44
Current Liabilities and Provisions	4	44,411,921.59	39,465,061.66
Total (Liabilities)		1,820,267,878.06	1,491,883,741.17
ASSETS			
Fixed Assets	5	1,284,242,640.97	1,301,880,240.90
Investments - CPF Fund	6	25,873,329.20	22,484,766.13
Current Assets, Loans, Advances etc.	7	510,151,907.89	167,518,734.14
Total (Assets)		1,820,267,878.06	1,491,883,741.17
Notes on Accounts	17		
SIGNATURES FOR NATIONAL BRAIN RESEARCH CENTRE, GURGAON (HARYANA)			

SANTOSH KUMAR CHOUDHARY
DY. FINANCE OFFICER

TANMOY BHATTACHARYA
OFFG. F & AO (CAO)

PROF. SUBRATA SINHA
DIRECTOR

As per our separate report
of even date attached

Place : New Delhi
Date : 23rd November, 2017

For N.C. MITTAL & CO.
Chartered Accountants
(FRN-000237N)

KAPIL MITTAL
PARTNER
Membership No. 503378

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGAON, HARYANA

INCOME AND EXPENDITURE ACCOUNT FOR THE YEAR ENDED March 31, 2017

	Schedule	Current Year	Previous Year
INCOME		Amount in (₹)	
Grants/ Subsidies (Revenue) from DBT		254,500,000.00	265,000,000.00
Fees/Subscriptions	8	1,353,863.50	3,295,614.00
Interest Earned	9	6,989,793.67	3,740,789.25
Other Income	10	3,533,235.00	4,012,960.00
Total Income (A)		266,376,892.17	276,049,363.25
EXPENDITURE			
Establishment Expenses	11	74,372,764.00	69,362,539.00
Other Administrative/Lab Expenses etc.	12	14,477,865.88	10,190,508.64
Repair & Maintenance	13	81,769,971.45	84,827,967.22
Training and Networking Expenses	14	35,645,391.06	37,440,063.36
Laboratory and Animal house consumables	15	31,192,065.46	24,931,087.71
Prior Period Items	16	6,834,783.00	3,975,902.66
Depreciation	5	33,044,815.00	33,894,933.00
Total Expenditure (B)		277,337,655.85	264,623,001.59
Balance Being Surplus/(Deficit) carried to Reserve & Surplus (A-B)		-10,960,763.68	11,426,361.66
SIGNATURES FOR NATIONAL BRAIN RESEARCH CENTRE, GURGAON (HARYANA)			

SANTOSH KUMAR CHOUDHARY
DY. FINANCE OFFICER

TANMOY BHATTACHARYA
OFFG. F & AO (CAO)

PROF. SUBRATA SINHA
DIRECTOR

As per our separate report
of even date attached

Place : New Delhi
Date : 23rd November, 2017

For N.C. MITTAL & CO.
Chartered Accountants
(FRN-000237N)

KAPIL MITTAL
PARTNER
Membership No. 503378

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGAON, HARYANA
RECEIPTS AND PAYMENTS FOR THE YEAR ENDED March 31, 2017

RECEIPTS	CURRENT YEAR	PREVIOUS YEAR	PAYMENTS		CURRENT YEAR	PREVIOUS YEAR
	Amount in (₹)	Amount in (₹)			Amount in (₹)	Amount in (₹)
I. Opening Balances			I. Expenses			
a) Cash in Hand	164,213.00	150,868.00	i) Establishment Expenses		8,825,278.00	12,156,149.00
b) Bank Balances			ii) Administrative Expenses		2,767,593.88	2,791,933.64
i) In Deposit Accounts	-	-				
ii) Saving Accounts	150,227,029.30	111,635,000.29	Payment Made Against Funds For Various Projects			
iii) CPF Investments	17,970,437.00	16,400,000.00	i) Recurring /Capital expenditure		590,601,262.53	500,371,143.72
			ii) Capital Grant Refunded to DBT		-	-
II. Grants Received			iii) Refund to RCGB		-	-
a) From Government of India						
Plan			III. Maintenance Cost			
i) Recurring Expenditure	254,500,000.00	265,000,000.00	i) Lab Maintenance Expenses		30,311,351.38	23,145,840.97
ii) Non-Recurring Expenditure	25,000,000.00	40,000,000.00	ii) Office Maintenance		52,088,484.00	48,245,809.00
			iii) Vehicle Running & Maintenance		631,069.00	565,729.00
Plan (Recurring)						
b) Fellowship Grant	1,506,706.50	3,124,964.00	IV. Investment and Deposit Made			
c) Delcon Projects (Including Interest)	883,910,787.00	406,374,007.88	i) Out of Earmarked/Endowment funds		214,000.00	162,660.00

III.	Receipt made against funds for various projects			V.	Expenditure of Fixed Assets & Capital Work-in-progress		
	i) Recurring Receipt/ Capital Grant	77,881,075.34	71,677,128.48		i) Purchase of Fixed Assets	35,756,376.50	8,393,727.35
	(Including Interest)						
				VI.	Training Expenses	2,934,731.06	2,436,457.32
IV.	Interest Received						
	i) On Bank Deposits	-	-	VII.	Other Payments(Specify)		
	ii) Savings Account	5,386,124.00	2,130,701.00		i) Advances to Supplier	7,367,793.24	13,365,844.37
	iii) On CPF Fund	1,567,379.00	1,570,437.00		ii) Advances to Staff	4,555,772.00	4,425,746.00
	iv) Other Interest	71,951.00	33,349.00		iii) Leave Encashment/ LTC/ Bonus	887,173.00	901,286.00
					iv) Security Deposit Paid	337,909.00	2,753,556.20
V.	Any Other Receipt				v) EMD Refunded	4,960,128.00	1,794,913.00
	Indirect Income				vi) TDS Paid	8,717,917.00	7,555,651.00
	i) Advance to Supplier Received	32,340.00	3,738,754.02		vii) Imprest	176,147.00	225,916.00
	ii) Advance to Staff Received	1,137,320.00	1,093,039.00		viii) Payment of Current Liabilities	165,417,767.32	150,236,607.02
	iii) Sale of Tender Documents	63,600.00	21,500.00		ix) Prepaid Insurance	571,613.00	895,911.00
	iv) Misc. Receipts.	369,528.00	657,091.00				
	v) Earnest Money Deposit Received	5,206,704.00	2,895,400.00				
	vi) Sale of Scrap	11,000.00	13,000.00	VIII.	Closing balances		
	vii) Guest House Charges	200,250.00	241,550.00		a) Cash in Hand	160,755.00	164,213.00
	viii) Hostel Deposit	386,000.00	373,000.00		b) Bank Balance		
	ix) CPF Fund Received	1,822,558.00	1,604,086.00		i) In Deposit Accounts		-
	x) Library Deposit	119,000.00	125,000.00		ii) Saving Accounts	494,595,608.23	150,227,029.30

xi) Current Liabilities Rec.	3,882,543.00	627,684.22	iii) CPF Investments	19,537,816.00	17,970,437.00
xii) Other Receipts	-	19,300,000.00			
TOTAL	1,431,416,545.14	948,786,559.89	TOTAL	1,431,416,545.14	948,786,559.89
SIGNATURES FOR NATIONAL BRAIN RESEARCH CENTRE, GURGAON (HARYANA)				-	

SANTOSH KUMAR CHOUDHARY
DY. FINANCE OFFICER

TANMOY BHATTACHARYA
OFFG. F & AO (CAO)

PROF. SUBRATA SINHA
DIRECTOR

As per our separate report
of even date attached

Place : New Delhi

Date : 23rd November, 2017

For N.C. MITTAL & CO.
Chartered Accountants
(FRN-000237N)

KAPIL MITTAL
PARTNER
Membership No. 503378

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGAON, HARYANA

SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE 1-CORPUS/CAPITAL FUND:					
		Amount in (₹)			
		Current Year		Previous Year	
1	Grant-in-Aid - Balance as at the beginning of the year		1,068,502,000.00		1,028,502,000.00
	Add: Contribution towards Corpus/Capital Fund	25,000,000.00		40,000,000.00	
			25,000,000.00		40,000,000.00
	Balance as at the year end		1,093,502,000.00		1,068,502,000.00

SANTOSH KUMAR CHOUDHARY
DY. FINANCE OFFICER

TANMOY BHATTACHARYA
OFFG. F & AO (CAO)

PROF. SUBRATA SINHA
DIRECTOR

As per our separate report
of even date attached

Place : New Delhi
Date : 23rd November, 2017

For N.C. MITTAL & CO.
Chartered Accountants
(FRN-000237N)

KAPIL MITTAL
PARTNER
Membership No. 503378

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGAON, HARYANA
SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE 2 - RESERVES AND SURPLUS:					
		Amount in (₹)			
		Current Year		Previous Year	
1	General Reserve				
	As per last Account	(204,178,468.93]		(215,604,830.59]	
	Addition during the Year	(10,960,763.68]		11,426,361.66	
	Less : Deductions during the year (deficit)	-	(215,139,232.61]	-	(204,178,468.93]
	Balance as at the year end		(215,139,232.61]		(204,178,468.93]

SANTOSH KUMAR CHOUDHARY
DY. FINANCE OFFICER

TANMOY BHATTACHARYA
OFFG. F & AO (CAO)

PROF. SUBRATA SINHA
DIRECTOR

As per our separate report
of even date attached

Place : New Delhi
Date : 23rd November, 2017

For N.C. MITTAL & CO.
Chartered Accountants
(FRN-000237N)

KAPIL MITTAL
PARTNER
Membership No. 503378

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGAON, HARYANA
SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE 3 - EARMARKED/ENDOWMENT FUNDS					
		Amount in (₹)			
		Current Year		Previous Year	
A.	Opening Balance of Project Fund	65,509,610.23		102,502,311.60	
	Add : Grants Received during the year	76,275,714.00		67,998,258.60	
	Less : Grants Refunded During the year	0.00		4,703,275.91	
		141,785,324.23		165,797,294.29	
	Add:Interest Earned	560,449.00		1,533,076.00	
	Any other addition during the year	0.00	142,345,773.23	0.00	167,330,370.29
	Less: Utilization/Expenditure towards objectives of funds				
	a) Capital Expenditure				
	Fixed Assets	44,606,263.83		50,038,966.61	
	Others	0.00		0.00	
	b) Revenue Expenditure				
	Salaries and wages	21,051,193.95		20,961,255.00	
	Other Administrative Expenses	40,905,491.76	106,562,949.54	30,820,538.45	101,820,760.06
	Total (a)		35,782,823.69		65,509,610.23
B.	Opening Balance of Fixed Asset Fund (Project)	417,596,391.58		444,757,974.16	
	Add: Addition During the year	44,698,763.83		50,038,966.61	
	Less: Deduction / Transferred During the year	0.00		4,570,178.32	
	Less: Depreciation for the period 2016-17	69,096,761.00	393,198,394.41	72,630,370.87	417,596,391.58
	Total (b)		393,198,394.41		417,596,391.58
C.	Opening balance of Donation received	2,631,788.00		2,631,788.00	
	Add: Additions during the year	0.00	2,631,788.00	0.00	2,631,788.00
	Total (c)		2,631,788.00		2,631,788.00
D.	Endowment fund created for Buildings Opening Balance	85,473,182.00		85,473,182.00	
	Add: Additions / (Payment) during the year	0.00	85,473,182.00	0.00	85,473,182.00
	Total (d)		85,473,182.00		85,473,182.00

E.	Contributory Provident Fund	12,140,138.00		10,698,712.00	
	Add: Additions / (Payment) during the year	1,608,558.00	13,748,696.00	1,441,426.00	12,140,138.00
	Total (e)		13,748,696.00		12,140,138.00
F.	DeLcon E-library Consortium				
	Opening balance of Consortium	4,744,038.63		24,197,834.13	
	Add : Grants Received during the year	881,948,576.00		405,673,921.88	
	Add : Interest Earned	1,962,211.00		700,086.00	
	Less: Utilization/Expenditure towards objectives of funds	521,996,520.65	366,658,304.98	425,827,803.38	4,744,038.63
	Total (f)		366,658,304.98		4,744,038.63
G.	Escrow Account-DBT				
	Opening balance	0.00		0.00	
	Less: Grant Received During the Year	0.00	0.00	0.00	0.00
	Total (g)		0.00		0.00
	Balance as at the year end (a+b+c+d+e+f+g)		897,493,189.08		588,095,148.44

SANTOSH KUMAR CHOUDHARY
DY. FINANCE OFFICER

TANMOY BHATTACHARYA
OFFG. F & AO (CAO)

PROF. SUBRATA SINHA
DIRECTOR

As per our separate report
of even date attached

Place : New Delhi
Date : 23rd November, 2017

For N.C. MITTAL & CO.
Chartered Accountants
(FRN-000237N)

KAPIL MITTAL
PARTNER
Membership No. 503378

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGAON, HARYANA

SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE-4 CURRENT LIABILITIES AND PROVISIONS					
		Amount in (₹)			
		Current Year		Previous Year	
A.	Current Liabilities				
1	Sundry Creditors	2,753,910.25		777,687.25	
2	Advances Received (Security deposit)	2,984,128.42		2,621,446.42	
3	Other Liabilities-TDS Payable	4,098.50		139,658.50	
4	Earnest Money Deposit	4,151,271.00		3,968,695.00	
5	Hostel Deposit	1,073,000.00		881,000.00	
6	Library Deposit	314,000.00		252,000.00	
7	Expenses Payable	21,718,800.40		19,590,060.47	
8	CPF Payable	49,859.00		43,798.00	
9	GIS Payable	3,004.00		2,954.00	
10	Salary Payable	5,358.00		5,314.00	
11	NPS(Employees Subscription)	13,139.00		24,090.00	
12	Audit Fees Payable	59,976.00		28,175.00	
13	Stale Cheque	383,752.22		316,874.22	
14	Labour Cess Payable	184,929.00	33,699,225.79	104,890.00	28,756,642.86
	Total (a)		33,699,225.79		28,756,642.86
B.	Provisions				
1	Gratuity	6,759,338.00		6,749,850.00	
2	Accumulated Leave Encashment	3,953,357.80	10,712,695.80	3,958,568.80	10,708,418.80
	Total (b)		10,712,695.80		10,708,418.80
	Balance as at the year end (a+b)		44,411,921.59		39,465,061.66

SANTOSH KUMAR CHOUDHARY
DY. FINANCE OFFICER

TANMOY BHATTACHARYA
OFFG. F & AO (CAO)

PROF. SUBRATA SINHA
DIRECTOR

As per our separate report
of even date attached

Place : New Delhi
Date : 23rd November, 2017

For N.C. MITTAL & CO.
Chartered Accountants
(FRN-000237N)

KAPIL MITTAL
PARTNER
Membership No. 503378

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGAON, HARYANA

SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE 5 - FIXED ASSETS/ DEPRECIATION											
	Rate of Dep.	GROSS BLOCK				DEPRECIATION			NET BLOCK		
		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	Total Depn. Upto 31.03.17	As at Current year-end	As at Previous year-end	Amount in (₹)
A. FIXED ASSETS		More than 6 Months	Less than 6 Months								
1	10%	0.00	318,590.00	0.00	71,887,574.00	23,562,706.67	4,816,557.00	28,379,263.67	43,508,310.33	48,006,277.33	
2	15%	2,536,279.45	31,771,162.18	0.00	305,485,644.95	143,297,376.02	21,945,403.00	165,242,779.02	140,242,865.93	127,880,827.30	
3	15%	0.00	0.00	0.00	2,086,342.00	1,409,099.80	101,586.00	1,510,685.80	575,656.20	677,242.20	
4	10%	157,303.00	1,265,449.00	0.00	39,550,753.00	17,915,660.84	2,100,237.00	20,015,897.84	19,534,855.16	20,212,340.16	
5	60%	26,212.00	1,308,669.00	0.00	723,1690.81	4,709,195.59	1,120,896.00	5,830,091.59	1,401,599.22	1,187,614.22	
6	15%	148,316.00	1,358,242.61	0.00	32,932,585.40	16,422,565.65	2,374,635.00	18,797,200.65	14,135,384.75	15,003,461.14	
TOTAL OF THE CURRENT YEAR		2,868,110.45	36,022,112.79	0.00	459,174,590.16	207,316,604.57	32,459,314.00	239,775,918.57	219,398,671.59	212,967,762.35	
B. FIXED ASSETS (PROJECTS)											
1	15%	41,398,599.53	3,300,164.30	-	764,365,632.25	302,070,476.85	69,096,761.00	371,167,237.85	393,198,394.40	47,596,391.57	
TOTAL OF THE CURRENT YEAR (C) (A+B)		44,266,709.98	39,322,277.09	-	1,223,540,222.41	509,387,081.42	101,556,075.00	610,943,156.42	612,597,065.99	630,564,153.92	
PREVIOUS YEAR											

D.	CAPITAL WORK IN PROGRESS																	
1	BUILDINGS																	
	Capital work-in-progress including advances,		668,974,084.73	914989.00	0.00	0.00	669,889,073.73	0.00	0.00	0.00	669,889,073.73	0.00	0.00	0.00	669,889,073.73	668,974,084.73		
	construction materials and building under																	
	construction (net of recovery)																	
E.	INTANGIBLE ASSETS																	
1	Patent and Copy Right (Application Fee)	25%	5,100,392.00	-	-	0.00	5,100,392.00	2,758,389.75	585,501.00	3,343,890.75	1,756,501.25	2,342,002.25						
	TOTAL (C+D+E)		1,814,025,712.07	45,181,698.98	9,322,277.09	0.00	1,898,529,688.14	512,145,471.17	102,141,576.00	614,287,047.77	1,284,242,640.97	1,301,880,240.90						

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TANMOY BHATTACHARYA
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DIRECTOR

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of even date attached

Place : New Delhi
Date : 23rd November, 2017

For N.C. MITTAL & CO.
Chartered Accountants
(FRN-000237N)

KAPIL MITTAL
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Membership No. 503378

NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGAON, HARYANA
SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE 6- INVESTMENTS - CPF FUND			
		Amount in (₹)	
		Current Year	Previous Year
1	FDR in Scheduled Bank	19,537,816.00	17,970,437.00
2	Balance with Savings Bank Account	6,335,513.20	4,514,329.13
	Total	25,873,329.20	22,484,766.13

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SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE 7 - CURRENT ASSETS, LOANS, ADVANCES ETC.					
		Amount in (₹)			
		Current Year		Previous Year	
A.	Current Assets				
1	Cash Balances in hand (Including Cheques/Drafts)		160,755.00		164,213.00
2	Bank Balances:				
	a) With Scheduled Banks:				
	-In Deposit Account	0.00		0.00	
	-In Saving Accounts (Core & Projects)	488,260,095.03		145,712,700.17	
	-In Deposit Against various Project Assets	0.00	488,260,095.03	0.00	145,712,700.17
3	Interest Accrued on FD(CPF)		1,196,628.46		1,481,965.00
	Total (a)		489,617,478.49		147,358,878.17
B.	Loans, advances and other assets				
1	Advances and other amounts receivable in cash				
	or in kind or for value to be received				
	a) Staff	6,686,226.06		8,077,848.55	
	b) Imprest	101,966.00		125,966.00	
	c) Advance to Parties	6,562,615.34		4,461,913.63	
	d) Others(Security & other Deposits)	2,091,414.20		2,161,491.20	
	e) Other Advances	92,625.00		92,625.00	
	f) TDS Receivable	4,427,969.80		4,344,100.59	
	g) Prepaid Insurance	571,613.00	20,534,429.40	895,911.00	20,159,855.97
	Total (b)		20,534,429.40		20,159,855.97
	Balance as at the year end (a+b)		510,151,907.89		167,518,734.14

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SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE 8 - FEES/ SUBSCRIPTIONS			
		Amount in (₹)	
		Current Year	Previous Year
1	Application Fees	598,971.00	433,000.00
2	Others (Specify)-Fellowship Grants	754,892.50	2,862,614.00
	Total	1,353,863.50	3,295,614.00

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NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGAON, HARYANA
SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE 9 - INTEREST EARNED			
		Amount in (₹)	
		Current Year	Previous Year
1	On Term Deposits :-		
	a) With Scheduled Banks	1,424,492.67	1,576,739.25
2	On Savings Accounts :-		
	a) With Scheduled Banks	5,386,124.00	2,130,701.00
3	On Advances	179,177.00	33,349.00
	Total	6,989,793.67	3,740,789.25

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SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE 10-OTHER INCOME			
		Amount in (₹)	
		Current Year	Previous Year
1	Projects Receipts	2,145,413.00	2,709,622.00
2	Tender Form	63,600.00	21,500.00
3	Miscellaneous (Scrap & Others)	488,004.00	486,611.00
4	Medical Contribution Recovery	191,100.00	184,260.00
5	Licence Fee Recovery	113,904.00	115,368.00
6	Establishment Charges	120,928.00	108,125.00
7	Guest House Charges	410,286.00	387,474.00
	Total	3,533,235.00	4,012,960.00

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NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGAON, HARYANA
SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE 11- ESTABLISHMENT EXPENSES			
		Amount in (₹)	
		Current Year	Previous Year
1	Salaries and wages and allowances	53,379,364.00	50,043,743.00
2	Bonus	145,068.00	142,477.00
3	Contribution to pension scheme	1,131,354.00	691,687.00
4	Staff welfare expenses	154,578.00	211,796.00
5	Children education reimbursement	1,098,000.00	1,017,451.00
6	Leave encashment	2,065,359.00	719,355.00
7	LTC expenses	1,085,194.00	721,224.00
8	Medical reimbursement	969,818.00	1,203,336.00
9	NPS(employer subscription)	2,732,074.00	2,769,440.00
10	overtime allowance	18,317.00	18,844.00
11	Skilled manpower	10,619,801.00	10,419,485.00
12	Medical insurance	765,505.00	902,505.00
13	Office expenses	208,332.00	501,196.00
	Total	74,372,764.00	69,362,539.00

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NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGAON, HARYANA
SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE 12- OTHER ADMINISTRATIVE EXPENSES			
		Amount in (₹)	
		Current Year	Previous Year
1	Postage, telephone and communication charges	789,849.00	803,375.00
2	Printing and stationary	1,147,369.00	1,094,501.00
3	Travelling expenses	2,411,792.50	1,664,640.00
4	Auditor remuneration	31,801.00	28,175.00
5	Hospitality/local meeting expenses	496,197.00	241,325.00
6	Legal and professional charges	645,632.00	872,330.00
7	Lease rent	4,444,048.00	1,000,000.00
8	Bank charges	14,524.63	9,326.14
9	Advertisement and publicity	506,117.00	402,610.00
10	Misc. expenses	316,833.00	582,196.50
11	Books and periodicals	79,294.00	89,318.00
12	Transportation charges	3,296,856.50	3,097,932.00
13	Conveyance reimbursement	68,640.00	85,780.00
14	Honorarium (others)	228,912.25	219,000.00
	Total	14,477,865.88	10,190,508.64

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SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE 13- REPAIRS AND MAINTENANCE EXPENSES			
		Amount in (₹)	
		Current Year	Previous Year
1	Electricity and water charges	47,690,321.00	49,223,529.00
2	Insurance others	529,703.00	1,591,277.00
3	Repairs and maintenance (office)	16,023,352.00	19,867,794.00
4	Manpower (house keeping)	2,358,447.00	1,379,149.00
5	Vehicle running and maintenance	297,609.00	195,906.00
6	Manpower (security)	4,277,353.00	6,617,108.00
7	Horticulture	2,239,947.00	1,846,267.00
8	Repairs and maintenance (buildings)	1,134,683.00	426,981.00
9	Repairs and maintenance (lab equipment)	5,768,433.45	2,876,733.22
10	Repairs and maintenance (office equipment)	211,132.00	58,070.00
11	Insurance charges vehicle	38,395.00	63,356.00
12	Repairs & maintenance office equipment(AMC)	600,893.00	154,486.00
13	Petrol, Diesel and CNG etc.	599,703.00	527,311.00
	Total	81,769,971.45	84,827,967.22

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SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE 14 - TRAINING AND NETWORKING EXPENSES			
		Amount in (₹)	
		Current Year	Previous Year
1	Subscription to journals	2,315,686.06	2,184,923.32
2	Training expenses	31,679,848.00	33,556,076.00
3	Contingencies (CSIR/UGC/DBT/ICMR students)	370,271.00	454,809.00
4	Conference & workshop expenses	1,140,051.00	1,122,111.04
5	Student medical expenses	139,535.00	122,144.00
	Total	35,645,391.06	37,440,063.36

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SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE 15 - LABORATORY AND ANIMAL HOUSE CONSUMABLES			
		Amount in (₹)	
		Current Year	Previous Year
1	Lab consumables and chemicals	27,958,577.26	23,006,896.71
2	Medicines and consumables animal	3,233,488.20	1,924,191.00
	Total	31,192,065.46	24,931,087.71

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SCHEDULE FORMING PART OF BALANCE SHEET AS AT March 31, 2017

SCHEDULE 16- Prior Period Items			
		Amount in (₹)	
		Current Year	Previous Year
1	Prior period expenses	6,834,783.00	3,975,902.66
	Total	6,834,783.00	3,975,902.66

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SCHEDULE-17

NATIONAL BRAIN RESEARCH CENTRE, MANESAR, GURGAON

**SIGNIFICANT ACCOUNTING POLICIES & NOTES ON ACCOUNTS FORMING PART OF THE BALANCE SHEET
AS AT 31ST MARCH, 2017 AND INCOME & EXPENDITURE ACCOUNT FOR THE YEAR ENDED 31ST MARCH,
2017**

SIGNIFICANT ACCOUNTING POLICIES & NOTES ON ACCOUNTS

1. Accounting Convention:

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

1.2 The NBRC is moving towards adopting 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:

2.1 All purchases of chemicals, glassware, consumables and printing & stationery have been booked/charged to consumption/ expenditure at the time of purchases.

3. Fixed Assets:

3.1 Fixed Assets are stated at historical cost.

3.2 Physical verification of assets had not been conducted during the year.

3.3 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.

3.4 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 2017. Pending completion of construction, the payments made to DC&SEM are being shown as Deposit under the head Building under Construction. 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.

3.5 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 FY 2012-2013 Depreciation is being charged as per Income Tax Act 1961 on W.D.V basis. As stated in FY 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. 6,90,96,761.00 (previous year Rs. 7,26,30,370.87) 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. 3,30,44,815.00 for current financial year (Rs. 3,38,94,933.00 for previous year) had been debited to Income & Expenditure Account.

5. Investments:

5.1 Investments in term deposits with banks are basically for Current Investments and are therefore valued on cost.

5.2 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.

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

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 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. 10,00,000/- 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. No amortization/write off have been done in respect of the assets acquired on lease. Arrears of Rs. 34,44,048.00 against lease amount for the period of 1999 to 2017 has been paid to IVCOL during the year for utilizing additional land as an approach road.

9. Retirement Benefits:

9.1 The NBRC is not registered with the Provident Fund authorities and it maintains a separate CPF Trust, which is yet to be recognized and the CPF fund required the separate accounting.

9.2 The NBRC has not made any provision for gratuity and leave encashment during financial year 2016-2017 as against the requirement of AS-15 issued by ICAI. However, the amount of gratuity and leave encashment to the extent of Rs. 67,59,338.00 and Rs. 39,53,357.80 respectively already exists on 31st March, 2017, (Rs. 67,49,850.00 & Rs. 39,58,568.00 respectively as on 31st March, 2016) 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. Loans & Advances:

Advances appearing under the head Current assets, Loans & Advances under Schedule-7 are subject to confirmation from parties.

12. Bank Balance:

Bank balance in Axis Bank Limited, Gurgaon (A/c No.056010100453998) & Punjab National Bank, Manesar (FCRA)

(A/c No. 4136000100008889) as on 31st March, 2017 of Rs. 47,02,67,825.86 & Rs. 10,86,657.54 respectively (Previous Year Rs. 13,53,90,801.46 & 10,73,959.54 respectively) 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. 77,21,007.00 for the financial year 2016-17 (previous year 2015-16 Rs. 39,75,902.66) 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 recipient. However, it was subsequently brought to notice of NBRC by said recipient 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. The matter is pending since.

15. Outstanding Balances of Closed Projects:

As on 31st March, 2017, Sixty-Six number of earmarked 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" in the balance sheet as on that date & are subject to reconciliation with the granting agencies.

16. Others

16.1 The Balance in the name of various parties under the head Advance to Suppliers & Receivable from customers and payable

to Sundry Creditors are subject to confirmation/ reconciliation by respective parties. The total amount payable to Creditors is Rs. 42,68,183.97 (previous year Rs. 7,77,687.25).

16.2 Schedules 1 to 16 along with Annexures 1 to 110 are annexed to and form an integral part of the Balance Sheet as at 31st March, 2017 and the Income and Expenditure Account for the year ended on that date.

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

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

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NATIONAL BRAIN RESEARCH CENTRE
NH-8, NAINWAL MORE, MANESAR, GURGAON, HARYANA
ANNEXURE OF PROJECT GRANTS AND EXPENDITURE FOR THE YEAR ENDED 31.03.2017

S. No.	NAME OF PROJECT	Opening Balance as on 01.04.2016	Grants received during the year 2016-17	Interest earned during the year 2016-17	Capital Exp. during the year 2016-17	Revenue Expenditure during the year 2016-17			Refund Unspent Balance	Closing Balance as on 31.03.2017
						Manpower	Others	Total Expenditure		
1	Distributed Information Centre	1,819,002.33	3,584,000.00	0.00	1,795,192.00	2,492,601.00	872,011.00	3,364,612.00	0.00	243,198.33
2	Programme of Co-Operation Between India and Syria Project	3558649.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3,558,649.00
3	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]
4	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]
5	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]
6	Material Malnutrition - Dr. Shyamala	[579,048.00]	0.00	0.00	0.00	0.00	0.00	0.00	0.00	[579,048.00]
7	M.Sc. Neuroscience (Dr. Aditya-DBT)	5,073.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	5,073.00
8	Stochastic Resonance - Prof. P.K. Roy	[471.00]	0.00	0.00	0.00	0.00	0.00	0.00	0.00	[471.00]
9	Dementia Meeting	2,364,225.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2,364,225.00
10	Comp. Analysis of Speech Imp. - Dr. Nandini Singh	[547,567.00]	0.00	0.00	0.00	0.00	0.00	0.00	0.00	[547,567.00]
11	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]
12	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]
13	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
14	BBNSC - Dr. Dhingra	144.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	144.00
15	BBNSC - Dr. Shyamala	[392,947.00]	0.00	0.00	0.00	0.00	0.00	0.00	0.00	[392,947.00]
16	BBNSC - Dr. Neeraj	296,937.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	296,937.00
17	BBNSC - Dr. Ellora	[403,419.00]	0.00	0.00	0.00	0.00	0.00	0.00	0.00	[403,419.00]
18	BBNSC - Dr. Soumya	1,246.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1,246.00
19	Cellular & Mole. Basis - Dr. Pankaj	[34,974.00]	0.00	0.00	0.00	0.00	0.00	0.00	0.00	[34,974.00]

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20	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
21	Japanese Enceph. Virus - Dr. Basu	451.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	451.00
22	Functional Role of E6-AP - Dr. Jana	168.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	168.00
23	Charac. of Molecular Interac. - Dr. Pravat Kumar Mandal	2,106.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2,106.00
24	Cognitive Neuro Science Workshop - Aditiya Murthy	[437,464.00]	0.00	0.00	0.00	0.00	0.00	0.00	0.00	[437,464.00]
25	EBM Including Alzheimer Disease - Dr. Vijaylaxmi	[230,717.00]	0.00	0.00	0.00	0.00	0.00	0.00	0.00	[230,717.00]
26	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]
27	Multilingualism - Dr. Nandini	823.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	823.00
28	DBT Grant - Dr. Kallol Dutta	7,920.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	7,920.00
29	INDO-US & NIH RO1 - Dr. Pankaj	142,087.58	0.00	0.00	0.00	0.00	0.00	0.00	0.00	142,087.58
30	CSIR - Dr. Nihar Ranjan Jana	73,089.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	73,089.50
31	Perception Engineering Project of DIT - Dr. Neeraj Jain	[1.31]	0.00	0.00	0.00	0.00	0.00	0.00	0.00	[1.31]
32	Functional Imaging Study of Dyslexia - Dr. Nandini C. Singh	[0.23]	0.00	0.00	0.00	0.00	0.00	0.00	0.00	[0.23]
33	Epilepsy Project of NBRC	12,465,913.01	36,201,000.00	286,587.00	32,423,227.13	7,958,066.00	7,010,449.58	14,968,515.58	0.00	1,561,757.30
34	Motivated Behaviour in Male Zebra Finches - Dr. Soumya	73,194.65	0.00	0.00	0.00	0.00	0.00	0.00	0.00	73,194.65
35	Multi Disiplinary 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
37	Understanding the Signaling Circuitries - Dr. Ellora Sen	[575,915.39]	0.00	0.00	0.00	0.00	0.00	0.00	0.00	[575,915.39]
38	Two Photon Microscope Facility for Advance Research - Dr. Neeraj Jain	14,458,925.56	0.00	0.00	0.00	0.00	8,177,635.62	8,177,635.62	0.00	6,281,289.94
39	Understanding the Psychological Function of Malin - Dr. Nihar Ranjan Jana	350.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	350.11
40	Neural Network Mechanism - Dr. Yoganarashimha	[1,324,592.66]	0.00	0.00	0.00	214,262.95	0.00	214,262.95	0.00	[1,538,855.61]

41	IBRO School Workshop - Prof. P.K. Roy	(672,839.00)	2,000.00	0.00	0.00	0.00	0.00	0.00	0.00	(670,839.00)
42	DST Serc School Workshop - Dr. Soumya Iyengar	36,376.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	36,376.00
43	Circadian System Linkage (DST) - Dr. Soumya Iyengar	0.39	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.39
44	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)
45	CSIR -II Study the Role of Neural Immune Respnce - Dr. Basu	(168,365.93)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	(168,365.93)
46	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
47	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)
48	DIT MCGILL Linkage (NKN) - Prof. Prasum Kumar Roy	-604,086.84	7,160.00	0.00	0.00	0.00	0.00	0.00	0.00	(596,926.84)
49	Role of Human Umbilical Cord Blood Stem (AIIMS) - Dr. Pankaj	55.44	0.00	0.00	0.00	0.00	0.00	0.00	0.00	55.44
50	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
51	DBT 5th Meeting of EGN-CDB - Dr. Shiv Kumar Sharma	67,875.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	67,875.00
52	DST ITPAR Workshop on Cognitive Neuroscience - Dr. Nandini C. Singh	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
53	DBT CSI Development and Validation of Screening Tools Project- Dr. Nandini	(1,044,510.00)	862,250.00	0.00	0.00	0.00	121,249.00	121,249.00	0.00	(303,509.00)
54	DBT Educational Neuroscience Meeting -Dr. Nandini C Singh	476.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	476.00
55	DBT ITPAR Grant-Dr. Nandini C.Singh	790,553.89	0.00	0.00	0.00	80,000.00	127,186.00	207,186.00	0.00	583,367.89
56	National Initiative On Glia Cell Research Project - Dr. Pankaj Seth	146,620.71	0.00	0.00	0.00	26,613.00	27,419.00	54,032.00	0.00	92,588.71
57	DBT BIRAC Under CRS Scheme Project Grant - Dr.Ranjit Giri	540,724.50	0.00	0.00	22,110.00	0.00	461,623.00	461,623.00	0.00	56,991.50
58	DBT Ramalingaswamy Fellowship - Dr.Saurav Banerjee	(120,570.12)	1,545,000.00	0.00	100,990.00	1,110,000.00	225,833.00	1,335,833.00	0.00	(12,393.12)

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59	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)
60	DST Inspire Faculty Award -Dr. Supriya Bhavani	(179,087.65)	166,898.00	0.00	0.00	0.00	0.00	0.00	0.00	(12,189.65)
61	DBT Tata Innovation Fellowship -Dr P.K.Roy	99,241.60	0.00	0.00	0.00	0.00	306,817.00	306,817.00	0.00	(207,575.40)
62	DBT INCRE Grant (NBRC) - Prof Subrata Sinha	1,460,444.00	325,836.00	12,873.00	0.00	0.00	0.00	0.00	0.00	1,799,153.00
63	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)
64	Wellcom Trust/DBT Indian Alliance - Dr. Amitabha Majumdar	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-
65	Wellcom Trust/DBT Indian Alliance -Dr. Anindya Ghosh Roy	9,035,486.34	0.00	0.00	1,883,398.91	0.00	830,892.50	830,892.50	0.00	6,321,194.93
66	Implementing Proteomic approach to understand the Etiology of Neuropathogenesis induced by Chandipura Virus infection - Dr. Anirban basu	878,475.68	0.00	0.00	0.00	0.00	901,056.21	901,056.21	0.00	(22,580.53)
67	Neuro -Cognitive networks underlying goal Directed Behavior - Dr. Arpan Banerjee	156,331.00	1,578,000.00	9,965.00	0.00	36,000.00	1,250,921.00	1,286,921.00	0.00	457,375.00
68	Role of Chromatin Remodelers in regulating associated with resistance to apoptosis under inflammatory and hypoxic conditions in glioma cells - Dr. Ellora sen	589,025.42	5,000.00	0.00	0.00	0.00	596,587.58	596,587.58	0.00	(2,562.16)
69	First Annual Conference of the Association for Cognitive Science - Dr. Nandini C. Singh	13,560.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	13,560.00
70	A longitudinal study to responsiveness to song based stimuli in children with autism behavior and diffusion tensor Imaging - Dr. Nandini C. Singh	476,365.00	0.00	0.00	0.00	21,161.00	188,180.00	209,341.00	0.00	267,024.00
71	Screening Committee Meeting under CSRI (CSI) - Dr. Nandini C Singh	14,978.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	14,978.00

72	Deregulation of micro RNA in cell and animal models of Huntington's disease: role of altered micro RNA in neuronal differentiation and cell cycle regulation - Dr. Nihar Ranjan Jana	(119,839.59)	311,000.00	0.00	0.00	0.00	194,160.00	194,160.00	0.00	(2,999.59)
73	DBT Workshop on Scientific Grant Writing - Dr. Pankaj Seth	(21,476.00)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	(21,476.00)
74	INDO-US Symposium on viral infection of the nervous system(IUSSTF) - Dr. Pankaj Seth	171,262.28	0.00	0.00	0.00	0.00	0.00	0.00	0.00	171,262.28
75	Non-invasive Imaging based detection and of brain oxidative (U.S. Airforce) - Dr. Pravat Kumar Mandal	350,787.85	0.00	0.00	0.00	245,839.00	104,949.00	350,788.00	0.00	(0.15)
76	Characterizing biomarkers of Alzheimer's disease :A longitudinal multi modal brain imaging study (Brain imaging) - Dr. Pravat kumar Mandal	(525,869.00)	4,615,000.00	17,604.00	0.00	2,331,930.00	303,206.50	2,635,136.50	0.00	1,471,598.50
77	National Programme on Preception Engineering - Phase II - Dr. Pravat Kumar Mandal	117,133.10	2,130,000.00	16,259.00	137,999.00	1,621,864.00	196,569.50	1,818,433.50	0.00	306,959.60
78	Influence of social cues on spatial cognition - Dr. Chetan Yadav	-4,873.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	(4,873.00)
79	National Programme on Preception Engineering - Prof. P.K. Roy	373,894.00	1,533,476.00	0.00	0.00	868,312.00	56,795.00	925,107.00	0.00	982,263.00
80	CSIR Japanese Encephalitis - Dr. Anirban Basu	(83,496.35)	500,000.00	0.00	0.00	0.00	451,720.00	451,720.00	0.00	(35,216.35)
81	Molecular Mechanism Of Microbial Activation - Dr. Anirban Basu	592,560.79	800,000.00	38,863.00	0.00	0.00	813,519.24	813,519.24	0.00	617,904.55
82	Multifaceted Kinase CDK5 - Dr. Aparna Dixit	-234,820.93	1,026,625.00	1,948.00	0.00	369,600.00	55,369.00	424,969.00	0.00	368,783.07
83	Vision Guide Speech Perception- Dr. Arpan Banerjee (DBT)	6,373.00	954,800.00	0.00	0.00	16,000.00	279,249.00	295,249.00	0.00	665,924.00
84	National Bioscience Award- Dr. Ellora Sen	-581.30	500,000.00	2,750.00	0.00	0.00	456,116.61	456,116.61	0.00	46,052.09
85	Tata Innovation Fellowship- Dr. Nihar Ranjan Jana	127,804.91	887,500.00	0.00	0.00	0.00	821,871.00	821,871.00	0.00	193,433.91

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86	Women Scientist Scheme -Dr. Sayali Ranade(DST)	-131,556.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	(131,556.00)
87	Innovative Young Biotechnologist Award 2013- Dr. Supriya Bhavanani	49,737.51	0.00	0.00	0.00	0.00	0.00	0.00	0.00	49,737.51
88	Innovation In Science Pursuit For Inspired Research(INSPIRE)- Dr. Yogita	583,882.18	1,659,335.00	0.00	8,398.00	991,680.00	268,670.00	1,260,350.00	0.00	974,469.18
89	Mechanisms Of Adult Brain Reorganisation- Dr. Neeraj Jain	238,404.39	1,266,000.00	8,597.00	55,599.00	840,835.00	56,223.00	897,058.00	0.00	560,344.39
90	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
91	A critical assessment of the dual stream models of visual information processing- DST - Dr. Dipanjan Ray	203,199.00	700,000.00	0.00	0.00	0.00	671,763.00	671,763.00	0.00	231,436.00
92	Tata innovation fellowship award- Dr. Anirban basu	4,331.81	883,739.00	7,708.00	0.00	0.00	852,140.00	852,140.00	0.00	43,638.81
93	Implications in tumor progression- Dr. Ellora sen	4,095,216.76	0.00	0.00	2,826,372.05	625,000.00	163,056.52	788,056.52	0.00	480,788.19
94	Workshop DST Csi- Dr. Nandini	2,326.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2,326.00
95	Tata innovation fellowship Award - Dr. Pravat Mandal	40,298.00	884,891.00	5,501.00	0.00	0.00	813,893.00	813,893.00	0.00	116,797.00
96	Crspri System - Dr. Sourav Banarjee	4,473,800.00	0.00	75,959.00	2,982,925.69	320,000.00	1,141,298.75	1,461,298.75	0.00	105,534.56
97	DBT Mirna Meditate Control - Dr. Sourav Banarjee	3,432,026.00	0.00	50,341.00	1,845,131.05	279,903.00	1,463,064.69	1,742,967.69	0.00	(105,731.74)
98	Ibro Workshop 2016 - Dr. Sourav Banarjee	2,160,447.90	120,000.00	0.00	0.00	0.00	2,860,101.96	2,860,101.96	0.00	(579,654.06)
99	Grant DBT 30 Year Commemorate	31,507.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	31,507.00
100	DBT BRAIN STORMING Dr. PANKAJ SETH	0.00	400,000.00	0.00	0.00	0.00	177,354.00	177,354.00	0.00	222,646.00
101	INDIAN ACADEMY OF NEUROSCIENCE(IAN-2016) Dr. PANKAJ SETH	0.00	4,086,204.00	0.00	0.00	0.00	4,307,481.00	4,307,481.00	0.00	(221,277.00)
102	A CROSS-CULTURE PERSPECTIVE(DBT-NETHERLANDS) -Dr. PRAVAT K MANDAL	0.00	2,061,000.00	0.00	524,921.00	535,333.00	162,903.00	698,236.00	0.00	837,843.00
103	DST-ANACOD Dr. PRAVAT K MANDAL	0.00	500,000.00	0.00	0.00	0.00	580,219.00	580,219.00	0.00	(80,219.00)

104	SPECIFIC BRAIN TEMPLATE DST Dr. PRAVAT K MANDAL	0.00	924,000.00	14,255.00	0.00	0.00	266,518.50	266,518.50	0.00	671,736.50
105	S&S LEARNING IN ZEBRA FINCHES Dr.SOUMYA IVENGAR	0.00	1,247,000.00	11,239.00	0.00	66,194.00	404,040.00	470,234.00	0.00	788,005.00
106	PDF-SERB(AKANSHA JALOTA)	0.00	960,000.00	0.00	0.00	0.00	447,965.00	447,965.00	0.00	512,035.00
107	PDF-SERB(AMIT NASKAR)	0.00	960,000.00	0.00	0.00	0.00	503,419.00	503,419.00	0.00	456,581.00
108	PDF-SERB(POONAM MEENA)	0.00	628,000.00	0.00	0.00	0.00	460,568.00	460,568.00	0.00	167,432.00
109	PDF-SERB(SUVADIP MALLICK)	0.00	960,000.00	0.00	0.00	0.00	425,214.00	425,214.00	0.00	534,786.00
110	PDF-SERB(PROF. SUBRATA SINHA(DIRECTOR))	0.00	500,000.00	0.00	0.00	0.00	48,214.00	48,214.00	0.00	451,786.00
	Total (A)	65,509,610.23	76,275,714.00	560,449.00	44,606,263.83	21,051,193.95	40,905,491.76	61,956,685.71	0.00	35,782,823.69
36	DELCON E-LIBRARY CONSORTIUM (B)*	4,744,038.63	881,948,576.00	1,962,211.00	92,500.00	1,783,029.00	520,120,991.65	521,904,020.65	0.00	366,658,304.98
	Grand Total (A+B)	70,253,648.86	958,224,290.00	2,522,660.00	44,698,763.83	22,834,222.95	561,026,483.41	583,860,706.36	0.00	402,441,128.67

SANTOSH KUMAR CHOUDHARY
DY. FINANCE OFFICER

TANMOY BHATTACHARYA
OFFG. F & AO (CAO)

PROF. SUBRATA SINHA
DIRECTOR

As per our separate report
of even date attached

Place : New Delhi
Date : 23rd November, 2017

For N.C. MITTAL & CO.
Chartered Accountants
(FRN-000237N)

KAPIL MITTAL
PARTNER
Membership No. 503378

Compiled and edited by Dr. V Rema and Kedar Singh Bajetha.
Front Cover: Courtesy Dr Arpan Banerjee.
Separators pages: Picture of *Caenorhabditis elegans* from Dr Anindya Ghosh Roy.
Back Cover: A herd of Neel Gai (*Boselaphus tragocamelus*), which is actually an antelope, was photographed grazing near NBRC by Rajeev Ramaswamy.



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