Contents

MANDATE

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

OBJECTIVES

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

From the Director's Desk

Why do we need to study the brain? Is it an existential requirement? Going by what the French philosopher, René Descartes said, 'I think, therefore I am' it is impossible to separate human existence from thinking – and by now, most of the world is fairly convinced that our thinking, for whatever it is worth, is done by the brain! Or is it a core utilitarian issue? As we grow older and the society becomes more complex and fragmented, a brain that is kept in reasonable shape for as long as possible, is essential for the adequate functioning and survival of any individual, and through this of the immediate family as well as the society. There are obviously many other reasons for taking up this vocation! The multi-layered complexities of this task, which are apparent at all levels from the molecular, structural and functional, to the cognitive and philosophical, make the goal even more daunting. This Annual Report of the activities of the National Brain Research Centre (NBRC) for the year 2011-2012 tries to portray how this young institution has approached its mandate to understand brain function and use this knowledge for a better understanding of brain disorders aimed towards the alleviation of human suffering. As a Deemed University, we also have a key role in human resource generation and developing a cadre of highly trained individuals who would approach the study of Neurosciences with core knowledge that has both breadth as well as depth and bring a fresh originality and insight into our research.

In spite of whatever we say about the changing patterns of burdens of disease in India, it is impossible to get away from infectious diseases. Ongoing research at NBRC on Japanese Encephalitis (JE) has demonstrated the critical regulatory role of Pattern Recognition Receptors (PRRs) which are expressed by host cells to identify viral particles and trigger an innate immune response following Japanese Encephalitis Virus infection. Further, Fenofibrate, a PPARa agonist that is commonly used as a hypolipidemic drug has been shown to reduce mortality and preclude neurological deficits in survivors in the murine model of JE. JE has also been instrumental in providing us with a model for understanding the fundamental aspects of neuroinflammation, which has a role not only in infection, but also in neurodegeneration and stroke.

The neuroAIDS laboratory at NBRC has made headway in understanding the crosstalk between neuron and astrocytes, particularly at the levels of gap junction channels. The HIV-1 transactivating protein (Tat) augments the expression of Connexins that are important components of gap junctions between these two important cells types of human brain. It is strongly believed that these findings will open new avenues of research in the area of neuroAIDS and provide a better understanding of cellular and molecular events that occur in the brains of HIV/AIDS-infected individuals.

One of the research groups at NBRC interested in understanding the pathogenesis of neurodegenerative diseases has found that dysfunction of ubiquitin ligase Ube3a may be associated with synaptic pathophysiology in a mouse model of Huntington's disease. This laboratory has also demonstrated the possible involvement of Wnt signaling pathways in Lafora disease pathogenesis.

The research group at NBRC working on prion disease has developed a new in vitro model system to study two devastating neurodegenerative diseases such as Alzheimer's disease and prion disease. They have developed mouse neurosphere cultures which express either beta amyloid peptide (which is the main hallmark of Alzheimer's disease) or replicating prion proteins (the main feature of prion disease) to study the biological implications of infected

CNS stem cells in the pathology of these diseases.

It is indeed sad that after so many decades of research in Neurooncology, the outcome of glial tumours, especially glioblastoma remains virtually as it was a decade ago. The identification of novel regulators of signalling pathways and their points of derangements provide a way for rational therapies. Research at NBRC has emphasised the role of inflammation driven signalling pathways in glioblastoma progression and their dysregulation, and also demonstrated novel aspects of their dynamics during hypoxia. As hypoxia is a hallmark of high grade glioma, this work has an important clinical relevance.

Extracellular signal-regulated kinase activity is crucial for long-term potentiation and memory. Research carried out on understanding memory formation and Alzheimer's disease has shown that a growth factor is involved in a feedback mechanism to keep the activity-dependent activation of this kinase sustained. In addition, this group has also shown that an alkaloid, sinomenine, can prevent microglial activation by amyloid beta and confer neuronal protection. This has relevance to Alzheimer's disease in which neuronal cell death is a prominent feature.

Research in the discipline of systems neuroscience at NBRC focuses on the somatosensory, motor, visual and auditory systems and mechanisms underlying spatial navigation. The research group working on the organization and plasticity of the sensorimotor system in mammals has developed a prototype of a brain-machine interface device, which directly uses brain signals for real-time online control of a robotic arm. This technology has great potential for developing assistive devices for patients with paralysis due to spinal cord injury or other causes.

Another group which has been working on the development of neural circuits of the prenatal human auditory cortex had earlier shown that relatively mature axons (capable of impulse conduction) were present in the human auditory cortex at 25 gestation weeks (GW), suggesting that auditory input may reach the auditory cortex by the end of the second trimester. This group has recently found that vesicular glutamate transporters Type1 and 2 (markers for cortico-cortical and thalamocortical synapses, respectively), are present in the human auditory cortex at this age as well. These results suggest that connections within the auditory cortex as well as those between the medial geniculate nucleus and auditory cortex in humans may start developing as early as 25G

Research on translational neuroscience and computational neuroimaging has resulted in the development of the technique of MRI based Elastometry using tissue porosity analysis, along with measurement of reactive stress/strain alteration of cerebral tissue while the ageing process takes place. Furthermore, CT/MR-based treatment planning methodology for optimizing radiotherapy performance has been constructed, using maximization of tumor control likelihood dynamics. Collaterally, this has shown the feasibility of a radiological tractography based estimation of endogenous stem cell mobility along brain parenchyma. This information is useful for optimizing neuroregenerative therapy in cerebral stroke using carbamylated erythropoietin or neuropoietin. This group of researchers has also adapted their recently patented MRI procedure of automated diagnosis of dementia, by generalizing the methodology across different populations in five countries, and across scanner systems of the three major manufacturers.

The group that specializing in Neurospectroscopy has developed a sensitive technique for measuring the levels of the oxidative stress marker glutathione precisely in different localizations in the brain using non-invasive Magnetic Resonance Spectroscopy (MRS) and has correlated it with clinical states. This group also maps brain pH by MRS spectroscopy and is attempting to establish the measurement of alkalinity in different areas of the brain as a biomarker for Alzheimer's disease.

The Speech and Language Laboratory has been involved in studying the development of cortical networks for reading Hindi and English in children between 8-10 years and how these networks are disrupted in children with dyslexia. They are also investigating the neural networks for processing musical speech and its possible application in music therapy to improve verbal communication in children with autism spectrum disorder.

The NBRC family has grown and we are pleased to welcome two new faculty members who joined us this year. Dr Sourav Bannerjee plans to employ a wide range of biochemical, cell biological, and biophysical approaches to study novel epigenetic mechanisms involving non-coding RNAs and the Ubiquitin Proteasome System that fine-tune synapse development and synaptic plasticity. Dr Sharba Bandyopadhyay's laboratory will be using electro-physiology, optical stimulation and Ca2+ imaging to study function and formation of auditory cortical micro-circuitry and the mechanisms by which such circuitry changes/adapts at different time scales. These studies will be important for

identifying common principles of adaptive computation and roles of specific elements such as inhibition in the brain leading to knowledge of understanding auditory perception and to assess causes of auditory deficits in different disease conditions.

We are proud to note that NBRC is completing 10 years as a Deemed University and as of March 31st, 2012, has awarded the degree of Doctor of Philosophy to 31 students. NBRC has also provided hands-on training to a number of summer trainees (selected by the Indian Academy of Science, Bangalore, Indian National Science Academy, New Delhi and National Academy of Sciences, Allahabad), to encourage them to pursue Neuroscience as a career. The 8th Foundation Day on 16 December 2011 was celebrated as usual by inviting students from five schools from Gurgaon / Manesar to attend a scientific poster presentation, demonstrations and quiz at NBRC. Most of these events were conducted by students of NBRC including a lecture on Neuroscience. The day was concluded with a public lecture entitled "Burden of Neurological Diseases: Challenges for Future Generations" by Professor Avindra Nath (Clinical Director of National Institute of Neurological Diseases and Stroke (NINDS), National Institute of Health, USA, a very distinguished neuroscientist who works on the pathophysiology of retroviral infections of the nervous system and the development of new diagnostic and therapeutic approaches for these diseases.

For the National Science Day (28 February, 2011), integrated PhD students, postdoctoral fellows and other project employees of NBRC presented talks on the basics of neuroscience to students of Kendriya Vidyalaya, NSG, Manesar, Government Girls Higher Secondary School, Manesar, Government Senior Secondary School, Pachgaon and Govternment College, Sidhrawali, Harryana.

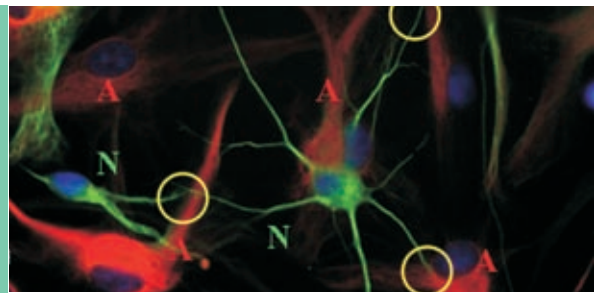
One of NBRC's mandates is to promote neuroscience in India through networking among institutions across the country. To achieve this mandate, NBRC sponsored the Brain Awareness Week in different institutions across the country. To make the general public aware about normal brain functions and the consequences of different brain diseases as well as the mechanisms underlying them, talks, poster sessions and demonstrations were organized at each of these institutions. The Brain Awareness Week also serves to educate school and college students and motivate them to pursue neuroscience as a career option.

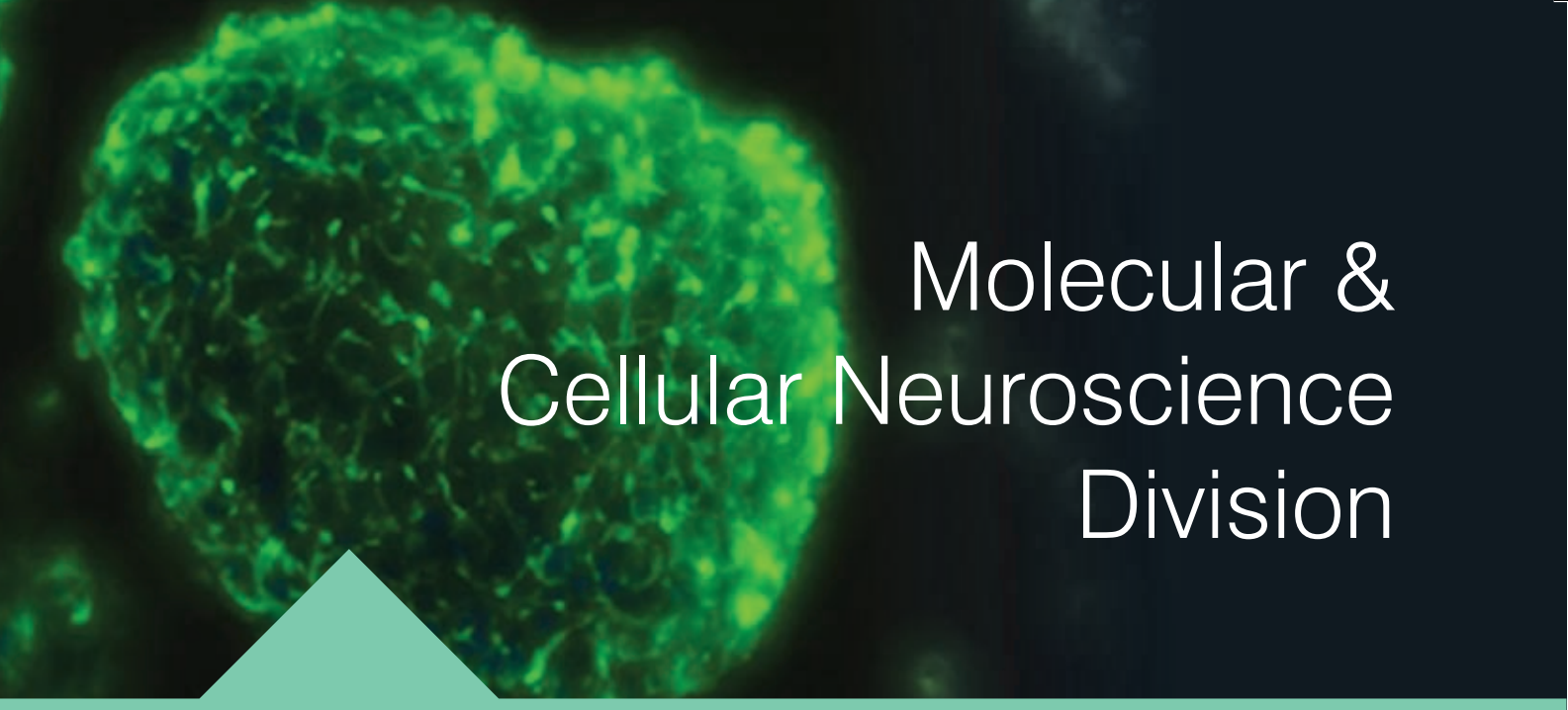
The multiple expectations from our institution demand a variety of roles from our faculty, staff and students – the creative, the educational and the promotional. As we move to next year one cannot but emphasise the spirit of cooperation and collaborative effort that is essential for our achieving further heights of accomplishment.

Prof. Subrata Sinha

RESEARCH REPORTS

Molecular & Cellular Neuroscience Division
Systems & Cognitive Neuroscience Division
Computational Neuroscience & Neuroimaging Division





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Dr. Nihar Ranjan Jana

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Dr. Ellora Sen

Dr. Shiv Kumar Sharma

Dr. Anirban Basu

Dr. Ranjit Kumar Giri

National Brain Research Centre

NBRC

Therapy of Glioma : Role of Hypoxia and Aberrant Gene Expression

Principal Investigator : **Subrata Sinha**

The cycle of hypoxia, necrosis, angiogenesis and proliferation is a feature of all tumours, more so of glioma. Grade IV Glioma, Glioblastoma multiforme is amongst the most hypoxic of all tumours. Hypoxia can range from the moderately hypoxic (1-2% oxygen), to profoundly anoxic regions (0.1 to 0.2% oxygen). Hypoxia induces pro survival and antiapoptotic signaling pathways, which then affect the response to therapy. It also results in genomic instability, leading the drug resistance and tumour progression. It is important to study the nature of hypoxia response in order to assess the strategies that are best suited for the management of hypoxic tumours. Hypoxia has also been shown to be linked with the expression of pro-inflammatory pathways.

The FAT1 gene is known to be tumour suppressor gene in Drosophila, and earlier studies by one lab had indicated that its human homologue may be associated with glial tumorigenesis. FAT1 gene expression was shown to be increased in cell lines derived from high grade but not low grade tumours and had an inverse relationship to the expression of a tumour suppressor gene PDCD4. Knocking down the FAT1 gene resulted in reduced cell migration and invasiveness. There is evidence that the FAT1 homologue acts as an oncogene (and not a tumour suppressor gene) in high grade glioma, and influences the pro inflammatory cytokine network in the cells. We also have indications of the differential regulations of the gene in hypoxia.

Publications

1. M. Mehndiratta, J.K. Palanichamy, A. Pal, M. Bhagat, A. Singh, **S. Sinha**, P. Chattopadhyay. **(2011)** CpG hypermethylation of the C-myc promoter by dsRNA results in growth suppression. **Molecular Pharmacology**, 8:2302-9.

Patent

Use of FAT1 gene and its products including RNA, protein and the derivatives of the same, as suitable molecules for either inflammation or cancer and the associated phenotype and the processes linking the same and also as a biomarker for the above processes (Indian patent filed, PCT in process). (Kunzong Chosdol, Bhawana Dikshit and Subrata Sinha).

Collaborators

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Recombinant antibodies for therapy

Principal Investigator : **Subrata Sinha**

Enhancing of specificity of drug delivery by recombinant antibodies and tumors specific promoter activation: Lack of specificity in tumor therapy manifests as toxicity, and the caised damage to normal tissue is a serious limitation that drastically reduces the efficiency of most chemotherapeutic regimes. Specificity could increased at the level of signalling pathways, targeted delivery systems and the tumor specific expression of siRNA capable of shutting down deleterious genes and tumor specific drug activation.

The oncoplacental isozymes of Alkaline Phosphatase (AP), Placental Alkaline Phosphatase (PAP) and its close relative, the Placental like Alkaline Phosphatase (PLAP), have been utilized for targeting. Earlier, we had shown that a Sendai Virosome targeted with a human recombinant scFv to PAP could specifically deliver drugs to cell lines that expressed the isozyme. This demonstrated its specificity with reference to the isozymes, Tissue Non Specific AP and Intestinal AP that are constitutively expressed on normal cells. This has been confirmed and the kinetics of cell death established. In addition, experiments are ongoing to establish the relative importance of endocytosis and membrane fusion to the internalization of the targeted Sendai Virosome. Normally Sendai Virosome are internalized by the non endocytic pathway of membrane fusion. However, antibodies are normally internalized by endocytosis. How antibody targeting could influence Sendai Virosome internalization is being studied.

The Placental like Isozyme (PLAP) is also activated in a number of tumors and is immunologically not distinguishable from PAP by the antibodies available so far. Hence antibodies targeting PAP also bind PLAP and vice versa. A combination of an NFKappaB enhancer with PLAP promoter has been cloned in a pGL3 vector. Genes cloned downstream to this hybrid construct have been shown to have a high degree of specific expression in the tumor cells studied. While the PLAP promoter gives the system specificity, the enhancer increases gene expression to levels equivalent to conventionally strong but non-specific promoter like the CMV promoter. Specificity has been demonstrated in-vitro in several PLAP expressing cell lines. Work is ongoing to combine the two modalities antibody and promoter activation for achieving a greater degree of specificity than is possible by a single modality.

Another aspect of work is the generation of potentially therapeutic recombinant antibodies to Hepatitis B. Previously antibodies to the S antigen were generated. Currently, antibodies are being generated to the neutralizing epitope of the pre S1 region. Work is ongoing with both human and mouse origin antibodies. This work was initiated at AIIMS and is being continued at NBRC.

Patent

A recombinant mouse - human Chimaeric Fab against Hepatitis B surface antigen: Indian and South African Patents granted (Biplab Bose, Navin Khanna, Subrata K. Acharya and Subrata Sinha).

Ongoing Funded Project (As Co PI)

i. Therapy of infectious and chronic diseases: Targeted gene delivery & long-term specific modulation of gene expression (DBT-COE) Was PI and Project Coordinator, currently Co-PI. Current Project Coordinator Prof. Debi P. Sarkar, Deptt. of Biochemistry, University of Delhi, South Campus, PI for AIIMS component, Dr. Parthaprasad Chattopadhyay.

ii. A comparison of gene expression in glioblastoma cell lines under short and long term exposure to hypoxia with reference to the key cellular regulatory and adaptive pathways (ICMR) was PI, currently PI Dr. Kunzang Chosdol.

iii. An in-vitro study of the role of FAT, A Drosophila tumor suppressor gene homologue, in human glial tumorigenesis. (DRDO), PI: Dr. Kunzang Chosdol, AIIMS.

iv. Hypoxia and Notch signalling in Glioblastoma: Implications for an adverse phenotype (DBT) PI Dr. Kunzang Chosdol.

v. Hypoxia and p53-HIC1 axis in stemness of glial tumors and cell lines (DBT) PI Dr. Parthaprasad Chattopadhyay.

vi. Promoter mediated tumor cell targeting by siRNA mediated gene silencing (DBT) PI Dr. Parthaprasad Chattopadhyay

Collaborators

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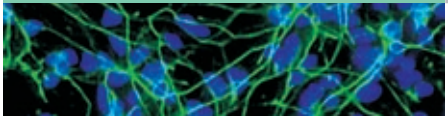

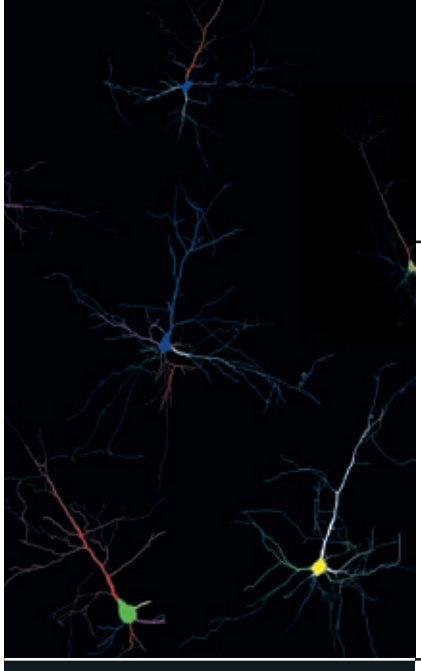

Understanding the Function of the Autism and Autism Spectrum Disorders Associated Ubiquitin Ligase UBE3A/E6-AP

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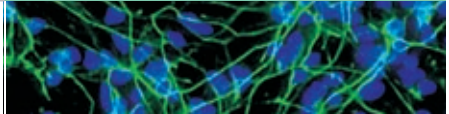
E6-AP encoded by UBE3A gene was first identified as a cellular factor associated in ubiquitin-mediated degradation of tumor suppressor p53 in cooperation with E6 oncoprotein of the human papilloma virus. Later, it is characterized as a HECT (homologous to E6-AP C terminus) domain family of ubiquitin ligase, an E3 enzyme of the ubiquitin proteasome system. Ube3a also functions as a transcriptional co-activator of steroid hormone receptors. Ube3a shows neuron specific imprinting and loss of function of maternally inherited Ube3a causes Angelman syndrome (AS). AS is a neurodevelopmental disorder characterized by severe mental retardation, susceptibility to seizures, speech impairment, ataxia and unique behavioural features such as inappropriate laughter and autistic features. Copy number variation of the UBE3A gene (duplication) has also been reported to be associated with autism. Ube3a maternal deficient mice exhibit many essential features of AS, including cognitive and motor dysfunction. These mice also exhibit defects in hippocampal long-term potentiation, altered function of hippocampal calcium/calmodulin-dependent protein kinase II and abnormal dendritic spine morphology. Studies in these mice provided further evidence that Ube3a is required for development of synapse, experience-dependent cortical plasticity and maturation of neocortex.

Past several years we are engaged in exploring the physiological function of Ube3a and how its defect could lead to AS. We are particularly working on (1) identification and functional characterization of novel substrates of Ube3a, (2) molecular mechanism of cognitive impairment in AS mice model, and (3) role of Ube3a in the progression of Huntington's disease.

Recently, we have observed that Ube3a-maternal deficient mice have significantly higher level of blood corticosterone, selective loss of GR and expression of GR-dependent genes like SGK1 and BDNF. These mice also exhibited increased anxiety-like behaviour, which could be due to chronic stress. Exposure of chronic restraint stress to Ube3a maternal deficient mice aggravated the anxiety-like behaviour. These findings suggest that chronic stress due to altered GR signalling might lead to anxiety-like behaviour and cognitive dysfunction in a mouse of model of AS. We have recently observed a significant decrease in adult hippocampal neurogenesis in Ube3a-maternal deficient mice as evident from the decreased numbers of BrdU-labelled as well as Ki67-positive cells. Ube3a-maternal deficient mice hippocampus also exhibited significantly decreased numbers of DCX-positive cells. The subventricular zone did not show any significant differences of BrdU or Ki76-labelled cells among wild type and Ube3a-maternal deficient mice brain. Our finding indicates that chronic stress might be linked with the decreased adult hippocampal neurogenesis in Ube3a-maternal deficient mice. We have also observed decreased number of parvalbumin-positive GABAergic interneurons in different regions of hippocampus and in amygdala. Currently we are investigating probable cause of



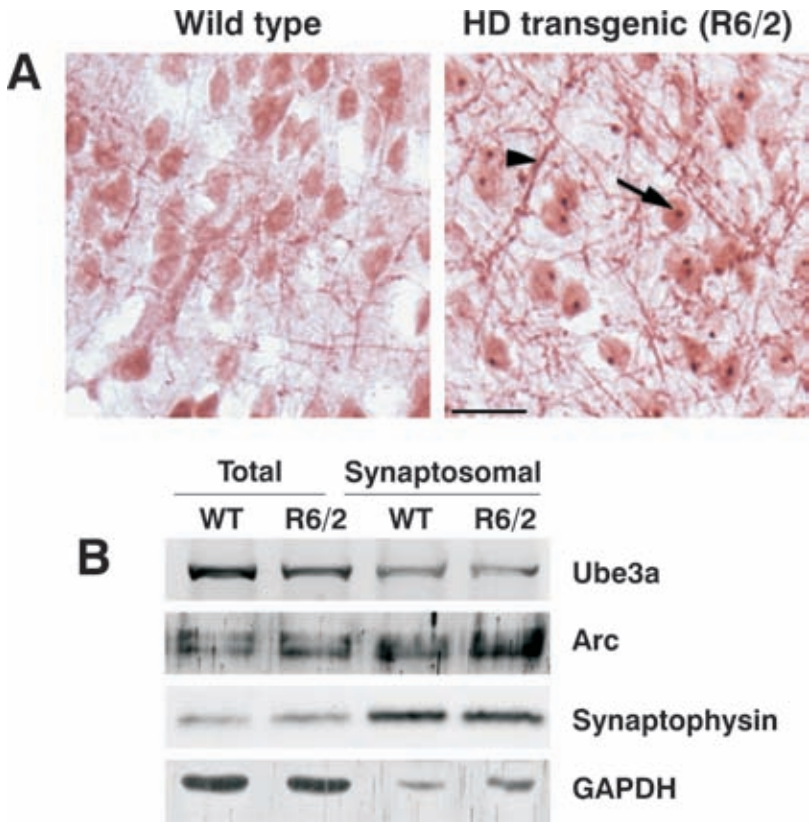


Figure 1

HD transgenic mice brain exhibits altered levels and localization of Arc.

A. Representative immunohistochemical staining of Arc in cortex of wild type and R6/2 mice brain (12 weeks old). Scale bar represents 10 µm. Arrow indicate the localization of Arc into nuclear aggregates and arrowhead points neuritic Arc (showed increased level in R6/2 brain).

B. Representative immunoblot of Ube3a, Arc and synaptophysin in the synaptoomal preparation obtaind from wild type and R6/2 mice (12 weeks old) total brain.

decreased number of parvalbumin-positive GABAergic interneurons in hippocampus and amygdala.

Earlier we have demonstrated that Ube3a function as a cellular quality control ubiquitin ligase. It has been found to degrade misfolded polyglutamine protein as well misfolded mutant α-synuclein. We have also shown that Ube3a strongly recruits to the mutant huntingtin nuclear aggregates in different brain regions of Huntington's disease (HD) mice resulting in significant loss of its functional pool. HD mice brain also exhibited increased levels of synaptic Arc (substrate of Ube3a, See Figure 1) and decreased levels of GluR1 and GluR2 (subtypes of AMPA receptor). These results indicated that the quality control and synaptic function of Ube3a is affected in HD brain. The functional relationship among Ube3a, Arc and GluR in mutant huntingtin expressing cells was further studied in mouse primary cortical neuronal culture upon transient transfection with mutant huntingtin plasmid. The mutant huntingtin expressing cell exhibited reduced numbers of neuronal processes, Ube3a was localized with mutant huntingtin aggregates and its staining was significantly reduced in cell soma and neuronal processes. Arc also co-localized with mutant huntingtin aggregates and its neuritic level was increased. In untransfected cortical neuron, GluR1 puncta was clearly visible in the neuronal processes, which was drastically reduced in mutant huntingtin expressing cell. The primary cultured neurons isolated from Ube3a-maternal deficient mice also exhibited increased level of Arc and decreased number of GluR1 puncta in comparison with wild type mice. These data suggests that the partial loss of function of Ube3a might be associated with abnormal synaptic function in HD transgenic mice brain. To further explore the role of Ube3a in HD pathogenesis, we are trying to generate Ube3a deficient HD transgenic mice.

Publications

1. N. R. Jana. Understanding the pathogenesis of Angelman syndrome through animal models. Neural Plasticity, 2012 (In Press).
2. S. K. Godavarthi, P. Dey, M. Maheshwari, N. R. Jana. Defective glucocorticoid hormone receptor signalling leads to increased stress and anxiety in a mouse model of Angelman syndrome. Human Molecular Genetics, 21, 1824-1834, 2012.
3. N. R. Jana. Protein homeostasis in aging: Role of ubiquitin protein ligases. Neurochemistry International, 60, 443-447, 2012.
4. J. Ghose, M. Sinha, E. Das, N. R. Jana and N. P. Bhattacharyya. Regulation of miR-146a by RelA/NFkB and p53 in STHdh (Q111)/Hdh (Q111) cells, a cell model of Huntington's disease. PloS One, 6: e23837, 2011.

Presentations

i. N. R. Jana. Understanding the pathogenesis of Angelman syndrome. Department of Physiology, Calcutta University, 2011.

ii. N. R. Jana, S. K. Godavarthi, P. Dey and M. Maheshwari. Hyperactivity of HPA axis and enhanced anxiety in a mouse model of Angelman syndrome. Annual meeting of Society for Neuroscience, Washington DC, 2011.

iii. N. R. Jana. Understanding the physiological function of Ube3a and pathogenesis of Angelman syndrome. India Brazil workshop on biomedical sciences, Rio de Janeiro, 2011.

Funding

i. Study the defect in neurogenesis and initial synapse formation in mouse model of Angelman mental retardation syndrome. Council of Scientific and Industrial Research. Govt. of India. Grant No: 37(1408)/10/EMR-II dt. 25-06-2010

ii. Role of E6-AP in the progression of Huntington's disease. Department of Biotechnology, Govt. of India (National Bioscience Award for Career Development). Grant No: BT/HRD/34/18/2008 dt. 16-04-2010.

iii. Understanding the role of ubiquitin-proteasome system dysfunction in the pathogenesis of Huntington's disease. Department of Science and Technology, Govt. of India (Indo-Japan cooperative science program). Grant No: DST/INT/JAP/P-71/2009 dt. 16-09-2009.

Collaborator

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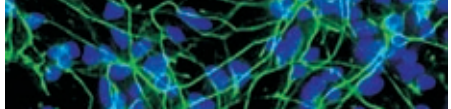

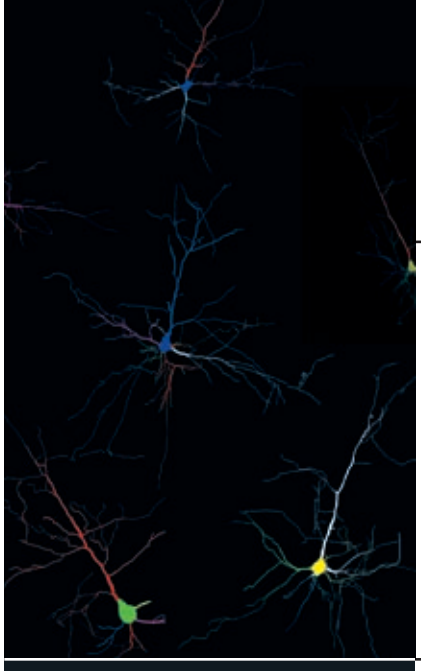

Understanding the Physiological Function of Malin, A Ubiquitin Ligase Mutated in Lafora's Progressive Myoclonus Epilepsy

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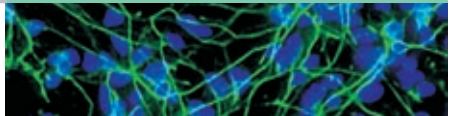
Lafora disease (LD) is an autosomal recessive progressive myoclonus epilepsy, usually manifest during teenage and patient dies within a decade of disease onset. The disease is clinically characterized by progressive increase in generalized tonic-clonic seizures, myoclonic and visual seizures, dementia, psychoses, muscles wasting leading the patient to a vegetative state and ultimately death. Pathological features of LD include gradual increase in accumulation of insoluble polyglucosan bodies (commonly known as Lafora bodies) and in neuronal loss. Lafora bodies are not only observed in brain but also in other non-neuronal tissues like liver, heart, skeletal muscle, skin etc.

LD is caused by mutations in the EPM2A or EPM2B (NHLRC1) genes encoding laforin (a protein phosphatase) and malin (a E3 ubiquitin ligase) respectively. Patients with mutations in either laforin or malin are clinically and pathologically indistinguishable, indicating that both proteins work together in some common signalling pathways and defect in those pathways could lead to disease manifestation. Emerging evidence indicates that both laforin and malin could play an important role in regulation of glycogen metabolism and autophagy. Knockout mice for both laforin and malin also exhibit progressive accumulation of Lafora bodies in various tissues including brain, defects in autophagic degradation pathway and widespread neurodegeneration. Current finding in LD mice models point towards the role of abnormal accumulation of Lafora bodies and impairment of intracellular protein degradation pathways in disease pathogenesis. But how exactly Lafora bodies induce neurodegeneration is not clear at present and the possible mechanism of dysfunction of protein degradation pathways in LD is also poorly understood. Since malin is an E3 ubiquitin ligase and its mutation leads to LD, it is hypothesized that the altered clearance of malin substrates might lead to disease pathogenesis. Therefore, identification of substrates of malin could open a new avenue in understanding the pathogenesis of LD. In the proposed project, we are trying to identify and characterize the new substrates of malin. In addition, we are also exploring the role of intracellular protein degradation pathways in LD pathogenesis.

Last year we have shown malin interacts with neuronatin and promotes its proteasome-mediated degradation. Malin also negatively regulates neuronatin - stimulated glycogen synthesis. We are continuing this study and observed that neuronatin is a misfolded-prone protein that aggregated easily in neuro2a cell upon proteasome inhibition. We are now studying the biological function of neuronatin and its involvement in LD pathogenesis. Using yeast-two hybrid screening followed by co-immunoprecipitation assay and immunofluorescence co-localization studies (see Figure 2) we have identified another novel interacting partner of malin i.e. dishevelled 2, a key mediator of Wnt signalling pathway. Overexpression of malin enhances the degradation of dishevelled 2 and inhibits Wnt signalling as evident from the down-regulation of β-catenin target genes and decrease in β-catenin-mediated transcriptional activity. Partial knockdown of malin significantly increases the level of dishevelled



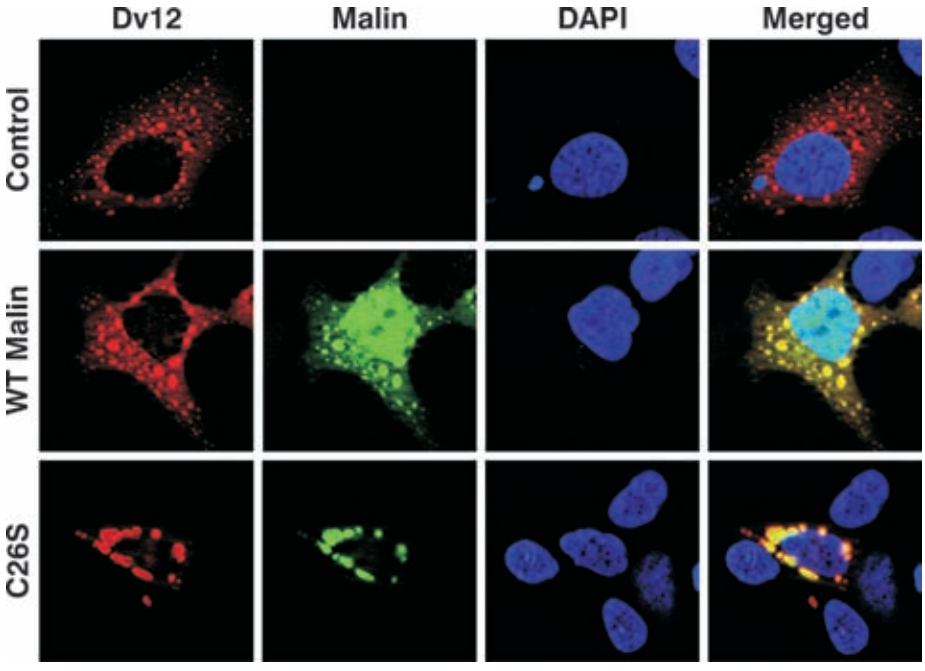


Figure 2. Malin and its mutants co-localize with Dvl2 vesicles. HEK293 cells were transfected with plasmids encoding wild type malin or its mutant along with Dvl2-FLAG (250 ng of each plasmid/well of 2-well chamber slide). Thirty-six hours later, cells were processed for double immunofluorescence staining using antibodies against Dvl2/V5 (to detect wild type malin) and Dvl2/myc (to detect C26S). FITC-conjugated secondary antibody was used to recognize wild type or mutant malin and Texas Red-conjugated secondary antibody was used to label Dvl2. Nuclei were counterstained with DAPI. Scale bar; 20 μm.

2 and up-regulates Wnt signalling. Several malin mutants are found to be ineffective in degrading dishevelled 2 and regulating the Wnt pathway. We have also found that malin enhances K48 and K63-linked ubiquitination of dishevelled 2 that could lead to its degradation through both proteasome and autophagy. Altogether, our results indicate that malin regulates Wnt signalling pathway through the degradation of dishevelled 2 and suggest possible deregulation of Wnt signalling in LD. Interestingly, both the substrates of malin (neuronatin and dishevelled 2) are associated with various aspect of brain development, which strongly suggests the involvement of malin in some aspect of brain development.

Publications

1. J. Sharma, S. Mulherkar, D. Mukherjee and **N.R. Jana**. Malin regulates Wnt signaling pathway through degradation of Dishevelled 2. **Journal of Biological Chemistry**, 287, 6830-6839, 2012.
2. *J. Sharma, S. N. Rao, S. K. Shankar, P. Satishchandra, and **N. R. Jana**. Lafora disease ubiquitin ligase malin promotes proteasomal degradation of neuronatin and regulates glycogen synthesis. **Neurobiology of Disease**. 44, 133-141, 2011.

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Presentations

i. N.R. Jana. Neuronatin in Lafora disease pathogenesis. RIKEN Brain Science Institute, Japan, 2012
ii. N. R. Jana. Understanding the pathogenesis of Lafora’s Progressive Myoclonus Epilepsy. Department of Physiology, Calcutta University, 2011.

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i. Understanding the physiological function of malin, a ubiquitin ligase mutated in Lafora’s Progressive Myoclonus Epilepsy. Department of Biotechnology. Govt. of India. Grant No: BT/PR13590/Med/30/286/2009 dt. 17-09-2010.

Collaborators

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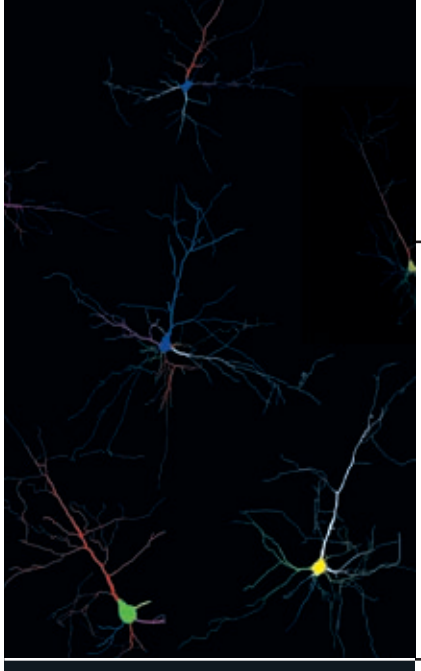

Cellular and Molecular Mechanisms of HIV-1 Neuropathogenesis

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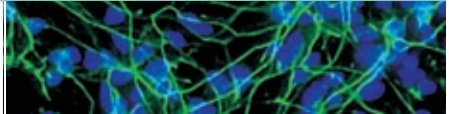
Over two and a half decades of global efforts to curb the increase in new cases of human immunodeficiency virus-1 (HIV-1) infections are finally showing some signs of hope. A small slowdown in number of new HIV-1 infections has been reported by some countries. Furthermore, advent of combinatorial antiretroviral therapy (cART) has reduced death and suffering of full blown HIV/AIDS cases in most of the HIV-1 patients. This has raised the hope that HIV/AIDS may no longer be a "death warrant", as the HIV-1 viral titers are reduced to undetectable levels in plasma at least in cases where cART is effective.

Among several problems associated with surviving AIDS patients or patients with milder AIDS symptoms, the cognitive and motor deficits are the most debilitating, yet commonly reported. Central nervous system (CNS) infection by HIV-1 cause glial cell mediated irreversible damage to the neurons and hence detailed investigations into glia-neuron interaction are warranted. HIV-1 induced damage to neuronal cells results in progressive motor and cognitive dysfunctions and other dementia like symptoms, collectively called HIV-associated neurocognitive disorders (HAND). In current times, although the severity of HIV associated dementia is far less as compared to the levels observed in the pre-cART era, the incidence of HAND is up to 50% amongst HIV/AIDS patients. We have earlier reported that HIV-1 viral protein Tat and drugs of abuse actually increase the damage to neurons. We are currently studying the co-morbid effects of chronic treatment of drugs of abuse and HIV-1 viral protein Tat on human neural precursor cells as well as neurons and find that the effects are far more severe than either one of them alone.

Our previous achievements have encouraged us to venture into more challenging research problems pertaining to the area of neuroAIDS. The last decade has placed the most abundant cell type of the brain, astrocytes, in limelight based on novel insights into several functions that astrocytes perform to support optimal neuronal functions. Neuron-glia interactions play an important role in maintenance of the normal brain physiology and function. Neuron-glia interactions are often perturbed in most of the neurodegenerative disorders hence better understanding of these interactions may provide new therapeutic targets. Gap Junction Channels are known to be one of the major mode of intercellular communication between neuron and glia as they allow the passage of various ions and second messengers, thereby regulating signaling pathways. Connexins are the key components of gap junction channels. Recent studies have reported an increase in Connexin-43 expression upon exposure of primary human astrocytes with live HIV virus which may have implications in HIV neuropathogenesis. However, the underlying signaling pathways and the consequences of the augmented gap junction communication remains poorly understood.

Venturing into the area of neuron-glia crosstalk studies we first met the pre-requisite of studying neuron-glia interactions by establishing human



neuron-astrocyte co-culture system in our laboratory. In an attempt to closely mimic the *in vivo* conditions of the human brain, we used co-cultures of astrocytes and neurons differentiated from human fetal brain derived neural precursor cells and validated the presence of connexins in this co-culture system. We studied expression of connexins at mRNA and protein levels, and introduced HIV-1 Tat protein to the co-culture system to explore the perturbation in neuron-glia communication via gap junction channels. Exposure of co-culture to HIV-1 Tat protein, significantly up-regulated the key proteins of gap junction channels, the connexins (Cx-26, Cx-36, Cx-40 and Cx-43). We employ live cell imaging techniques to study the functional aspects of the gap junction intercellular communication with help of fluorescence emitting dyes. We also observed that up-regulation of connexins, following exposure to HIV-1 Tat resulted in increased apoptosis and provide a basis to the astrocyte mediated indirect damage to the neurons as observed in neuroAIDS autopsy brain samples. Furthermore, alterations in connexin levels also affect cell proliferation as evidenced by a cell proliferation marker, Ki67 in primary cultures of human brain cells. In addition to this, we are also exploring the role of aquaproins that are abundantly present on astrocytes, particularly Aquaporin-4 (AQP-4) in HIV-1 neuropathogenesis. We are actively pursuing these interesting leads further to investigate the role of neuron-glia communications in HIV-1 neuropathogenesis.

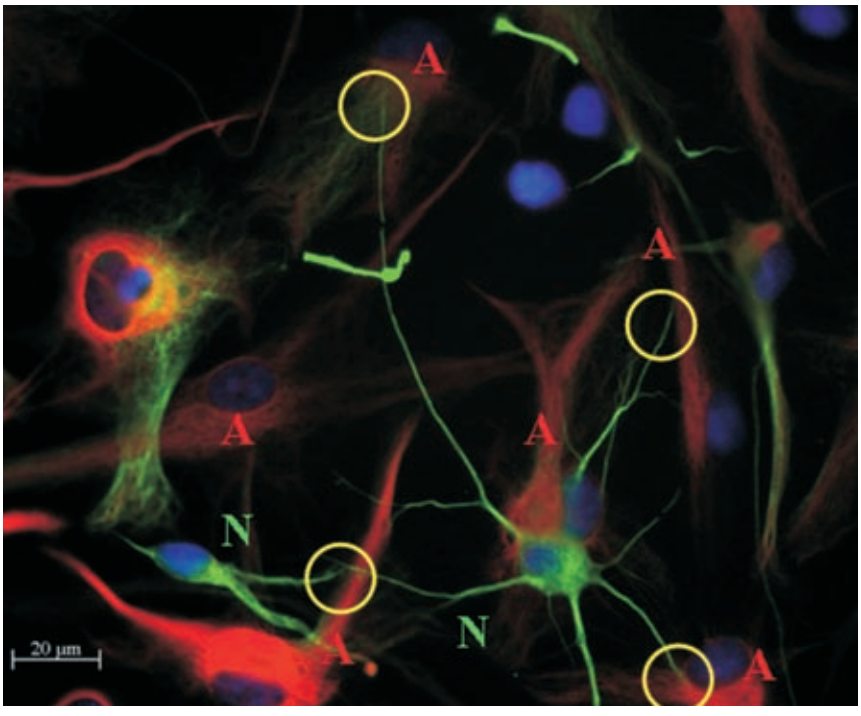


Figure shows human neuron-astrocyte co-culture following immunofluorescence of 4% paraformaldehyde fixed co-culture. The neuron seen in green (FITC) is immunolabeled with neuronal cell specific marker Tuj-1, while astrocytes are seen in red (Texas red) that are immunolabeled with astrocyte marker glial fibrilary acidic protein (GFAP). Note that a neuron (green) denoted as "N" extends projections to form connections with neighbouring astrocytes (red) denoted as "A". The yellow circles denote the sites of connections established between neurons and glia and points of possible cross-talk between these two important cell types of the brain.

We strongly believe our findings will open new avenues of research in this area and will provide better understanding of cellular and molecular events that occur in brains of HIV/AIDS patients. It is also hoped that insights gained through these studies would offer a window to design therapeutic intervention to reduce the glia mediated neuronal damage caused by HIV and its proteins.

Publications

Research Papers

1. V. Chennupati, D. Datta, M.R Subba Rao, N. Boddapati, M. Kayasani, R. Sankaranarayanan, M. Mishra, **P. Seth**, C. Mani, and S. Mahalingam (2011). Signals and Pathways Regulating Nucleolar Retention of Novel Putative Nucleolar GTPase NGP-1(GNL-2). **Biochemistry** 50 (21): 4521-4536.
2. L. Durgadoss, P. Nidadavolu, K.R. Valli, U. Saeed, M. Mishra, **P. Seth**, and V. Ravindranath (2012). Redox modification of Akt mediated by the dopaminergic neurotoxin MPTP, in mouse midbrain, leads to down-regulation of pAkt. **FASEB J** 26(4): 1473-1483.
3. M. Pant, P. Garg and **P. Seth** (2012). Central Nervous System Infection by HIV-1: Special Emphasis to NeuroAIDS in India. **Proceedings of National Academy of Science. (India)** 82 (1):81–94.

Book Chapter

1. M. Mishra and **P. Seth**. Cellular and Molecular Basis of Neurocognitive Deficits in HIV/AIDS. In: Expanding Horizons of Mind Science(s). Publishers - Nova Science Publishers, Inc, NY, USA, Chapter 21, Pages 383-405, 2012.

Presentations

i. P. Seth and P. Garg. Neuron-Glia Crosstalk in HIV-1 Neuropathogenesis. Symposium on The Consequences if substance abuse and HIV on Stem Cell Biology at 17th Society of Neuro Immune Pharmacology Scientific Conference, April 9, 2011, Clearwaters, Florida, USA. Invited Speaker.

ii. P. Seth, S. Malik and H Khalique. PDGF Attenuates HIV-1 Tat & Morphine Induced Damage to Human Neurons. Department of Neuroscience, School of Medicine, Temple University, Philadelphia, USA, April 12, 2011. Invited Speaker.

iii. P. Seth and P. Garg. Neuron-Glia Interactions in NeuroAIDS. Children's Hospital of Philadelphia, Philadelphia, USA, April 13, 2011. Invited Speaker.

iv. P. Seth. HIV-1 finds a New Hiding Place, the Brain. Brain Awareness Program at Government Girls College, Gurgaon, India. September 8, 2011. Guest Speaker.

v. P. Seth and M. Mishra. Neural Progenitor Cells in Management of Alzheimer 's disease. Alzheimer's Disease Symposia, Department of Neurology, King George's Medical College, Lucknow, Dec 3, 2011. Invited Speaker.

vi. HIV-1 and Drugs of Abuse - it takes two to tango. At Applied Physiologist and Pharmacologists of India, at All India Institute of Medical Sciences, New Delhi, Dec 15, 2011 Invited Speaker.

vii. P. Seth and S. Malik. Free Radicals in HIV-1 Neuropathogenesis. National Seminar on Reactive Oxygen Species, Department of Biochemistry, Lucknow University, Lucknow, Dec 24, 2011. Invited Speaker.

viii. NeuroAIDS: Past, Present and Possible Future. Pankaj Seth. Indian Institute of Science Education and Research, IISER-Kolkata, Feb 8th, 2012 Guest Faculty.

ix. P. Seth, S. Malik, P. Garg, M. Pant and M. Fatima. Understanding NeuroAIDS Using Cellular and Molecular Approaches. Golden Jubilee Symposium, Department of Biochemistry, Panjab University, Chandigarh, February 10-11, 2012. Invited Speaker

x. P. Seth and S. Malik. HIV-1 and Drugs of Abuse - Implications in NeuroAIDS. 5th Symposium on Molecular Medicine at Special Centre for Molecular Medicine, Jawaharlal Nehru University, New Delhi Feb 17-18, 2012. Invited Speaker.

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i. S. Malik, R. Saha and P. Seth. Role of forkhead box transcription factors in human immunodeficiency virus protein-Tat and illicit drug exposure induced neuronal apoptosis. XXIX Annual Conference of Indian Academy of Neurosciences, October 30 - November 1, 2011 at DIPAS, New Delhi, India.

ii. P. Garg, M. Pant and P. Seth. Novel Insights into Neuron-glia Communication in NeuroAIDS. XXIX Annual Conference of Indian Academy of Neurosciences, October 30 - November 1, 2011 at DIPAS, New Delhi, India.

Funding

i. Characterization of Human Fetal Brain Derived Neural Stem Cells as a Model for Studying Neurodegenerative Diseases.Grant number: BT/PR6615/MED/14/857/2005. Grant award date: Dec 2006 (Ended Dec 2011). Department of Biotechnology, Ministry of Science & Technology, Govt. of India.

ii. Role of CNS opportunistic infections in subsequent development of HIV dementia.Grant number: 1 R01 NS055628-04. Grant award date: July 2008. National Institute of Neurological Disorders and Stroke, National Institutes of Health, USA.

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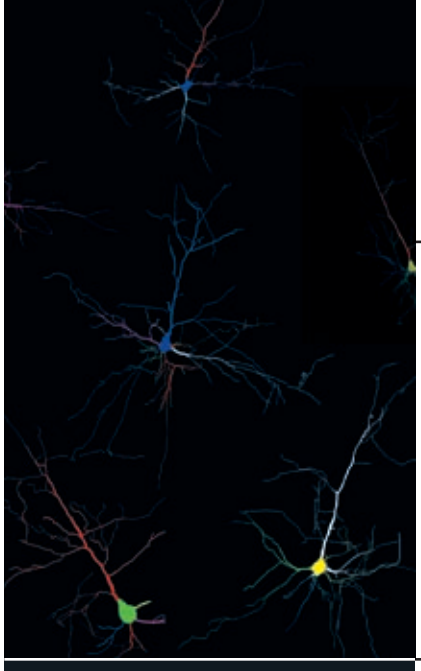

Understanding Aberrant Transcriptional Circuitries and Signaling Cascades in Glioblastoma Multiforme

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The regulation of tumor cell behavior in response to its microenvironment is a major factor influencing the properties and outcome of a malignancy. Glioblastoma multiformes (GBM) represents one of the most malignant brain tumors characterized by intense proliferation and poor prognosis. As inflammation is an indispensable participant in tumor progression, the focus of our group is to understand the importance of inflammatory mediators on the transcriptional regulation of genes associated with GBM survival and resistance to apoptosis. The aim is to understand how aberrant transcriptional circuitries and signal transduction pathways contribute to the progression GBM. The highly resistant nature of GBM to chemotherapy has also prompted us to identify new treatment strategies that target aberrant signaling pathways.

(i) Inhibition of Casein Kinase 2 induces p53 dependent cell cycle arrest and sensitizes glioblastoma cells to Tumor Necrosis factor (TNFα)-induced apoptosis t hrough SIRT1 inhibition

Glioblastoma multiforme are resistant to TNFα-induced apoptosis and blockade of TNFα-induced NFκB activation sensitizes glioma cells to apoptosis. As Casein kinase-2 (CK2) induces aberrant NFκB activation and since we observed elevated CK2 levels in GBM tumors, we investigated the potential of

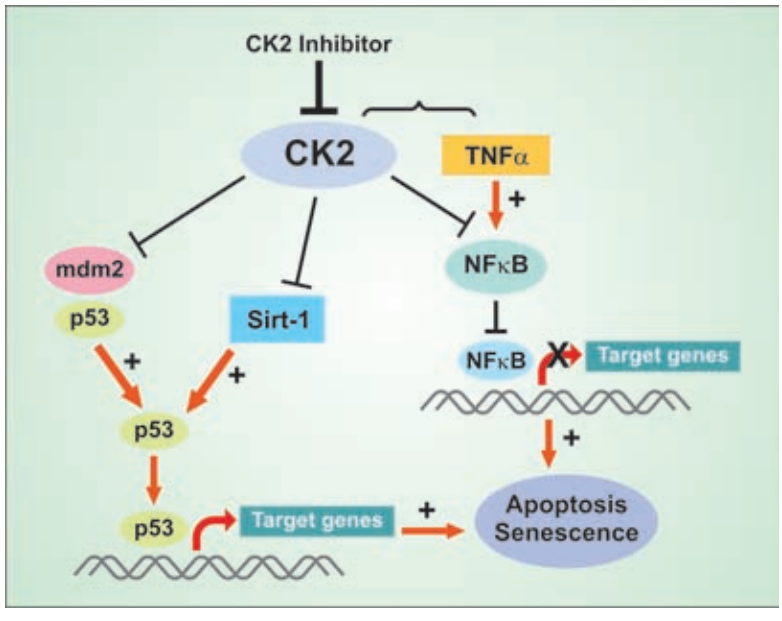
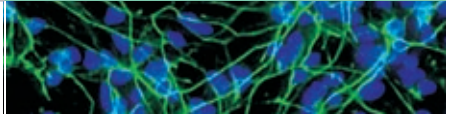


Figure1.

Proposed model demonstrating the role of CK2 in glioma cell apoptosis and resistance to therapy. CK2 inhibition induces glioma cell death via activation of p53 through SIRT1 inhibition and sensitizes glioma cell to TNFα via down regulation of TNFβ-induced NFκB activity.



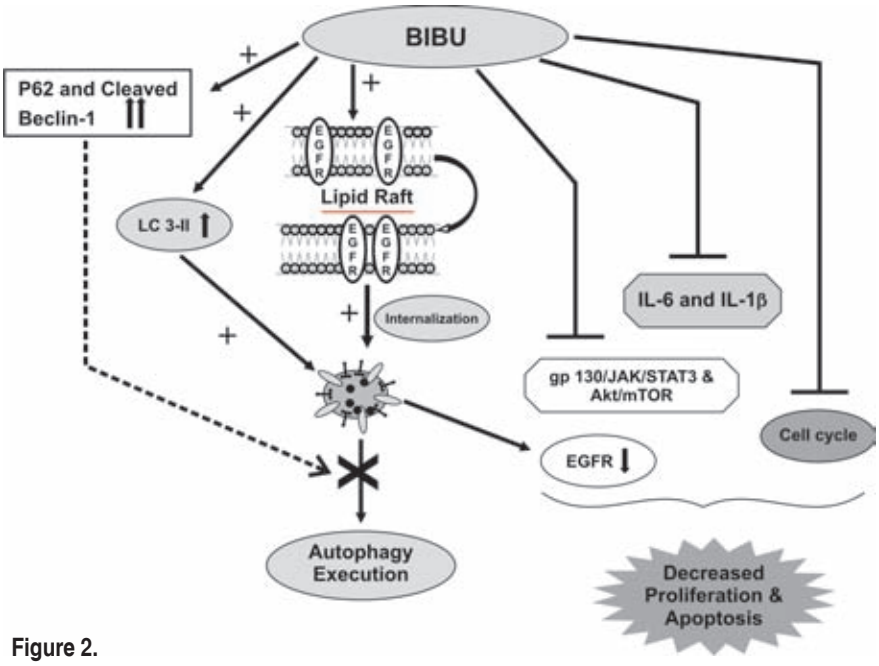


Figure 2.

Proposed model for induction of apoptosis and non-productive autophagy in glioma cells by EGFR inhibitor BIBU.

CK2-inhibitors (CK2-Is) - DRB and Apigenin in sensitizing glioma cells to TNFα-induced apoptosis. CK2-Is and CK2 siRNA reduced glioma cell viability, inhibited TNFα-mediated NFκB activation, and sensitized cell to TNFα-induced apoptosis. Importantly, CK2-Is activated p53 function in wild type but not in p53 mutant cells. Activation of p53 function involved its increased transcriptional activation, DNA binding ability, increased expression of p53 target genes associated with cell cycle progression and apoptosis. Moreover, CK2-Is decreased telomerase activity and increased senescence in a p53 dependent manner. Apoptotic gene profiling indicated that CK2-Is differentially affect p53 and TNFα targets in p53 wild type and mutant glioma cells. CK2-I decreased MDM2-p53 association and p53 ubiquitination to enhance p53 levels. Interestingly, CK2-Is down-regulated SIRT1 activity and over-expression of SIRT1 decreased p53 transcriptional activity and rescued cells from CK2-I induced apoptosis. This ability of CK2-Is to sensitize glioma to TNFα-induced death via multiple mechanisms involving abrogation of NFκB activation, reactivation of wild type p53 function and SIRT1 inhibition warrants investigation.

(ii) EGFR inhibitor BIBU induces apoptosis and defective autophagy in glioma cells

The importance of aberrant EGFR signaling in glioblastoma progression and the promise of EGFR-specific therapies, prompted us to determine the efficacy of novel EGFR inhibitor BIBU-1361 [(3 - chloro - 4 - fluoro-phenyl) - [6 - (4 - diethylaminomethyl - piperidin - 1 - yl) - pyrimido [5,4 - d] pyrimidin - 4 - yl] - amine] in affecting glioma survival. BIBU induced apoptosis in a caspase dependent manner and induced cell cycle arrest in glioma cells. Apoptosis was accompanied by decreased EGFR levels and its increased distribution towards caveolin rich lipid raft microdomains. BIBU inhibited pro-survival pathways Akt/mTOR and gp130/JAK/ STAT3; and decreased levels of pro-inflammatory cytokine IL-6. BIBU caused increased LC3-I to LC3-II conversion and triggered the internalization of EGFR within vacuoles alongwith its increased co-localization with LC3-II. BIBU caused accumulation of p62 and increased levels of cleaved forms of Beclin-1 in all the cell lines tested. Importantly, BIBU failed to initiate execution of autophagy as pharmacological inhibition of autophagy with 3-Methyladenine or Bafilomycin failed to rescue BIBU mediated death.

BIBU mediated increase in EGFR distribution towards caveolin rich lipid raft microdomains is concomitant with its increased internalization within vacuole like structures and co-localization with LC3-II. This coupled with increased accumulation of p62 and cleaved forms of Beclin-1 possibly prevented the successful execution of productive autophagy. In addition, BIBU (i) decreases EGFR, Akt/mTOR and gp130/JAK/ STAT3 levels and (ii) induces cell cycle arrest and triggers glioma cells apoptosis. The ability of BIBU to induce apoptosis and prevent execution of autophagy warrants its investigation as a potent anti-glioma target.

Publications

Reasearch Articles

1. D. Dixit, V. Sharma, S. Ghosh, V.S. Mehta, and **E. Sen.** Inhibition of Casein Kinase 2 induces p53 dependent cell cycle arrest and sensitizes glioblastoma cells to Tumor Necrosis factor (TNFα) induced apoptosis through SIRT1 inhibition. **Cell Death and Disease;3:e271. doi: 10.1038/cddis.2012.10.**

2. R. Tewari, S. Roychoudhury, S. Ghosh, V.S. Mehta and **E. Sen.** (2012). Involvement of TNFα induced TLR4-NFκB and TLR4-HIF-1α feed-forward loops in the regulation of inflammatory responses in glioma". **Journal of Molecular Medicine**; 90(1):67-80
3. S. Sinha, N. Koul, D. Dixit, V. Sharma and **E. Sen.** (2011). IGF-1 induced HIF-1α-TLR9 cross talk regulates inflammatory responses in glioma. **Cellular Signaling**. 23 (11):1869-1875.04
4. V. Sharma, D. Dixit, S. Ghosh and **E. Sen.** (2011). COX-2 regulates the proliferation of glioma stem like cells. **Neurochemistry International.**; 59(5):567-71.

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5. **E. Sen** (2011). Targeting inflammation induced transcription factor activation: An open frontier for glioma therapy. Invited Review in **Drug Discovery Today**. 16(23-24):1044-51.

Presentations

International

i. R. Tewari, S. Roychoudhury, V.S. Mehta and E. Sen. Involvement of TNFα induced TLR4-NFκB and TLR4-HIF-1α feed-forward loops in the regulation of inflammatory responses in glioma". Shanghai Symposium: Signaling, Inflammation and Cancer, Shanghai 25-28 July, 2011.

ii. E. Sen and D. Dixit. Role of Casein Kinase 2 (CK2) in resistance of Glioma cells towards TNF-alpha mediated apoptosis. 19th Euroconference on Apoptosis, Stockholm,14-17 September, 2011.

iii. S. Ghosh and E. Sen. Role of β-catenin mediated chromatin remodeling in TNF-α induced transcriptional regulation of MHC Class I genes. Spetses Summer School on Chromatin and Systems Biology, Greece 17-23 September, 2011.

iv. D. Dixt and E. Sen. Role of Casein Kinase 2 (CK2) in resistance of Glioma cells towards TNFα mediated apoptosis. Annual Meeting of Society for Neuroscience, Washington DC, 12-16 November, 2011.

National

i. E. Sen. The T-L-R connection. National Conference on CME in Immunology, West Bengal State University WBSU, 4th Nov 2011

ii. E. Sen. The NFκB-p53-SIRT1 nexus in glioma: More than meets the eye??? 5th Symposium on "Frontiers in Molecular Medicine" Special Centre for Molecular Medicine , JNU, 18th February 2012

iii. E. Sen. Inflammation and tumorigenesis : An evolving concept "Bioepoch" School of Biotechnology, JNU, 24th February 2012

iv. E. Sen, Sadashib Ghosh and Arkoprovo Paul. Role of Cofilin in Modulating Apoptotic Signals in Glioblastoma Multiforme. Recent Advances in Chemical and Physical Biology, SINP, Kolkata, 5th -7th March, 2012

Funding

i. Oligodendrocyte Differentiation from Neural Stem Cells - Implication in CNS repair. Funded by DBT, Govt. of India. BT/PR6615/MED/14/857/2005.

ii. Understanding signaling circuitries involved in transcriptional regulation of genes associated with survival and immune response in an inflammatory environment: Implications in glioblastoma progression. Funded by DBT, Govt. of India. BT/PR12924/MED/30/235/2009

Awards

i. Prof. BK Bachawat Travel Grant for Young Scientists (2012) to Ellora Sen by Christian Medical College, Vellore, India

ii. IBRO international travel grant 2011 to Deobrat Dixit for attending Society for Neuroscience, Washington DC, 2011.

Degree Awarded

Ph.D. Richa Tewari (2011) Ph.D. Nitin Koul, MBBS (2011)

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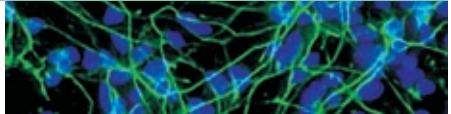

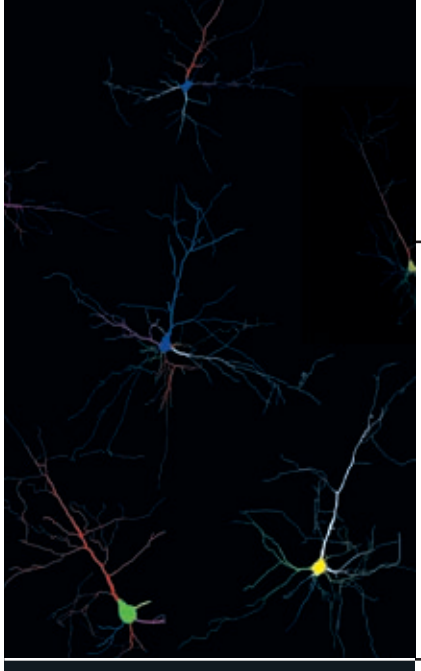

Activity-Dependent Protein Modifications, Long-term Potentiation and Memory

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Activity-Dependent Activation of Extracellular Signal-Regulated Kinase

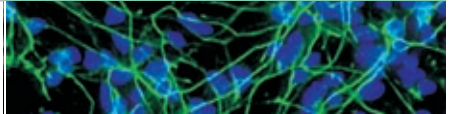
It has been well established that post - translational modifications in proteins play crucial roles in synaptic plasticity and memory. One modification, phosphorylation, is known to play critical roles in these processes. Among the several kinases that are important for long-lasting synaptic change and memory, the extracellular signal-regulated kinase (ERK) has received special attention due to the fact that it can regulate diverse processes involved in synaptic plasticity and memory. Although ERK is activated by different stimuli relevant for long-term potentiation (LTP) and memory, the mechanisms of ERK activation are not completely understood. Using hippocampal slices, we are examining the processes involved in ERK activation. We earlier reported that KCl depolarization induces a sustained ERK activation. This sustained ERK activation requires protein synthesis, transcription and receptor tyrosine kinase activity. We have conducted more experiments to examine the mechanisms that contribute to depolarization-induced sustained ERK activation. Further experiments showed that KCl depolarization indeed enhances the levels of a growth factor at the sustained ERK activation time point. Importantly, we found that blocking the activity of this growth factor blocks sustained ERK activation. Thus, there appears to be a feed-back mechanism in depolarization-induced sustained ERK activation.

Synaptic Mechanism of Memory: Long-Term Potentiation in the Hippocampus

Long-term potentiation (LTP) is a long-lasting increase in synaptic strength. This synaptic phenomenon is widely studied as a candidate cellular mechanism of memory formation. We use hippocampal slices to study processes involved in LTP. In these experiments, we stimulate the CA3 region of the hippocampus and record the response in the CA1 region. We use a commonly used pattern of stimulation of the CA3 fibres. It is well known that massed and spaced trainings induce differential pattern of memory. Keeping in line with our key interest in examining mechanisms of differential memory formation by massed and spaced trainings, we apply LTP-inducing stimuli either in a massed or spaced pattern, and record LTP. We earlier reported that, consistent with earlier findings, the two patterns of stimulations induce differential pattern of LTP in the hippocampal slices. We then tried to examine whether modifying molecular machinery has any effect on the pattern of LTP induction by massed stimulation. Our results suggest that increasing the levels of a particular post-translational modification of proteins enhances the extent of LTP by massed stimulation. These results suggest that this post-translational modification may contribute to differential induction of LTP by the two patterns of stimuli.

Pattern-Dependent Memory Formation

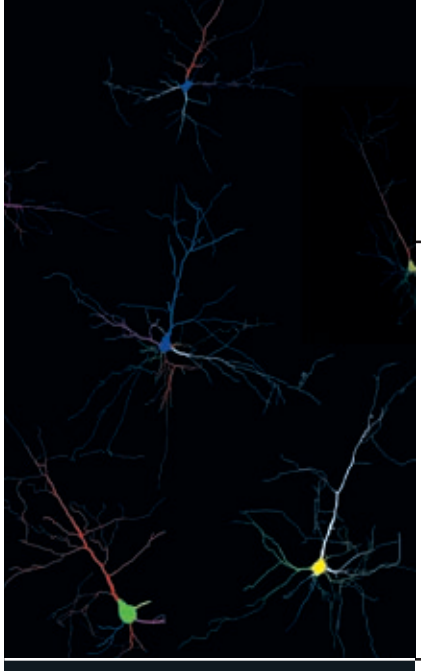
It is well established that the pattern in which the training trials are applied during training plays a major role in determining the strength and duration of memory. It is typically observed that in a multi-trial task, the spaced training in which the training trials are widely spaced in time produce good long-term memory.



In contrast, the same number of trials applied in a massed pattern where there is little or no temporal spacing between trials produce weak memory. We are interested in examining the mechanisms that contribute to the differential effects of massed and spaced training on memory formation. For our studies, we use spatial memory task using the Morris water maze system. In this task, the animals try to find a platform to escape out of water. They use spatial cues present in the surrounding to remember the location of the platform hidden in opaque water. After establishing the procedure in our lab, we conducted experiments directed towards identification of processes involved in better memory formation by spaced training. We earlier reported that, as shown by others, the massed pattern of training is less effective in inducing memory than the spaced training. We then asked-can the memory induced by massed pattern of training be enhanced by pharmacologically increasing particular modification of proteins? We find that indeed it is possible to enhance memory induced by massed pattern of training by changing the levels of post-translational modification of proteins. These results suggest that the particular post - translational modification under study plays important roles in determining the extent of memory by the two training paradigms.

Funding

This work is supported by NBRC core.



Alzheimer's Disease: Neuroprotection Against Amyloid Beta-Induced Toxicity

Principal Investigator
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Research Fellow
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Narayanan

Considerable efforts are devoted towards understanding what causes memory impairment conditions. Among different memory loss conditions, Alzheimer's disease (AD) is the most common amongst the elderly. The social and economic burden of this disease is evident from the fact that the number of people suffering from this condition is constantly increasing. The pathological features of this disease include amyloid plaques which are extracellular, and neurofibrillary tangles which are present intracellularly. Amyloid beta (A-beta) peptide is a primary constituent of the plaques found in AD brains. This peptide is widely considered to play a casual role in the development of this disease. It has become clear now that amyloid beta exists in different forms. Among these, the oligomeric form of amyloid beta is now considered to play major role in the development of the disease at least in the initial stages. The oligomeric A-beta causes neuronal cell death

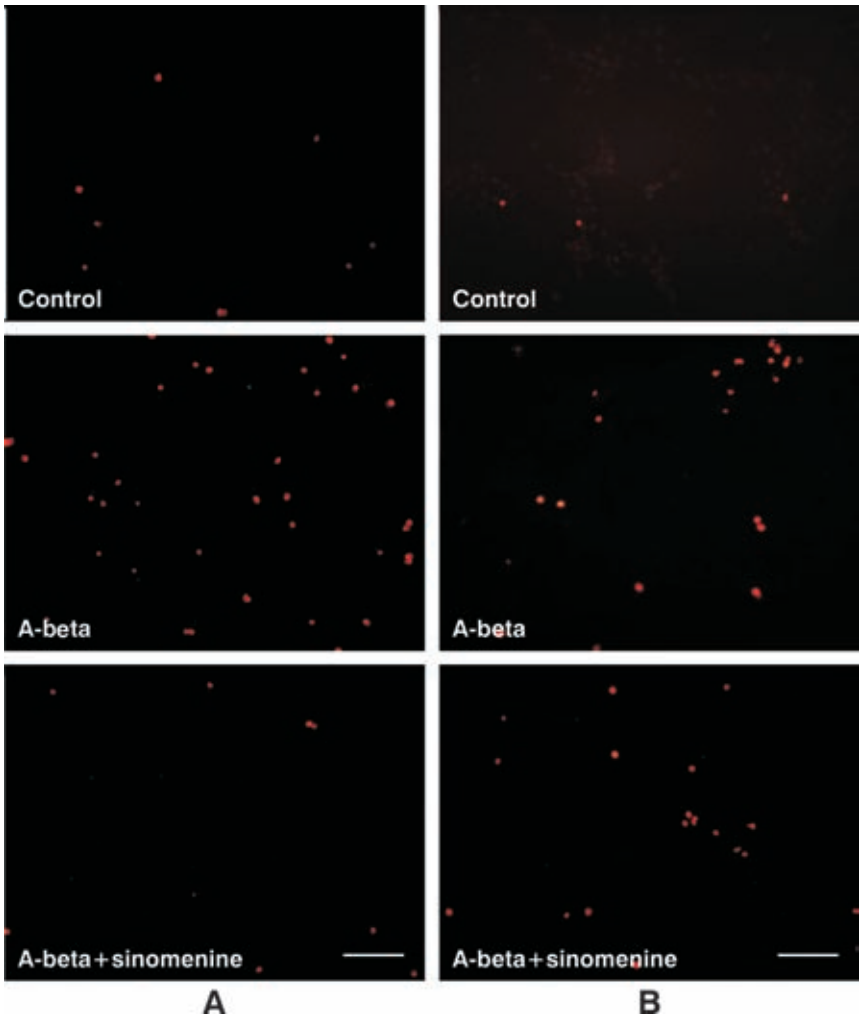
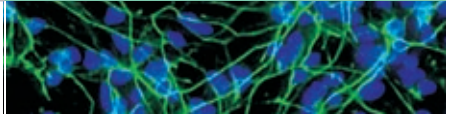


Figure 1.

Sinomenine protects hippocampal cells against A-beta-induced indirect toxicity (A), but has no effects on direct toxicity (B). A. The HT22 cells were treated with the conditioned medium from control, A-beta-treated or A-beta+sinomenine treated BV2 cells. The cells treated with the conditioned medium from A-beta-treated BV2 cells showed large number of TUNEL-positive cells. The number of TUNEL-positive cells was reduced in the samples which were treated with the conditioned medium from A-beta+ sinomenine-treated BV2 cells, indicating protection by sinomenine against indirect toxicity. B. The HT22 cells were treated with A-beta or A-beta+sinomenine. The number of TUNEL-positive cells in the A-beta treated or A-beta+sinomenine treated cells was similar, indicating lack of protection against direct toxicity.



and impairs synaptic plasticity and memory. Thus, in our studies we use oligomeric form of A-beta. We prepare oligomeric A-beta using the commercially available A-beta (1-42).

Effects of an Alkaloid on Amyloid Beta-Induced Neurotoxicity

The neuronal cell death is one of the prominent features in AD, and A-beta plays a causal role in this process. For this reason, a lot of effort is directed towards examining the mechanisms of amyloid-beta-induced cell death. Significant effort is also directed towards identification of compounds that can prevent or delay cell death. A-beta causes neuronal cell death both directly and indirectly. In the indirect mode of cell death, A-beta acts on the microglial cells and causes release of toxic molecules such as reactive oxygen species (ROS) and nitric oxide. The release of inflammatory molecules also is a consequence of A-beta acting on microglial cells. These toxic substances then affect the viability of neurons. This mode of neuronal cell death is also believed to play important roles in neuronal cell death caused by A-beta and development of the AD pathology. We earlier showed that a curcumin metabolite protects primary neurons against A-beta-induced direct cell death. With regards to indirect cell death, we reported also that an alkaloid (sinomenine) was able to inhibit A-beta-induced release of ROS, nitric oxide and inflammatory molecules from microglial (BV2) cells. Also, we showed that the alkaloid was able to inhibit neuronal toxicity caused by the conditioned medium (which contains toxic molecules) from A-beta-treated microglial cells. The effect of alkaloid was confirmed using two different assays for cell viability. The indirect toxicity experiments were performed on a hippocampal cell line (HT22) as well as primary hippocampal cells. We have conducted more experiments in this aspect. We examined the effects of the alkaloid on the levels of toxic substances in the A-beta-treated BV2 conditioned medium. Our results showed that the alkaloid reduced the levels of toxic molecules in the conditioned medium of A-beta treated BV2 microglial cells. In addition, we examined the effects of simultaneous treatment of sinomenine and A-beta on A-beta-induced ROS generation in BV2 cells. The results showed that a pre-treatment with sinomenine was necessary for its effects on ROS generation.

Since the alkaloid was effective in protecting neuronal cells against indirect toxicity, we next asked whether the alkaloid had any effects on A-beta induced direct cell death. We found that the A-beta-induced cell death in hippocampal cell line was unaffected by the alkaloid. This observation was confirmed in two different assays that measure cell viability. Thus, whereas the alkaloid prevents indirect neuronal cell toxicity, it has no effects of direct cell death caused by A-beta.

Effects of Amyloid Beta on Growth Factor Signaling

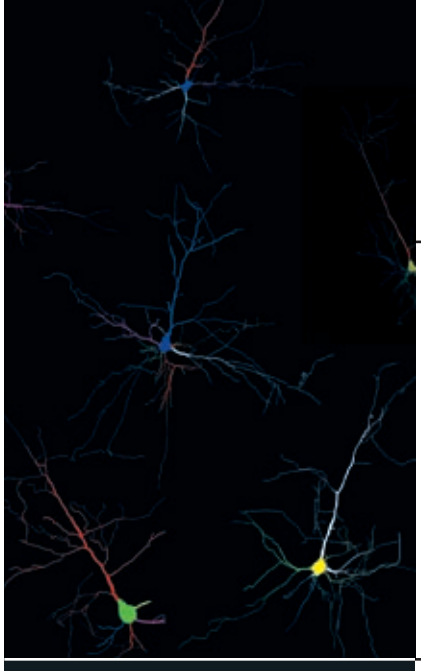
Several previous studies have shown that growth factor signaling plays crucial roles in the development of synaptic plasticity and memory. Since AD is a memory impairment condition, we asked how A-beta affects growth factor signaling. To examine the effects of A-beta on growth factor signaling, we use primary hippocampal neurons since hippocampus is critical for different kinds of memory. These neurons are treated with the growth factor with or without A-beta. The samples are then processed for examination of activation state of important signaling molecules. We found that the growth factor-induced activation of extracellular signal regulated kinase (ERK) is impaired by A-beta. ERK is one of the important kinases that has been shown to critically regulate synaptic plasticity and memory in several different model systems. We then examined other events in the growth factor signaling pathway. Our results show that molecules, which are critical for synaptic plasticity and memory, are affected by A-beta. We have also attempted to find out the step in the growth factor signaling cascade that is affected by A-beta. Our results thus suggest that the inhibitory effect of A-beta on growth factor signaling may be one of the contributing factors for the deficits in synaptic plasticity and memory in this devastating disease.

Publication

1. S.M. Shukla and **S.K. Sharma** (2011) Sinomenine inhibits microglial activation by Aβ and confers neuroprotection. **J Neuroinflammation** 8:117.

Funding

This work is supported by Council of Scientific and Industrial Research and NBRC core.



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

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While the blood–brain barrier (BBB) protects the central nervous system (CNS) from peripheral immune and inflammatory activation, the CNS is also able to induce the protective innate immune system in response to injury, including trauma, infection, stroke and neurotoxins. This acute inflammatory response is short-lived and generally beneficial in neutralizing potential threats to the CNS by minimizing cellular damage. On the other hand, a sustained chronic neuroinflammatory response can be detrimental and initiate neuronal damage, neuronal circuits impairments, astrocytic and microglia involvement and neurodegeneration via long-lasting formation and accumulation of neurotoxic

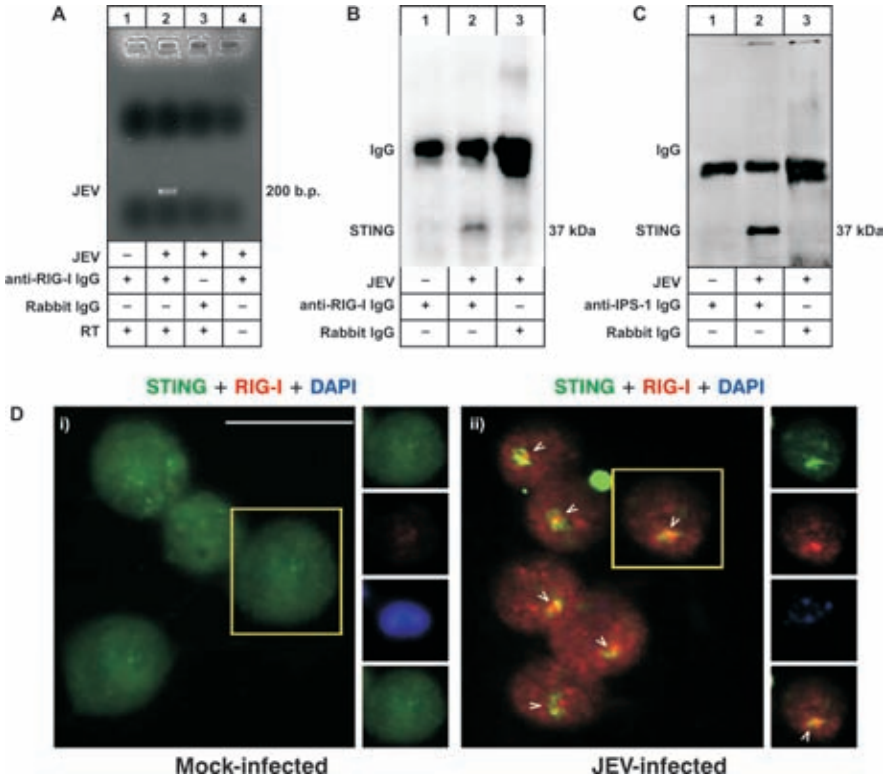
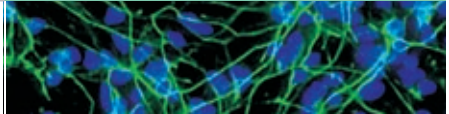


Figure1.

Viral RNA interacts with RIG-I that in turn interacts with STING and IPS-1. A, Interactions between RIG-I and viral protein was observed by RT-PCR with RNA obtained from JEV-infected cell extracts by the method as described under experimental procedures. Viral mRNA band was visualized only in the sample which was conjugated with anti-RIG-I antibody. Image is representative of 3 independent experiments. B-C, STING - RIG-I and STING - IPS-1 interactions following JEV infection were observed by CoIP. Protein extracts from mock-infected and JEV-infected cells were allowed to form complexes with incubated anti-RIG-I or anti-IPS-1 antibodies. The protein-antibody complexes were eluted followed by detection for STING by immunoblotting. The shown immunoblots are representative of 3 independent experiments. D, Mock-infected and JEV-infected cells were double stained for STING and RIG-I. Merged images show clear STING and RIG-I interactions (yellow), marked by arrowheads. Un-merged images of the cell (inset) shows STING (green) and RIG-I (red) expressions, separately. Magnification ×40; scale bar is 25 μ; images are representative of 3 independent experiments.



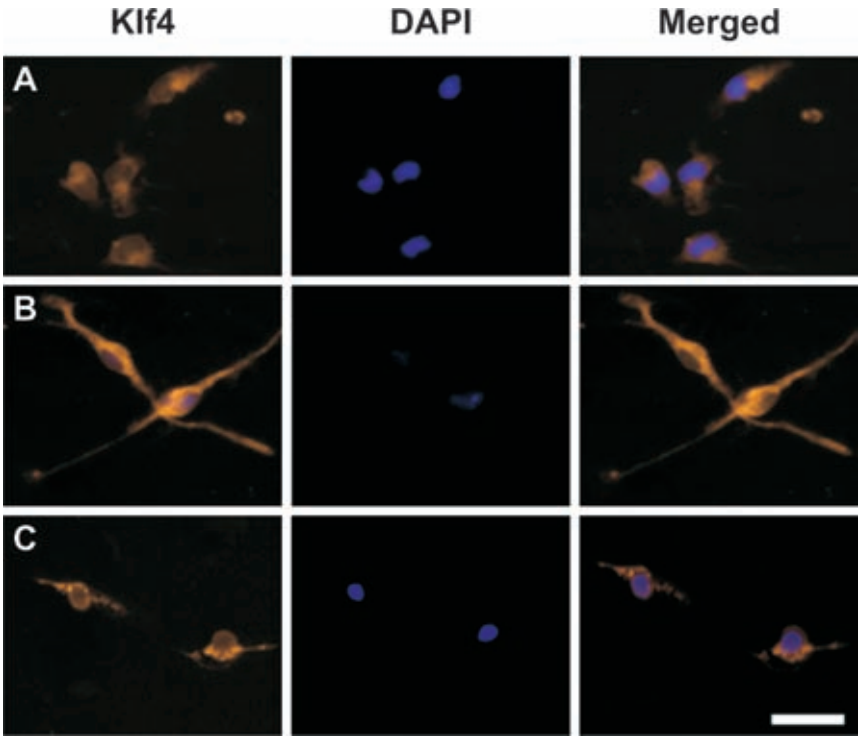


Figure 2.
Effects of Honokiol on the Klf4 expression in LPS treated primary microglia. Primary microglia isolated from P0-P2 BALB/c mice treated with 500ng/ml of LPS and 10μM of HNK were analysed by immunocytochemistry. (A) Fluorescent images of untreated primary microglia treated with a sham mixture of 1XPBS and DMSO in 1:1 ratio. (B) Primary microglia treated with LPS for 12h and (C) LPS treated primary microglia co-treated with HNK for 12h. Images showing the staining for Klf4 (Alexa fluor 594; Rhodamine Channel), DAPI (Blue) and Merged images (Right panel). Scale bar-20μm

proinflammatory mediators. The recognition of microglia as the brain's intrinsic immune system, and the understanding that chronic activation of this system leads to pathologic sequelae, has led to the modern concept of neuroinflammation.

Our research question evolves around the understanding the molecular basis of host-pathogen interaction in viral infection of the brain and the signaling events associated with neuro-inflammation. In last few years our research have been primarily focused on neuropathology of host pathogen interaction in Japanese encephalitis Virus (JEV), causative agent of most common Viral encephalitis in Asia-pacific region.

JEV a member of the flaviviruses, is the most common cause of arthropod borne human encephalitis in Asia. Flaviviruses infecting the CNS are known to trigger inflammation and cause neuronal death. This is mediated in part by direct virus-induced apoptosis/necrosis or by a 'bystander' mechanism resulting from the inflammatory milieu. JEV is able to infect neurons, although their role in JEV infection has not been clearly defined. A detailed understanding of the disease pathogenesis is therefore crucial for the prevention of the neurological sequel mediated by JEV in human beings.

Neuroinflammation associated with Japanese encephalitis (JE) is mainly due to the activation of glial cells with subsequent release of proinflammatory mediators from them. The recognition of viral RNA, in part, by the pattern recognition receptor retinoic acid-inducible gene I (RIG-I) has been indicated to have a role in such processes. We have showed that neurons are one of the potential sources of proinflammatory cyto/chemokines in JEV-infected brain that are produced via RIG-I dependent pathways. Ablation of RIG-I in neurons leads to increased viral load and reduced release of the cyto/chemokines.

We have also showed that RIG-I acts with STING in a concerted manner following its interaction with Japanese encephalitis viral RNA to induce a type 1 interferon response. Knock-down of STING showed that the expressions of various inflammatory signaling molecules were down-regulated along with increased intracellular viral load. Alternatively, over-expressing STING decreased intracellular viral load. Our results indicate that at the sub-cellular level, interaction between the pattern recognition receptor RIG-I and the adapter molecule STING, is a major contributor to elicit immunological responses involving the type 1 interferons in neurons following JEV infections.

We have further showed that NLRP3 inflammasome is a key mediator of neuroinflammation in murine Japanese Encephalitis. Our results identify a mechanism, mediated by Reactive Oxygen Species (ROS) production and potassium efflux as the two danger signals that link JEV infection to caspase-1 activation resulting in subsequent IL-1β and IL-18 maturation. Our study further identified the role of NLRP3 inflammasome mediated caspase-1 activation and subsequent IL-1β and IL-18 production during JEV infection. We have also shown that replication competent JEV is crucial for activating this complex as UV treated JEV does not increase caspase-1 activity or the production of inflammatory cytokines.

Besides studying fundamental aspects of JE neuropathology we are always keen to do translational research to develop newer generation of therapy for JE. Recently in collaboration with Prof Vijayalakshmi Ravindranath from Center for Neurosciences, Indian Institute of Science, we have showed that Fenofibrate, a PPARγ agonist that is commonly used as a hypolipidemic drug, reduces mortality and precludes neurological deficits in survivors in murine model of Japanese encephalitis viral infection. Given the prevalence of this infection in endemic areas, the high mortality and morbidity that it causes among children and the lack of effective curative therapies, fenofibrate with its well established safety profile could offer an inexpensive, safe and effective prophylactic therapy for JEV infection.

Alongside with neurobiology of JE, our laboratory is also deeply engaged in basic research to understand the transcriptional regulation of microglial activation. Earlier we have identified a novel transcription factor Krüppel-like factor 4, which regulates microglial activation and subsequent neuro-inflammation. Recently we have showed that Honokiol (HNK), a biphenolic anti-inflammatory agent used as traditional herbal medicine inhibiting Krüppel-like factor 4 to abrogate microglial activation. We have found that honokiol can substantially downregulate the production of pro-inflammatory cytokines and inflammatory enzymes in LPS stimulated microglia. In addition, honokiol also downregulates LPS induced up regulation of both Klf4 and pNF-κB in these cells. We also found that overexpression of Klf4 in microglial cells suppresses the anti-inflammatory action of honokiol. Our findings strongly suggest that Klf4 is one of the key players of inflammation and therefore is one of the key targets of therapeutic intervention in neurodegerative diseases which has distinct pathology of inflammation.

Publications

Research articles

1. N. Sehgal, K.L. Kumawat, **A. Basu** and V. Ravindranath (2012) Fenofibrate reduces mortality and precludes neurological deficits in survivors in murine model of Japanese encephalitis viral infection. **PLoS One** 7(4): e35427
2. A. Nazmi, R. Mukhopadhyay, K. Dutta, and **A. Basu** (2012) STING mediates neuronal innate immune response following Japanese encephalitis virus infection. **Scientific Reports**, 2:347
3. D.K. Kaushik, R. Mukhopadhyay, K.L. Kumawat, M. Gupta and **A. Basu** (2012) Therapeutic targeting of Kruppel like factor 4 abrogates microglial activation. **Journal of Neuroinflammation** 9(1), 2012:57
4. D.K. Kaushik, M. Gupta, K.L. Kumawat, and **A. Basu** (2012) NLRP3 inflammasome: Key mediator of neuroinflammation in murine Japanese Encephalitis. **PLoS One** 7(2); 2012:e32270.
5. A. Nazmi, K. Dutta, and **A. Basu** (2011) RIG-I Mediates Innate Immune Response in Mouse Neurons Following Japanese Encephalitis Virus Infection. **PLoS One** 6(6):e21761
6. A. Nazmi, K. Dutta, S. Das, and **A. Basu** (2011) Japanese Encephalitis Virus Infected Macrophages Induces Neuronal Death. **Journal of Neuroimmuno Pharmacology** 6(3):420-33

Reviews

7. S. Ghosh, and **A. Basu** (2012) Network Medicine in Drug Design: Implications for Neuroinflammation. **Drug Discovery Today** 17(11-12):600-7
8. I.M. Ariff, A. Mitra and **A. Basu** (2012) Epigenetic regulation of self-renewal and fate determination in neural stem cells. **Journal of Neuroscience Research** 90(3):529-39 (Cover photo) *

* In press last year

Presentations

i. A. Nazmi and A. Basu (2012) MPYS (STING) mediates neuronal innate immune response following Japanese encephalitis virus infection. 5th Congress of the Federation of Immunological Societies of Asia Oceania; 14th -17th March 2012, New Delhi, India.
ii. A. Basu (2012) Microglia; A friend in need may not be a friend indeed.BIOSPARKS 2012, School of Life Sciences, JNU, New Delhi, 14-15th March, 2012.

iii. K. Dutta, A. Nazmi, R. Mukhopadhyay and A. Basu (2012) Involvement of the RLR pathway in neuronal immunity following Japanese encephalitis virus infection. 43rd Annual meeting of the American Society for Neurochemistry; 3rd –7th March 2012, Baltimore, USA.

iv. D.K. Kaushik, and A. Basu (2012) Therapeutic targeting of Krüppel like factor 4 abrogates neuro-inflammation. 43rd Annual meeting of the American Society for Neurochemistry; 3rd –7th March 2012, Baltimore, USA.

v. A. Basu (2012) Modulation of neural stem cell fate following Japanese encephalitis virus infection. Biotech 2012, Annual Conference "Current Advances in Biotechnology and Medicine", Institute of Liver and Biliary Sciences, New Delhi 24th-25th February, 2012.

vi. I.M. Ariff, S. Das, and A. Basu (2012) Japanese Encephalitis virus infection and Neural stem/progenitor fate determination. 19th Biennial meeting of the International Society of Developmental Neuroscience; 11th - 14th January 2012, Tata Institute of Fundamental Research, Mumbai, India.

vii. D.K. Kaushik, and A. Basu (2012) Kureppel like factor 4, a zinc finger transcription factor is associated with microglial activation and subsequent neuro-inflammation. 41st Annual meeting of Society for Neuroscience; 12th-16th November 2011, Washington DC, USA.

viii. A. Basu (2011) Nervous about immunity: neuronal signals control innate immune response.CME in Immunology, Organized by West Bengal State University, 4-5th November.

ix. A. Basu (2011) Transcriptional Regulation of Microglial activation: Inflammation in Hypoxia. XXIX Annual Meeting of Indian Academy of Neurosciences, New Delhi, 30th Oct- 1st Nov. 2011.

x. A. Basu (2011) JE Virus infects brain: Murder in triplicate NERVE 2011, Haffkine Institute, Mumbai, 27-28th September, 2011.

xi. D.K. Kaushik, and A. Basu (2011). Upregulation of Krueppel like factor 4 in microglia is associated with its activation and successive neuro-inflammation. 23rd Biennial ISN-ESN meeting, 28th August-1st September 2011, Athens, Greece.

xii. A. Basu (2011) Evaluation of Minocycline as a therapy in an experimental model of Japanese Encephalitis.Department of Pediatrics, CSM Medical University, Lucknow, 13th June, 2011.

xiii. K. Dutta, M.K. Mishra, S. Das and A. Basu (2011) Therapeutic implications in Japanese encephalitis- taking Minocycline from the bench to the bedside. 2nd Molecular Virology meeting, 29th-30th April 2011, Indian Institute of Science, Bengaluru, India.

xiv. D. Adhya, K. Dutta, and A. Basu (2012) Immune evasion by Japanese encephalitis virus – a novel strategy for persistent peripheral infection. 2nd Molecular Virology meeting, 29th-30th April 2011, Indian Institute of Science, Bengaluru, India.

xv. A. Basu (2011) Inflammation and neuro-genesis in Japanese Encephalitis.2nd Molecular Virology Forum meeting, IISC, Bangalore, 29-30th April, 2011.

Funding

i. Host–Directed Drug Targeting: Implication of Suppressors of cytokine signaling (SOCS) in the pathogenesis of Japanese Encephalitis [Funded by Department of Biotechnology (awarded along with the National Bio Science Award for Career Development)].

ii. To study the role of Neuronal innate immune response in Japanese encephalitis virus infection [Funded by CSIR (27(0238)/10/EMR-II)].

iii. To elucidate the role of inflammasome and other molecular events leading to Hypoxia induced neuro inflammation [Funded by Life science Research Board, DRDO (No LSRB-213/EPB/2010)].

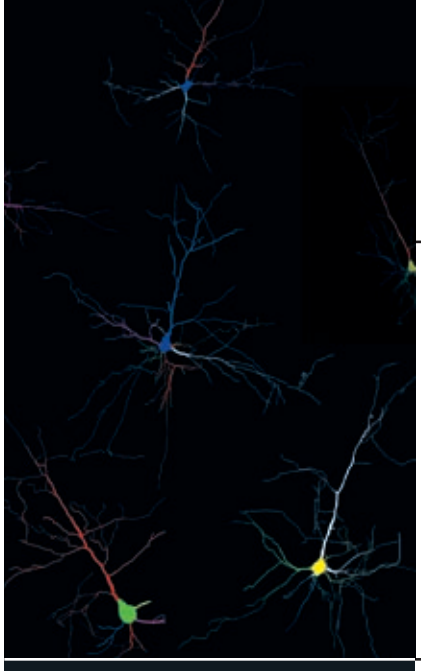
Awards

Elected as a Fellow of the National Academy of Sciences, India.

Deepak Kumar Kaushik, ISN Travel Award, to attend 23rd Biennial Meeting of ISN-ESN, Athens, 2011.

Deepak Kumar Kaushik, DST Travel Award, to attend Society for Neuroscience meeting, Washington DC, 2011.

Dr Kallol Dutta, IBRO and DST Travel Award, to attend 43rd Annual meeting of American Society for Neurochemistry, 3-7th March, Baltimore.



Development of a Novel in vitro Model of Alzheimer's Disease Employing Neurosphere Culture from TgAPPswePS1ΔE9 mice.

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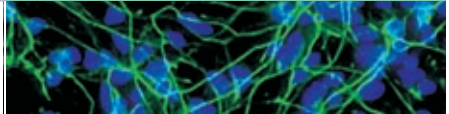
Lab. Attendant
Lalit Bidla

Alzheimer's disease (AD) is the most common cause of dementia worldwide. Increased formation of beta amyloid (Aβ) peptides is the key feature in both sporadic (SAD) and familial Alzheimer's disease (FAD). Genetic studies of early onset FAD have identified three causative genes: amyloid precursor protein (APP), Presenilin 1 (PSEN1) and presenilin 2 (PSEN2). Mutation/s in these genes affects the production and aggregation of more fibrillogenic $A\beta_{1-42}$ peptides that forms the backbone of the amyloid (Aβ) cascade hypothesis. Very little is known about exact role of beta amyloid peptides towards neurotoxicity. In order to study the mechanisms associated with AD neurodegeneration in humans, transgenic animals expressing human FAD genes were developed. Though these transgenic mice show beta amyloid deposits, astrogliosis, impaired learning abilities and mild cognitive impairment, exact role of beta amyloid peptides towards neurotoxicity remains puzzled. Moreover, the effect of beta amyloid on various mature brain cells is not known. Therefore, an alternative model that retains the capacity to generate major cell types of brain and generates human beta amyloid peptides endogenously is needed.

Furthermore, several publications have demonstrated the presence of neural stem cells in adult brain both in animals and in humans. These CNS stem cells posses the potential to differentiate towards major cell types of brain except microglia in vitro and in vivo. It is not clear why these cells fail to replenish the neuronal cell loss seen in AD, especially in hippocampus where CNS stem cells are enriched. Thus, we hypothesize that beta amyloid peptides might be affecting the normal functioning of CNS stem cells. So, to recapitulate most of the pathological features of AD, such as, de novo beta amyloid production and to study its effect on major cell types of brain cell types my lab is working towards developing an alternative in vitro model employing CNS stem cells. According to Aβ cascade hypothesis, Aβ peptide is the central and key molecule in the development of AD. Therefore, endogenous production and multimerization of human Aβ peptides are essential features in developing AD model in vitro.

My lab has developed 4 separate neurosphere lines. Two of these were positive for huAPPswe and huPS1ΔE9 gene (Tg +ve) and two are negative (Tg –ve) which served as wild type controls. Our results demonstrated that, Tg +ve lines express huAPPswe and huPS1ΔE9 transgenes at mRNA level (by RT-PCR) which are not present in Tg -ve neurosphere lines.

Western blot analysis of neurosphere lysates and immunofluorocytochemistry (IFCC) analysis indicated the expression human APP protein and its fragments only in Tg +ve neurosphere lines but not in transgenic negative lines. However, presence of beta amyloid peptides in neurosphere lysates was not detected in any transgenic positive neurosphere lysates. This could be because of release of Aβ peptides to extracellular space, the culture media. Western blot analysis of human Aβ peptides from culture supernatants of both Tg –ve and Tg +ve active neurosphere cultures indicated the presence of human Aβ peptides in all Tg +ve neurosphere lines but not at all in Tg -ve lines. These Aβ peptides are seen both as monomers as well as oligomers. Moreover, resolution of Aβ peptides in Tris-Bicine Urea gel followed by western blot analysis



clearly demonstrated the presence of human Aβ40 and Aβ42 in Tg+ve (NS1 and NS3) but not in Tg-ve NS lines and Aβ42 to Aβ40 ratio is higher than any other in vitro model of AD.

Intracellular Aβ load is another pathological feature of various cells in AD brain. Immunofluoroscent staining of adherent cells from neurosphere cultures demonstrated Tg +ve neurosphere lines have significant increased immunosignal towards 6E10 antibody than Tg -ve neurosphere lines without Formic acid (FA) treatment. Upon FA treatment, Tg +ve cells showed dramatic increased immunosignal over non-treated counterparts, whereas Tg -ve cells showed little increased signal than non-treated cells. Increased immunosignal in Tg+ve neurosphere cultures might be due to the presence of Aβ peptides in beta-sheet isoforms or in oligomeric form that required epitope retrieval by FA prior to its interaction with 6E10 antibody. Taken together, the results strongly indicate the expression, protein misfolding and accumulation of human Aβ peptides in Tg +ve neurosphere cultures in parallel with transgenic mice brain. Collectively, it indicates the genesis of a newer in vitro model for AD that has the potential to address other pathological effect of Aβ peptides on other adult brain cells like neurons, astrocytes and oligodendrocytes.

Presentations

i. **R.K. Giri** and P.S. Ghate. Utilization of neurosphere cultures to model Alzheimer's disease in vitro. **Annual Meeting of Society for Neuroscience, Washington DC, USA, 2011**.

ii. P.S. Ghate and **R.K. Giri**. Neurosphere culture as a novel In vitro model for Alzheimer's Disease. **Annual Meeting of Indian Academy of Neuroscience, New Delhi, India, 2011. Best Research Paper Presentation Award**

iii. **R.K. Giri**. Utilization of Neurosphere Culture in the Development of a Novel in vitro model of Alzheimer's Disease, **McLaughlin Research Institute, Great Falls, Montana, USA, 2012**.

Funding

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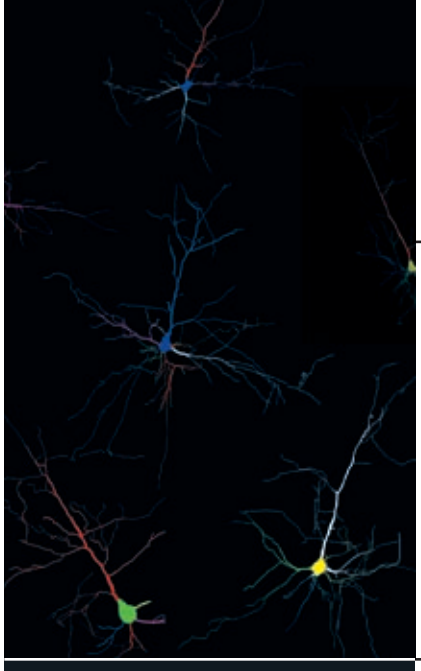

Changes in Epigenetic Factors in Terminally ill RML-Scrapie Infected C57BL/6J mouse

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Prion Diseases are a group of fatal but rare neurodegenerative disorders. It comprises Kuru, Cruetzfeldt-Jakob Disease (CJD), Gerstmann-Straussler-Scheinker syndrome (GSS) and fatal familial insomnia (FFI) in humans; scrapie in sheep and goat, and bovine spongiform encephalopathy (BSE) in cattle. The key event in the pathogenesis of prion disease is the post-translational conversion of normal cellular prion protein (PrPC) to pathological, infectious and alternatively folded isoforms (PrPSc). Infectivity associated with PrPSc makes this a unique neurodegenerative disease. Spongiform degeneration, glial proliferation and neuronal loss, are hallmark pathology of prion disease. However, very little is known about the mechanisms by which PrPSc mediates PD-associated pathology. Genes which are not required in matured neurons but required in cell cycle, are re-activated in various neurodegenerative diseases and are correlated with neuronal death, suggesting the alteration of normal genetic programme is a prerequisite condition of neuron loss in neurodegenerative disease. The gene expression programs governing cellular proliferation, differentiation and cell death involve multiple epigenetic changes beyond the level of transcription factor recruitment. Major epigenetic mechanisms include DNA methylation and histone modification. The acetylation and deacetylation of core histones on chromatin are most important histone modifications and are essential for many biological processes, including proliferation, differentiation and gene silencing. Such events are not reported in PD. To understand the effect of prion replication on histone acetylation at spatial level my lab have developed a robust mouse model of prion disease.

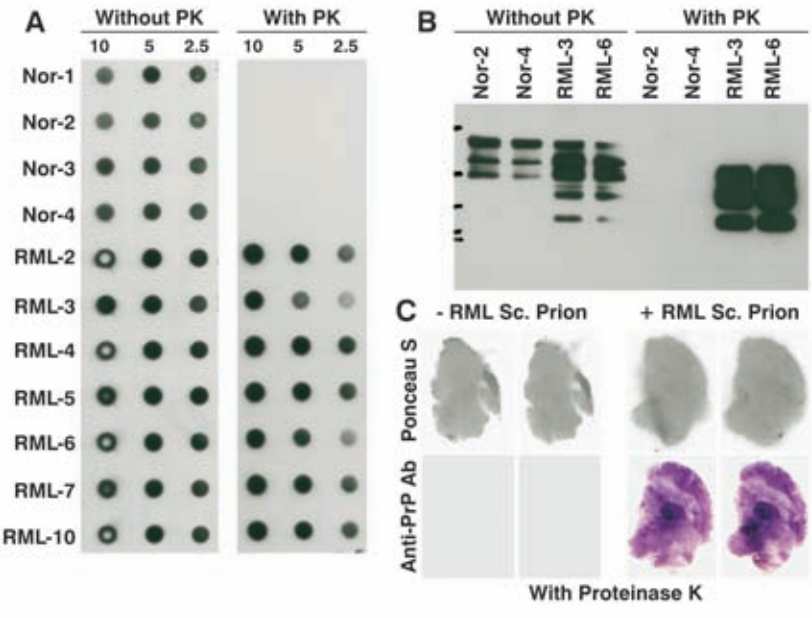
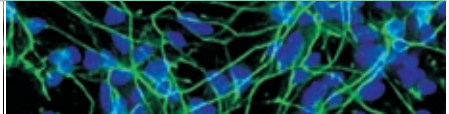


Figure 1.

Detection of proteinase-K resistant Prion protein in RML scrapie infected C57BL/6J mice brain by dot blot (A), western blot (B) and by brain histoblot (C) using an antibody specific for mouse prion protein.



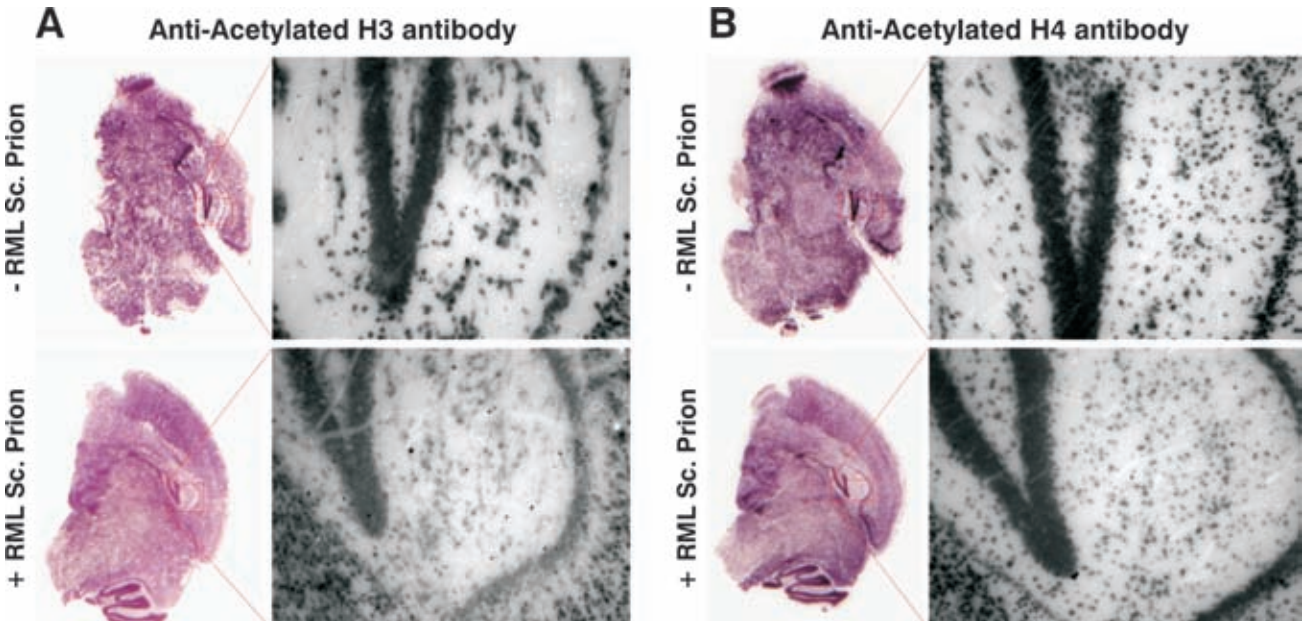


Figure2.

Decreased levels of acetylated histone-3 (A) and acetylated histone-4 (B) in C57BL/6J mice brain by brain histoblot analysis.

10 C57BL6/J mice were injected with RML scrapie mouse prions and allowed to manifest the disease completely. All animals were monitored regularly and pathological symptoms were recorded. Animals during advanced stage show plastic tail, circling and ataxic phenotype, typical to prion disease. Brains from terminally sick animals were harvested and frozen immediately in liquid nitrogen. Brain sections or brain homogenates were obtained. Similar samples were also obtained from age matched control mice. Brain histoblots were obtained from brain sections, dot blots and western blots were obtained from brain lysates and were immuno-blotted with anti-PrP antibody. Our results clearly demonstrated the presence of Proteinase-K resistant PrPSc only in RML scrapie prion infected mice brain but not at all in normal mice brain (Figure 1).

Funding

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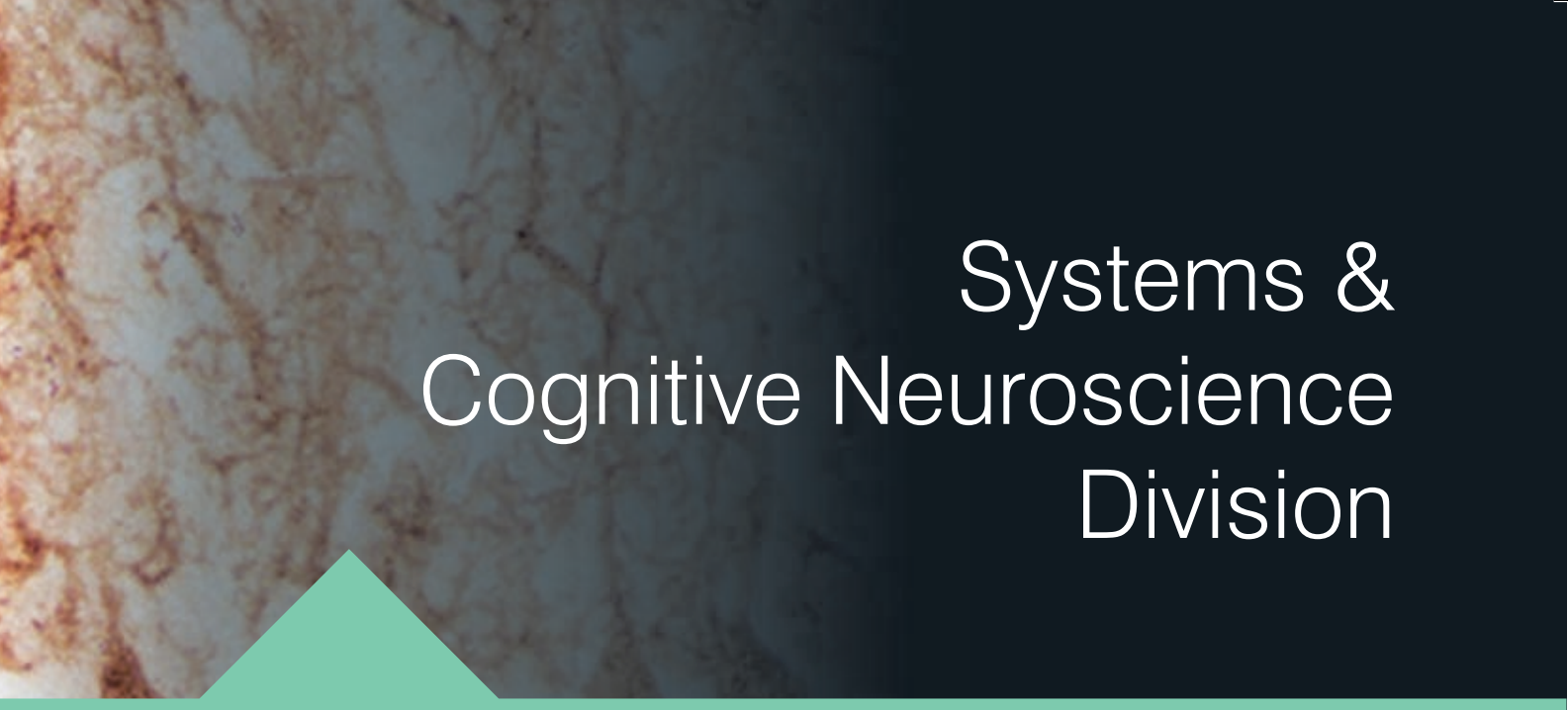

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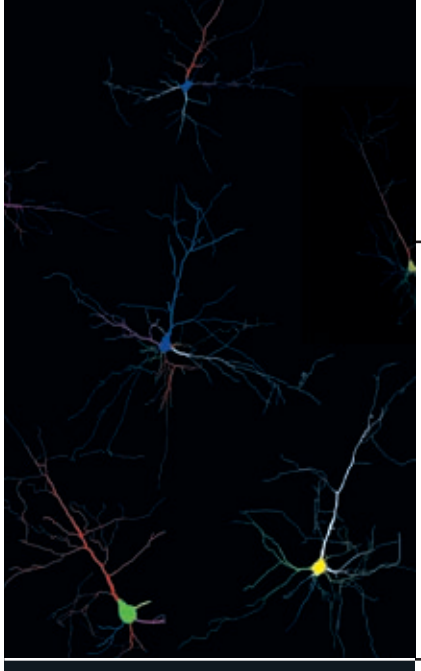

Organization of the Somatosensory and Motor Systems and Effects of Spinal Cord Injuries

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Spinal cord injuries result in large-scale changes in the brain organization. For example, following injuries to the dorsal columns of the spinal cord at cervical levels, the topographically organized sensory inputs in the somatosensory cortex undergo changes such that the face inputs expand and reactivate the deafferented hand region. Research work in our laboratory is focused towards understanding how these injuries affect the organization and information processing in the somatosensory and motor systems. We use a combination of neurophysiological, neuroanatomical and behavioural approaches in our laboratory. To understand the effects of spinal cord injuries on the brain, we perform unilateral lesions of the dorsal columns of the spinal cord, leaving spinothalamic and other ascending and descending pathways intact. The behavioural effects of these lesions are restricted to the inability of the monkeys to form a precision grip. In the previous years we have shown that sensory loss due to lesions of the dorsal columns leads to reorganization not only in the primary somatosensory area 3b, but also in other somatosensory areas such as S2 and PV, and the motor motor area 4. The work done during the year is described below.

fMRI reveals large-scale brain reorganization

Generally in animal models, the brain reorganization is studied using electrophysiological techniques Although these techniques provide data at high resolution, they have

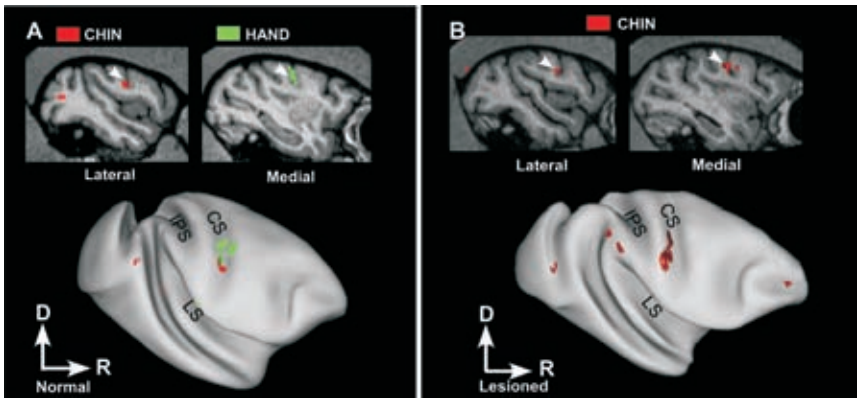
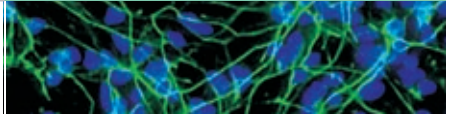


Figure 1.

BOLD response in area 3b of the cortex of a normal monkey and a monkey with chronic lesion of the dorsal columns. (A) The top panels show the BOLD response in a normal monkey following light cutaneous stimulation of the chin (in red on left) and the hand (in green on right). As expected, the chin area is lateral to the hand area. The bottom panel shows locations of these regions on a partially inflated reconstruction of the brain. (B) The top panels show the BOLD response following light cutaneous stimulation of the chin (left) and more vigorous stimulation of the chin (right) in a monkey with long-standing lesion of the spinal cord. Stimulation of the hand did not result in any BOLD response. Instead the vigorous stimulation of the chin resulted in a response in the medial region where hand area is expected. This can be clearly seen in the bottom panel where the BOLD signal is superimposed on the partially inflated brain reconstruction. CS, central sulcus; IPS, intraparietal sulcus; LS, lateral sulcus; D, dorsal; R, rostral.



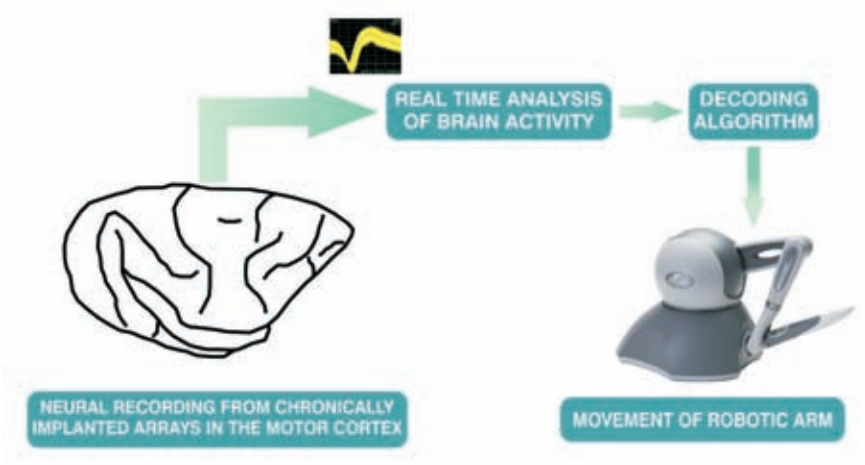


Figure 2.

A schematic showing principal components of the brain-machine interface device. The neuronal signals are recorded from the brain, analysed in real-time using a previously optimized algorithm to decode the information, and the output is used to perform the task such as moving a robotic arm.

the limitation that only small parts of the brains can be sampled at a time. We are establishing the use of functional magnetic resonance imaging (fMRI) to complement other techniques. We used standard clinical 3T scanner magnet to detect changes in the brain organization in anesthetized monkeys. Since under these conditions the signal to noise ratio (SNR) is poor, we used special acquisition sequences. In order to increase the filling factor to improve SNR we used the standard human knee coil instead of the head coils. The skin on the hand or the chin was stimulated using a manually controlled bristle brush. We show that the BOLD signal can reveal normal somatotopic organization in area 3b in anesthetized monkeys using fMRI, with a medial hand representation bordered by a lateral face representation (Fig. 1A). We also performed experiments in monkeys with long-standing unilateral lesions of the dorsal columns of the spinal cord. The goal was to develop technology for using fMRI to determine the extent of the brain reorganization where the signal is extremely weak. Electrophysiological studies have shown that neurons in the reorganized cortex respond only weakly and require stronger stimuli. Our results using fMRI show that stimulation of the chin not only evoked responses in the normal face region in area 3b, but also in the deafferented hand region (Fig. 1B). In monkeys with complete injuries to the dorsal columns of the spinal cord no BOLD response could be evoked in the somatosensory cortex by stimulation of the skin of the hand. Thus the face inputs expand into the hand region after spinal cord injuries as detected by fMRI tools.

Development of Brain-Machine Interface Devices.

Brain reorganization after chronic injuries has implications for developing therapeutic interventions for recoveries from spinal cord injuries. Our efforts have also been concentrated towards developing technology for assistive devices for patients with spinal cord injuries using brain machine interface devices. The goal here it to develop technology for obtaining neuronal signals from the brains of the patients

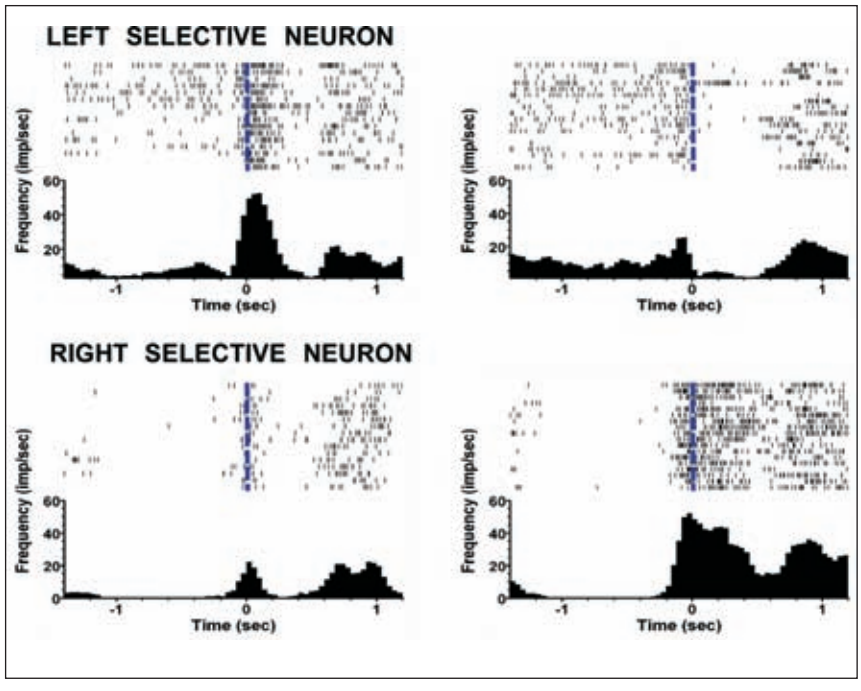


Figure 3.

Action potentials of two neurons in the premotor cortex recorded when the monkey was engaged in a centre-out reach task. The top graph of each panel shows a raster plot and the bottom graph shows the histogram. The vertical dashed blue lines indicate the time of the movement onset to which the rasters are aligned. The top two panels show the firing pattern of a left-selective neuron when the monkey moved its arm to the left (left panel) or to the right (right panel). The bottom panels show firing pattern of a right direction selective neuron. Note that neurons increase their firing rate before and during the movement.

with paralysis, analyze those signals in real-time, and to use this time varying signal content for driving computer controlled devices such as a robotic arm (Fig. 2).

Currently we are using normal monkeys to develop this technology. The monkey was trained on a bidirectional delayed centre-out reach task, in which the monkey had to move his hand from a central position to either in the left or the right direction based on a cue. Subsequently we implanted arrays of microwire electrodes in the premotor cortex, the area of the brain involved in movement planning. We recorded both the spike signals (Fig. 3) and local field potentials (Fig. 4) when the monkey was engaged in the task. The signals were analyzed and an algorithm was developed based on 250 ms of data (sampled at 1 kHz) prior to the start of movement. The feature vector used was the power spectrum summed over specific frequency bands using linear discriminant analysis for pattern recognition. Half the number of trials were used for training the algorithm. It was then tested on the remaining trials. We obtained 90% prediction accuracy for the trials where the monkey reached to the left and 93% accuracy for the trials where the monkey reached to the right. The output was then successfully used to drive movement of the 'Sensible' robotic arm in real-time. Efforts are on to further optimize the system.

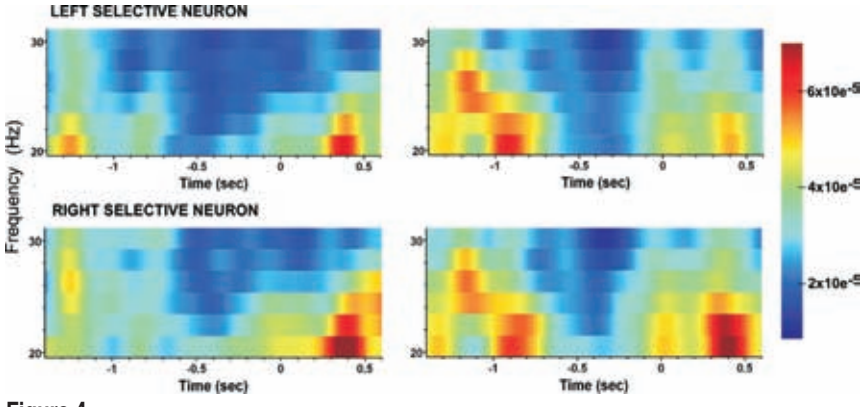


Figure 4.

Power spectrograms of the local field potentials recorded on two electrodes where the neurons showed left selective activity (top) or right selective activity (bottom).

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1. N. Jain and S. Tandon (2011). Plasticity of the somatosensory system following spinal and peripheral injuries. In Expanding Horizons of the Mind Sciences (Eds. Tandon PN, Tripathi RC and Srinivasan N, Eds). Nova Science Pub, NY. pp 93-104.

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i. A. Dutta, N. Kambi, P. Raghunathan, S. Khushu and N. Jain (2011). Functional magnetic resonance imaging (fMRI) of the normal somatosensory cortex in adult macaque monkeys and its reorganization following spinal cord injuries. Neuroscience 2011, Annual Meeting of the Society for Neuroscience, USA. Nov 12-16, Washington, DC, USA.

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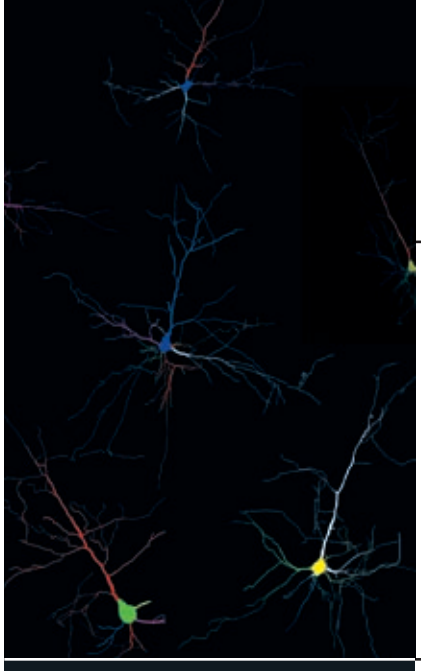

Development of the Human Auditory Cortex

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We had earlier found that axons in all layers of the auditory cortex were immunoreactive for heavy and medium chain neurofilaments by 25 GW and the density of the neurofilament-rich plexus in the cortical wall became adult-like during the first postnatal year in humans (9 postnatal months). Although neurofilament-positive axons are found throughout the developing auditory cortex, their origins (whether cortico-cortical or thalamocortical) are not known. To answer this question, we studied the expression of vesicular glutamate transporter (type 1 isoform, VGLUT1 and type 2 isoform, VGLUT2) in the auditory cortex of postmortem human brains at different ages. Earlier studies have shown that VGLUT1 is expressed in the supragranular and infragranular layers primarily in cortico-cortical synapses whereas VGLUT2 is known to predominate in layers IV and VI of the cortex and acts as a marker for thalamocortical synapses. We found that mRNA for both VGLUT1 and VGLUT2 was present in the presumptive human auditory cortex in the second trimester and during the postnatal period (1 year - adulthood). Further, immunohistochemistry revealed that an anti-VGLUT1 antibody labeled the supragranular and infragranular layers of the developing auditory cortex intensely, whereas Layer IV appeared to be sparsely labeled at 25GW. Additionally, VGLUT2 was present on axon terminals and cells

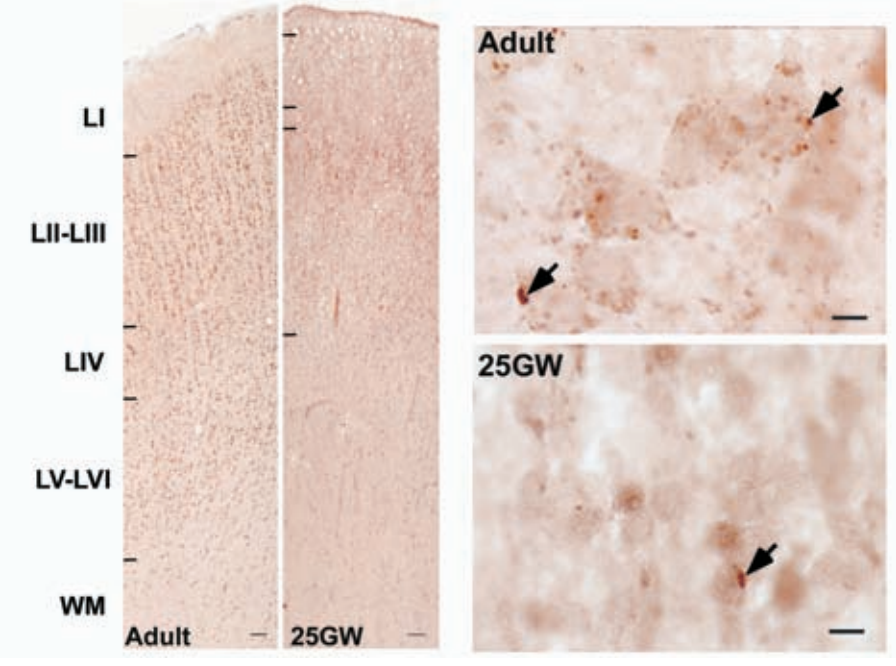
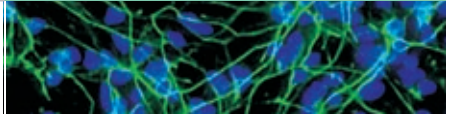


Figure1.

Coronal sections of the human auditory cortex (left panels) demonstrate that Layer IV was highly positive for the vesicular glutamate transporter (type II, VGlut-2) in an adult, whereas faintly staining cells could be seen in LV and LVI at 25GW. High power views demonstrate that stellate cells in Layer IV which receive thalamocortical input from the medial geniculate nucleus of the thalamus were positive for VGlut-2 in adults (arrows). Neurons in LIV of the auditory cortex at 25GW also demonstrate the characteristic punctate staining for VGlut-2 (arrow), although significantly less than in adulthood. Scale bars for low power images = 200μm, scale bars for high power images = 100μm.



in Layer V and Layer VI at 25GW. Very sparse label was also seen in the middle layers of the developing auditory cortex (deeper parts of Layer III, Layer IV and superficial parts of Layer V) beginning at this age (Figure 1). We also found that a small number of Layer V pyramidal neurons were immunopositive for VGLUT2 at 37GW in addition to labeled axon terminals in the middle cortical layers. There was a marked increase in the density of VGLUT2 immunoreactive fibers centered at Layer IV at 9 postnatal months. Our results suggest that VGLUT1-positive synapses within the human auditory cortex (which are present at cortico-cortical connections) are present as early as 25 days. Further, thalamic axons which utilize glutamate may begin to innervate the human auditory cortex as early as 25GW and gradually increase to adult levels by the first postnatal year. These results strengthen our earlier findings showing that auditory input from the medial geniculate nucleus may reach the auditory cortex during the second trimester.

Funding

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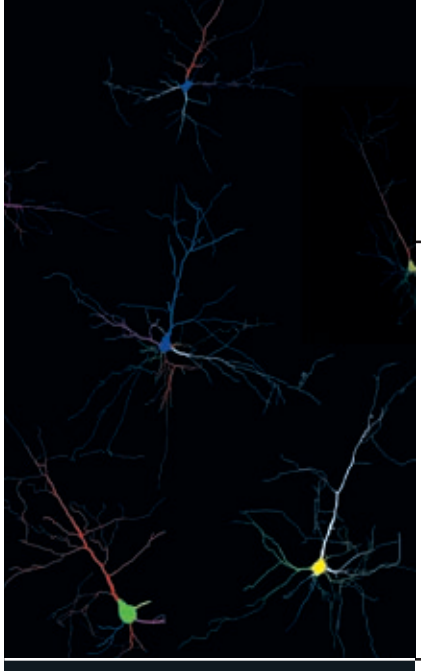

The Role of the Opioid System in Neurogenesis and Behaviour in Adult Zebra Finches

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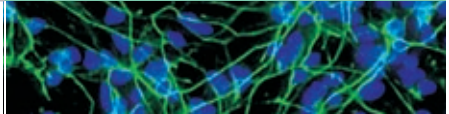
We have been using zebra finches as a model system to study the phenomenon of adult neurogenesis as well as vocalization. Neural circuits important for vocalization (amongst others) are continuously remodeled in the brains of these birds as a result of the turnover of neurons in specific song control pathways. We have found that the opioid system in zebra finches (consisting of endogenous opioids and their receptors) modulates adult neurogenesis in zebra finches. Additionally, the opioid system also modulates different kinds of behavior, including vocalization in adult male zebra finches. We had earlier studied the effects of systemic injections of different doses of naloxone on female-directed and undirected songs, calls and other behaviours in adult male zebra finches. We found that systemic administration of low doses (2.5mg/kg body weight) of naloxone for a period of 4 days led to a decrease in both directed and undirected song, whereas other behaviours were not affected. Interestingly, an even greater decrease in undirected singing was observed following the administration of 10mg/kg body weight of naloxone, although there was no effect of this dose on directed song. We also found changes in spectral features of song (decrease in goodness of pitch, frequency and amplitude modulation) and temporal features of song (increase in the duration of intersyllable intervals, Khurshid et al., 2010a). These results suggested that naloxone administration led to a decrease in the motivation to sing, since μ-ORs were present in the VTA-SNc (ventral tegmental area- subtantia nigra complex) and other areas important for motivation and reward. On the other hand, changes in the quality of song (spectral and temporal features) may have been the result of blocking μ-ORs expressed in song control nuclei such as HVC and RA. In order to determine the site of action of naloxone in the brain which led to the changes in song behaviour, we decided to inject naloxone specifically into different brain regions and then study changes in the behaviour of adult male birds.

We started by injecting naloxone directly into Area X (a nucleus of the avian basal ganglia) in awake singing male birds which contains a high density of μ- opioid receptors. Each bird's songs were recorded prior to the experiment to measure the baseline song. Stereotaxic coordinates from a zebra finch brain atlas as well as electrophysiological recordings were used to implant a cannula unilaterally into Area X in adult male zebra finches. After the birds recovered from surgery and started singing, they were placed in a sound-attenuated recording chamber. A microdialysis probe was inserted into the cannula and a syringe pump was used to infuse different doses of naloxone (50, 100 and 200ng/kg body weight) directly into Area X in one hemisphere while birds were singing to females. Specialized software (SA+, version 1.02) was used to count the number of songs sung (i) with the probe in place within Area X, (ii) after saline infusion and (iii) saline + different doses of naloxone. Preliminary data from three experimental birds showed that there was a small increase in the number of songs with increased doses of naloxone when the cannula was placed in the ventrolateral part of Area X on



one side. In contrast, when the cannula was placed in LMANshell (a song control region rostral to Area X, n = 4), there were no significant changes in the number of directed songs and calls with increasing doses of naloxone. We also found that amongst the spectral features there was a decrease in the mean pitch of songs sung during naloxone infusion just above Area X whereas this feature increased when naloxone was injected directly into Area X. Our results suggest that blocking opioid receptors in Area X during directed song affects the number of songs as well as the quality of song. However, larger sample sizes would be required to confirm whether these changes are significant. Whereas the mechanisms underlying the increase in singing have to be studied in further detail, it is possible that blocking opioid receptors in Area X leads to the release of dopamine from VTA-SNc neurons which are further downstream in this pathway, since the release of dopamine is known to trigger directed song.

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2. P. Haldipur, U. Bharti, S. Govindan, S. Sarkar, **S. Iyengar**, P. Gressens, S. Mani **(2011)**. Expression of sonic hedgehog during cell proliferation in the human cerebellum. **Stem Cells and Development**, 21(7):1059-1068.
3. P. Haldipur, U. Bharti, C. Alberti, C. Sarkar, G. Gulati, **S. Iyengar**, P. Gressens and S. Mani **(2011)**. Preterm Delivery Disrupts the Developmental Program of the Cerebellum. **PloS ONE**; 6(8).

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i. S Iyengar: Song Learning in Birds. Brain and Cognition Workshop (sponsored by DST and IUSSTF), IISc, Bengaluru, July, 2011.

ii. N Ramanathan and S Iyengar: Role of δ-opioid receptors on female directed song and other behaviours in male zebra finches. Poster presented at the 8th Horizons in Molecular Biology International PhD Student Symposium, Göttingen, Germany, September, 2011.

iii. S Sen, L.S Hameed, N. Ramanathan and S. Iyengar (2012) Role of the Endogenous Opioid System in modulating Adult Neurogenesis in Zebra Finches (Taenopygia guttata). Poster presented at the 19th Biennial Meeting of the International Society for Developmental Neuroscience, Mumbai, India. Theme: Neurodevelopment and Neurological diseases, January, 2011.

iv. S Iyengar: BirdSong and Learning. Fifth DST-SERC school in Neuroscience (Learning and Memory), NIMHANS, Bangalore, Manesar, February, 2011.

Funding

i. Effects of altering the level of neuronal proliferation on the learning and production of behavior in male Zebra finches: Basic biology of stem cells grant awarded in 2007. This work is supported by DBT funds.

ii. “Opioid Modulation of song in Male zebra finches” awarded in 2010 (DST). This work is supported by NBRC Core and DST funds.

iii. “Neurobiology and Understanding the Circadian System Linkage of Cognitive Performance in an Avian Model System” awarded in 2010 (DST). This work is supported by NBRC Core and DST funds.

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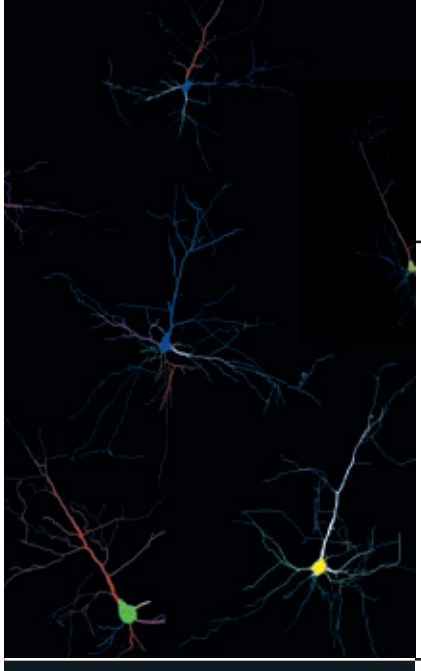

Retinal Circuitry: In Health and In Disease

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Retinal degenerative diseases such as Retinitis Pigmentosa and Age-Related Macular Degeneration have high incidence rates, and are among the leading causes of blindness. These diseases have varied etiology but are characterized by degeneration and loss of photoreceptors. While photoreceptors progressively degenerate, the inner retinal neurons, especially retinal ganglion cells (RGCs), which send visual signals to the brain, are relatively preserved, at least initially. Based primarily on this, several novel therapeutic strategies, such as stem cell transplantation and implantation of a prosthetic device have been designed. A retinal prosthesis is an electronic device designed to transform visual information into a spatiotemporal set of electrical stimuli which are applied to the surviving retinal neurons via an array of microelectrodes. The underlying assumption is that the information about the specific components of the visual scene would be correctly encoded as electrical stimuli which will be transferred to specific retinal neurons, and thus produce artificial vision in blind patients. Similarly, the transplanted stem cells are expected to differentiate into photoreceptors which would functionally integrate with the host neurons. Both of these approaches have shown great promise in recent years, but are yet to produce the desired clinical outcome. We believe that the clinical success of these treatment approaches is linked to our understanding of how the retinal circuitry develops and functions, normally as well as in retinal degeneration. Our lab is interested in addressing these fundamental questions, with emphasis on their relevance to treatment of the retinal degenerative diseases.

We have been studying the role of Müller glial cells in rescue and recovery of photoreceptors in retinal degeneration. Müller cells have been reported to express stem cell-like properties, and they differentiate into retinal neurons following retinal degeneration. In fact, in teleost fish the Müller cells are able to fully

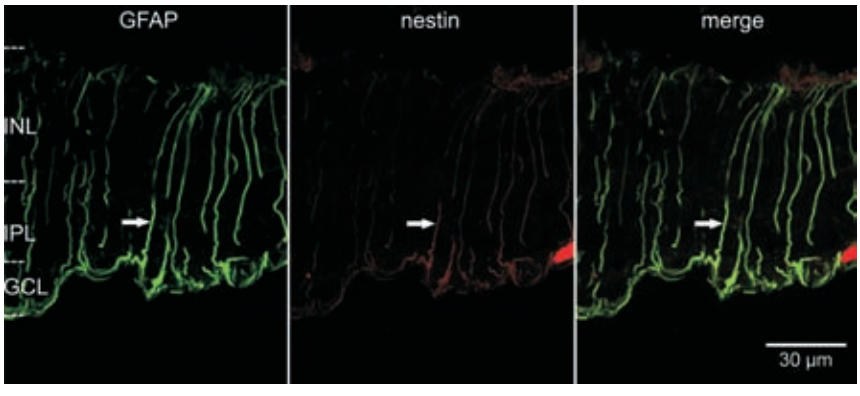
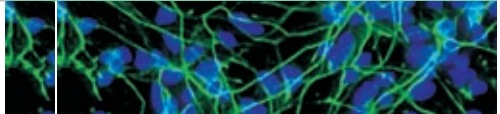


Figure 1.

Mueller glial cells in adult rd1 mouse express a progenitor cell marker, nestin. A representative image of adult rd1 mouse retina, double-immunolabeled for GFAP (green) and nestin (red). Mueller cell processes hypertrophy and overexpress GFAP (left panel). A vast majority of them also express a progenitor cell marker, nestin (middle panel) for up to six months of age, suggesting that Mueller cells remain undifferentiated in rd1 mouse for several months. Arrow points to one such process.



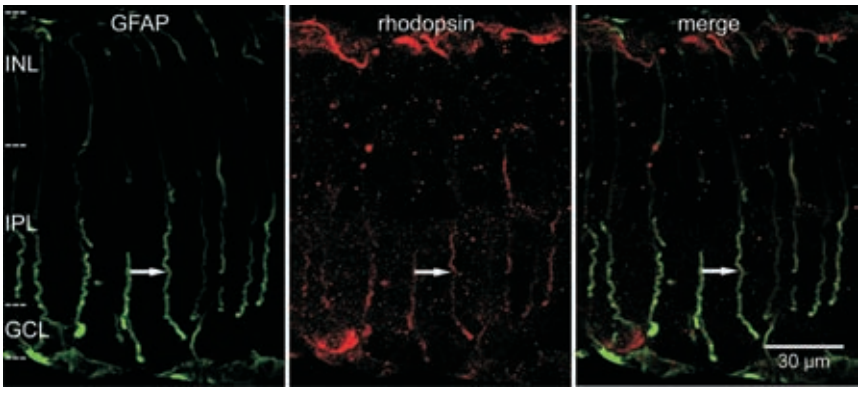


Figure 2.

Mueller glial cells in adult rd1 mouse express a mature rod photoreceptor marker, rhodopsin. A representative image of adult rd1 mouse retina, double-immunolabeled for GFAP (green) and rhodopsin (red). Many of the radial processes of Mueller cells, identified by their expression of GFAP (left panel), expressed a mature rod marker, rhodopsin in rd1 mouse (middle panel). Arrow points to one such process. Interestingly, Mueller cells did not express several non-rod retinal markers, such as PKCα, recoverin and β-III-tubulin (not shown), suggesting that these cells tend to differentiate selectively into rod photoreceptors in rd1 mouse.

regenerate the retina. However, the neurogenic capacity of these cells is limited in mammals and other vertebrates. We have found that Müller cells continue to remain undifferentiated (express a stem cell marker, nestin) in rd1 mouse retina (Fig. 1).

Furthermore, we found that starting at third postnatal week, Müller cells express rhodopsin, a mature rod photoreceptor marker, which continued up to at least one year of age in rd1 mouse (Fig. 2).

Interestingly, Müller cells did not express several other non-rod neuronal markers of retina, such as PKCα, β-III-tubulin or recoverin. Together, these results suggest that Müller cells show a propensity to differentiate selectively into retinal neurons (rods) that are the primary targets of the PDE6β mutation in rd1 mouse. Although the functional significance of rhodopsin expression by Müller cells is not completely clear, these results have implications for novel therapeutic strategies for retinal degeneration.

In another project, we have been studying retinal remodeling that ensues after photoreceptor degeneration. We have continued to investigate the mechanisms underlying rhythmic spike bursts that are observed in retinal ganglion cells after photoreceptor loss (Fig. 3).

We believe that these investigations would not only help finding more sophisticated ways to artificially stimulate the ganglion cells using retinal prostheses, but will also provide insights about how normal inner retinal circuitry functions. We are testing the hypothesis that aberrant firing in the ganglion cells originates in the impaired synaptic interaction between bipolar cell and amacrine cell inputs to the ganglion cells. We are testing this by using several experimental approaches, such as quantiative immunohistochemistry, Western blotting, recording excitatory and inhibitory postsynaptic potentials in ganglion cells, pharmacological intervention of the excitatory and inhibitory neurotransmission in inner retina, and by studying how these spike bursts progress during development.

We showed previously that a vast majority of M1 type of intrinsically-photosensitive retinal ganglion cells (ipRGCs) do not express a transcription factor, Brn3b, whereas all non-M1 type of ipRGCs express this factor (Jain et al., 2012). Considering that M1 cells have been reported to mediate non-image-forming vision whereas non-M1 cells

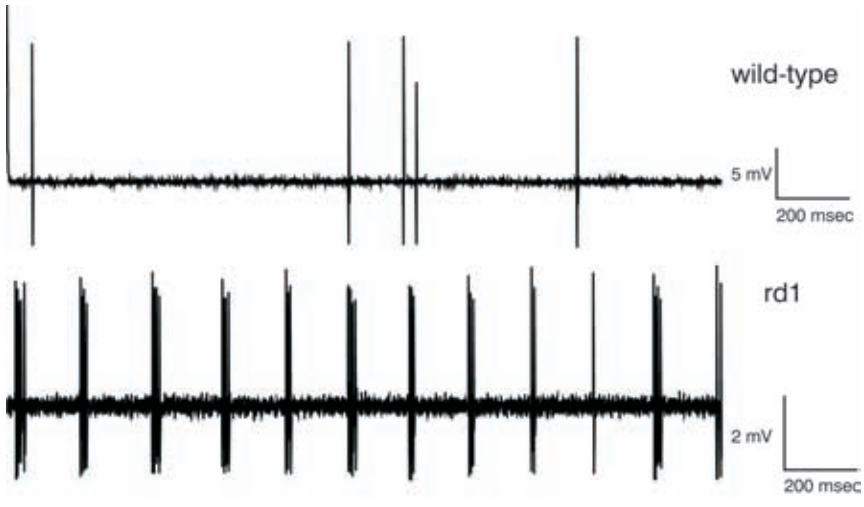


Figure 3.

Mueller glial cells in adult rd1 mouse express a mature rod photoreceptor marker, rhodopsin. A representative image of adult rd1 mouse retina, double-immunolabeled for GFAP (green) and rhodopsin (red). Many of the radial processes of Mueller cells, identified by their expression of GFAP (left panel), expressed a mature rod marker, rhodopsin in rd1 mouse (middle panel). Arrow points to one such process. Interestingly, Mueller cells did not express several non-rod retinal markers, such as PKCα, recoverin and β-III-tubulin (not shown), suggesting that these cells tend to differentiate selectively into rod photoreceptors in rd1 mouse.

additionally mediate image-forming vision, our results implied that Brn3b is expressed exclusively by RGCs that mediate image-forming vision. We have now found that in the absence of photoreceptors in rd1 mouse, even M1 cells start to express Brn3b (Dhingra et al., ARVO poster, 2011). This has led us to perform a series of experiments to understand the interplay between classical photoreceptors and ipRGCs in mediating non-image-forming visual functions, such as pupillary reflex (PLR) and circadian rhythm under different light conditions. For example, we are testing the hypothesis that classical photoreceptors play a critical role in PLR at all physiologically-relevant light intensities. The current view is that while classical photoreceptors mediate PLR at low light intensities, ipRGCs take over this function at high intensities. We are testing our hypothesis by studying expression patterns of Brn3 transcription factors in ipRGCs and by studying PLR, in two (a genetic and an inducible) mouse models of retinal degeneration.

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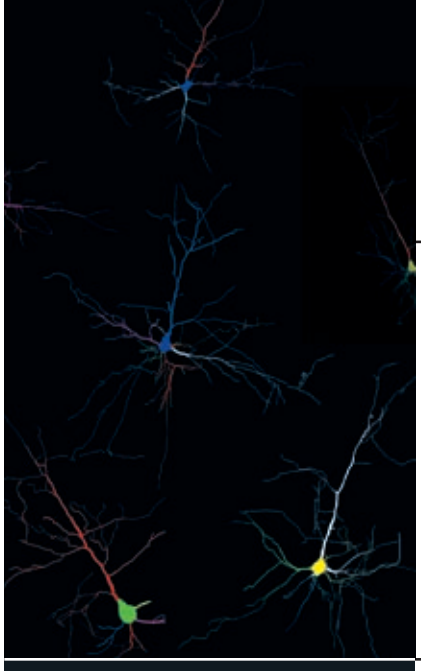
Presentations

i. N.K. Dhingra, V. Jain and R. Guruswamy: M1 type of intrinsically-photosensitive retinal ganglion cells express Brn3 transcription factors in rd1 mouse. ARVO, Fort Lauderdale (USA). May, 2011 (poster).

Funding

This work is supported by Department of Biotechnology, Govt of India, and National Brain Research Centre.



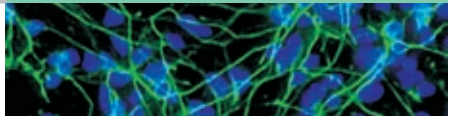
Neural Network Mechanisms Underlying Spatial Learning and Navigation

Principal Investigator
Yoganarasimha Doreswamy

Research Fellows
Apoorv Sharma
Guncha Bhasin
Chetan Yadav

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, which enables us to know where we are and helps in reaching a place we intend to go. Through in vivo neurophysiological studies in rodents, we hope to understand the neural mechanisms underlying spatial memory and navigation, which will eventually lead to better understanding of the memory deficits observed during aging, brain injury and neurodegenerative diseases. The hippocampus plays a major role in learning and memory, especially in episodic-memory, context-dependent learning, learning of spatiotemporal sequences. Spatially active place cells of the hippocampus selectively fires at specific location in an environment, suggesting formation of a "cognitive map" of the surrounding environment. By interaction with head direction system, they play a very critical role in spatial memory and navigation, thus forming an outstanding model system for studying the neural network mechanisms by which the brain constructs the cognitive representations from multimodal inputs. Head direction cells (present in anterodorsal & laterodorsal thalamic nuclei, lateral mamillary nucleus, postsubiculum and retrosplenial cortex) 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. Like place cells, the head direction cells are also controlled by a complex interaction between idiothetic cues and external landmarks. Coupling between head direction cells and place cells has been reported, where the preferred firing locations or directions of place cells and head direction cells remain strongly coupled to each other even when they become completely uncoupled from external landmarks. Further, the head direction system is suggested to govern the orientation of the hippocampal spatial representation relative to the external environment. Thus, the specific role of hippocampus in spatial memory can be delineated by studying the functional properties of its input areas, which will reveal the nature of information processing at these inter-related brain areas.

Two major parallel input streams, from the lateral and medial entorhinal cortex, convey non-spatial and spatial information to the hippocampus. The lateral entorhinal cortex receives major input from the perirhinal cortex, which is connected with unimodal sensory areas and appears to be involved in the processing of configurations of objects. The medial entorhinal cortex receives major input from the dorsal presubiculum and retrosplenial cortex, which contain directionally and spatially tuned neurons, and from postrhinal cortex, which is connected with visuospatial regions of the neocortex and has been linked to contextual processing. Based on anatomical connectivity, subicular complex has been considered as both an afferent and efferent area of the hippocampus. Subicular complex receives projections from the hippocampus; but also connects to superficial layers of the entorhinal cortex, which are the input layers to different subfields of the hippocampus. Subicular complex, consisting of subiculum proper, presubiculum, postsubiculum and parasubiculum, receives sensory inputs from different cortical areas and connects to the hippocampus and entorhinal cortex, two major brain areas involved in processing



of spatial information. Subicular complex neurons show directional and locational correlates and theta modulated place by direction cells have been reported in postsubiculum, which may act as internal units allowing updating of position from one location to another based on the current directional heading. The subicular neurons also encode head angular velocity and running speed, two properties that are necessary to allow self-motion information to update representation of head direction and location. Further, anterodorsal thalamic nuclei, containing head direction cells which encode the current heading direction, reciprocally connects to postsubiculum area. Considering the anatomical connections with other brain regions involved in spatial and directional information processing, it is essential to understand the functional properties of subicular complex as the subiculum may act as an interface between these brain areas in the integration of spatial and directional information. Our lab is interested in characterising the network properties and the exact role played by different sub-regions of the subicular complex in learning and memory processes.

We have installed and standardised 96-channel high density electrophysiology system in our laboratory to study information processing in rodent brain in vivo, which allows simultaneous recording of neuronal spiking activity as well as local field potentials at various brain areas in awake freely behaving animals, through multitetrode recording technique. Figure 1 shows the picture of a custom-made microdrive constructed in the laboratory, containing 2 reference electrodes and 18 independently movable tetrodes to target specific brain areas/layers for neurphysiological recordings. Figure 2 shows the set-up in behavioural recording room, where the rats are trained to run clockwise on an elevated circular track having four different textures, placed in the centre of the room surrounded by a black circular curtain running from ceiling to the floor. Various salient distal landmarks are either hanged or placed on the floor at the periphery of the curtain. Presently, neurophysiological studies are in progress to understand the functional properties of subicular complex neurons during spatial navigation.

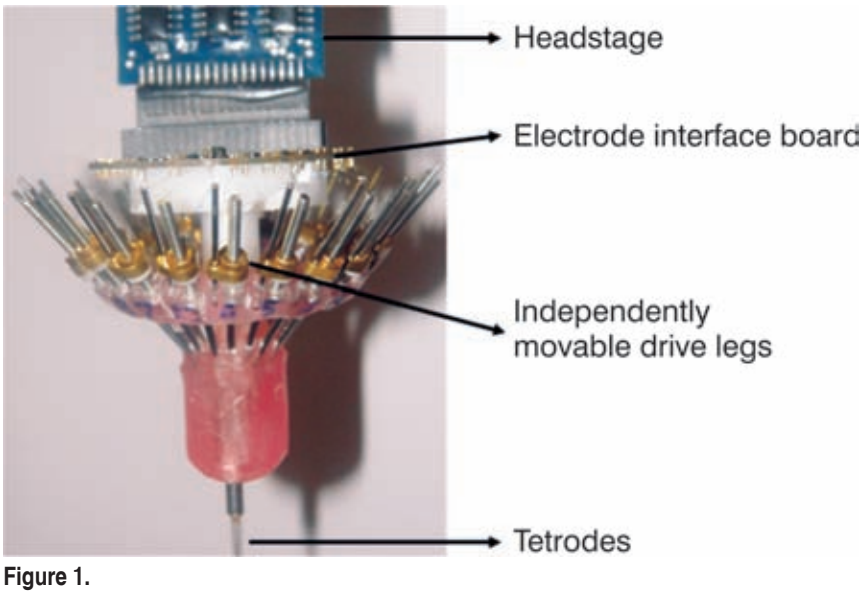


Figure 1.

Figure 2.

Presentation

i. D. Yoganarasimha: Invited lecture on “Spatial Memory and Navigation” at International Brain and Cognition Workshop (5 July to 14 July 2011), Centre for Neuroscience, Indian Institute of Science, Bangalore, India.

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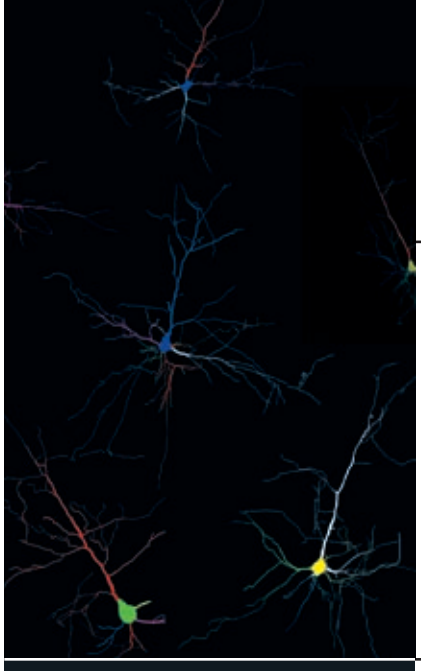
National Brain Research Centre
NBRC



On the road to being a biliterate: Reading networks in Hindi - English children

Principal Investigator
Nandini Chatterjee Singh

Research Fellow
Sarika Cherodath

Background

While much is known on how the developing brain learns to read a single orthography, precious little is known about the development of cortical networks in children learning to read two distinct orthographies simultaneously. We used functional neuroimaging (fMRI) to uncover cortical pathways for reading in children learning to read Hindi, written in Devanagari and English, written in the Roman script. Hindi, a transparent orthography like Italian relies primarily on letter-to-sound assembly, whereas English, an opaque orthography depends largely on lexically mediated processing.

Cortical activations were imaged while 18 right-handed children in the age range 8-10 years read words and nonwords in English and Hindi. Participants read 60 words and 60 nonwords alternating with rest, during which the subjects fixated on a string of symbols. A total of 240 volumes were acquired for each language task and the analysis was performed using SPM5 with a MATLAB interface. Behavioural assessment included of phonological awareness and naming fluency skills in both languages. Vocal reaction times for word and nonword reading for the tasks in the scanner were assessed using a MRI-compatible microphone.

The behavioural performance of the participants in the phonological awareness tasks in both languages showed no significant differences. In fact, the phonological awareness scores in both languages showed a strong correlation. Our neuroimaging results revealed a strongly bilateral cortical reading network comprising occipital cortices, precentral and postcentral areas and cerebellum that is shared across the two languages, with Hindi being more spatially extensive and bilateral than English (Fig. 1)

An interesting and surprising finding was the robust recruitment of the left hippocampus while reading both words and nonwords. Recent theories of reading development suggest that it plays an important role in decoding process in children during word reading, until they become skilled readers.

Phonological awareness, which is the ability to manipulate sounds and which is believed to be a

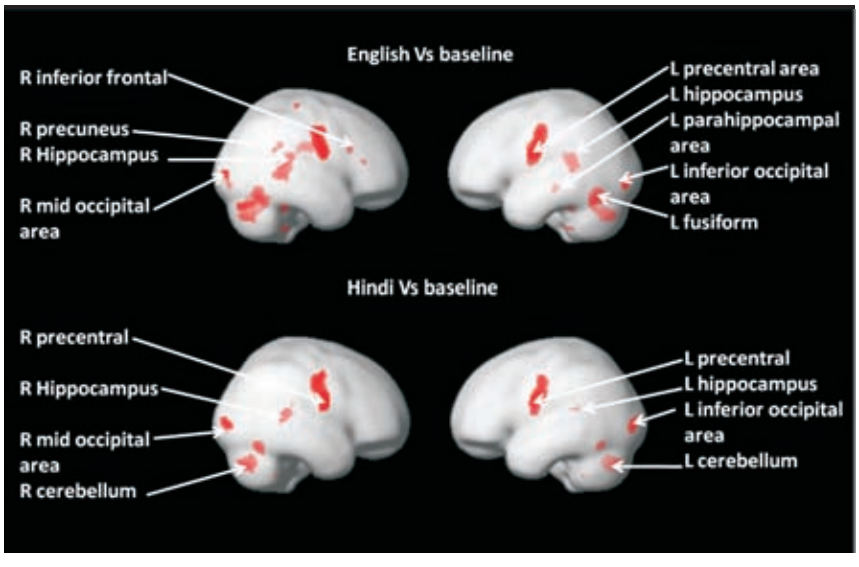
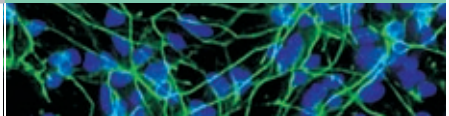


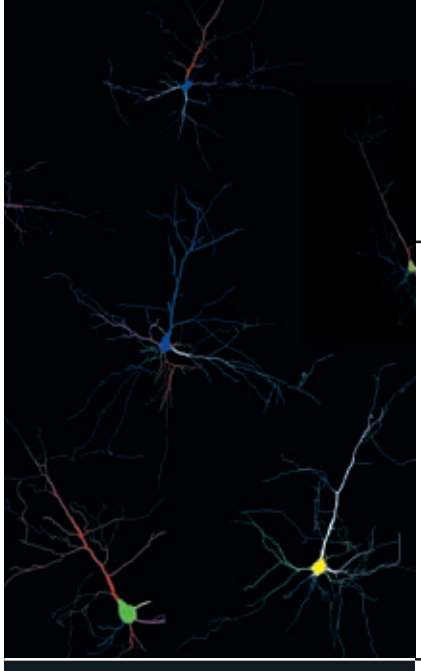
Figure 2.
Neural circuits for reading words in English and Hindi for children between 8-10 years



strong predictor of reading skills showed correlations with non-overlapping regions for the two languages. In English, the highest correlation was observed in the right mid temporal area, known to be involved in phonological decoding and articulation in bilinguals with English as their L2. Hindi showed correlations in the right precuneus, which has been reported in reading visually complex, syllabic scripts like Japanese and Korean.

Conclusions

Expertise in reading Hindi seems to be dependent on visuo-spatial processing skills as opposed to English, which demands greater knowledge of sound-letter mapping rules and articulatory effort. Our results suggest for the first time that reading skills across different languages might rely on different processes and has important implications for dyslexia in biscriptals.



Neural Correlates of a New Vernacular: Reading Romanagari

Principal Investigator
Nandini Chatterjee Singh

Post Doctoral Fellow
Chaitra Rao

Research Fellow
Avantika Mathur

Background

The phenomenal proliferation of internet access and mobile telephony, combined with inaccessibility of native language software has led non-English language users to represent the local language in Roman (English script). This practice has fostered the use of vernacular writing systems such as Romanagari (portmanteau of Roman and the Hindi script Devanagari), Romaji (Japanese Kanji), Aralish (Arabic) and Greeklish (Greek). Although scant research exists on these vernaculars, evidence suggests that with increasing exposure, readers begin treating Romanized words similarly to real words. However, decoding Romanized words for meaning appears to require greater cognitive effort. Our study marks the first attempt to assess the underlying neurobiological correlates of processing a native language transcribed in a non-native script, by comparing functional magnetic resonance imaging (fMRI) activation patterns for word recognition in native (Hindi) and non-native languages (English) with a Romanized variant of the native language. The choice of Romanagari—Hindi written in Roman script is propitious in view of the steadily growing population of internet and mobile phone users in India. Newspapers currently estimate the number of Romanagari users at over 500 million.

Cortical activations were recorded when fourteen Hindi-English bilinguals (mean age = 20yrs), all regular users of mobile phone short message service (SMS) judged if presented stimuli were concrete nouns in three language conditions, Romanagari (Hindi words, Roman script: 'shor' meaning NOISE), Devanagari (Hindi words and script:) and English (shore). All stimuli were Hindi/English homophones.

Behavioural responses [Fig.2 (A)] revealed that participants' mean reaction time (RT) and percentage accuracy differed significantly (both $p<.001$) across the three language conditions. Paired comparisons showed participants to be more accurate and faster in Devanagari compared to both English and Romanagari.

The fMRI data corroborated the cognitive load-based explanation, revealing multiple additional clusters of activation unique to Romanagari, as well as more spatially extended activation in common regions (Fig. 2(B). Thus, Devanagari, Romanagari and English stimuli commonly

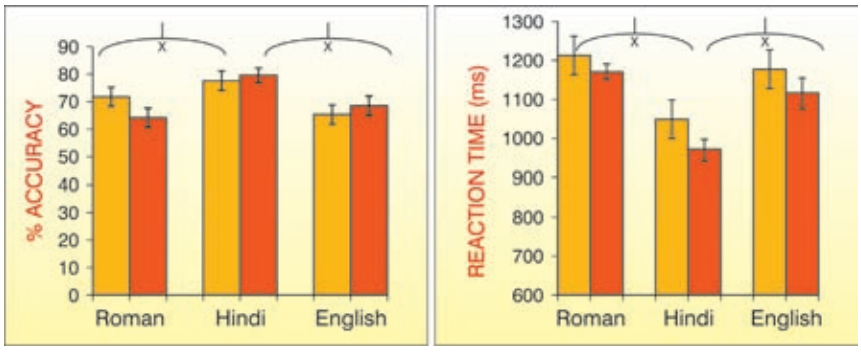
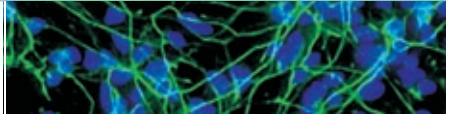


Figure 2 a.

Behavioural response latency and accuracy, and corresponding fMRI activation patterns of participants. Left panel - % accuracy, Right panel - reaction time to concrete (orange) and non-concrete items (yellow)



activated regions previously identified in word recognition studies – bilateral occipital areas, left inferior frontal gyrus, left superior temporal pole, right insula and cerebellum. In addition, a common network of attention-related areas also emerged, including bilateral inferior frontal and left inferior parietal regions, as well as mid-cingulum.

We propose that the greater time and effort required for judging concreteness in Romanagari reflects the higher cognitive load of accessing Hindi through Roman script. On this view, incomplete semantic access in Romanagari leads to erroneous rejection of concrete items. In conclusion, the present data constitute strong support for the thesis that processing vernacular writing systems like Romanagari imposes an additional attentional demand on the cognitive system, whose signature is evident not only behaviourally but also at the neural level.

We speculate here that the continued popularity of Romanized vernaculars like Romanagari derive their appeal from their ability to bridge sociocultural divides – for example, between native and non-native users of a language or between first and second generation immigrants, as well as to their ease of encoding (as opposed to decoding). Future longitudinal research tracing the evolution of behavioural as well as neural processing of Romanized vernaculars can yield fresh insights on the development of brain language processing networks.

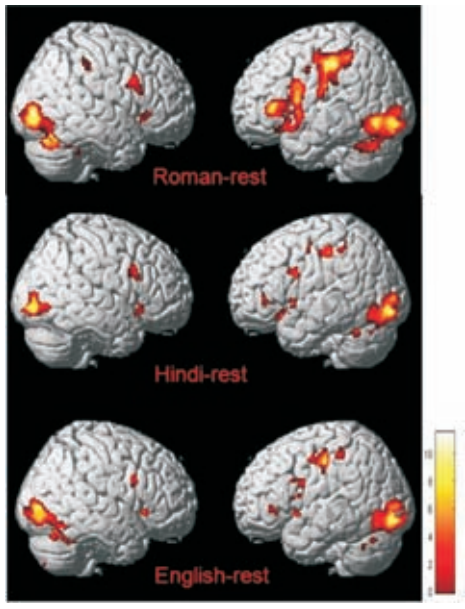


Figure 2 b.

preferential activation for task over baseline (rest) in Romanagari (Roman), Devanagari (Hindi) and English at FDR corrected /p/<.001

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Presentations

i. N.C. Singh – On the read to being a biliterate – cortical reading networks in children learning two scrips, British Dyslexia Association, Harrogate, UK, June 2011

ii. N.C. Singh - Word processing in a non-linear alphasyllabary – the reading network for Devanagari, Invited talk at the symposium entitled Language, Literacy and Cognitive Development: current issues for a science of education' 15-17the December 2011, Bangalore, India.

iii. N.C. Singh - "Brain and Behaviour: How do they correlate during reading scripts", Invited talk at 'Chaperons', the Annual Festival of Ambedkar Centre for Biomedical research, Delhi University, Delhi, 19th March 2012.

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Collaborator

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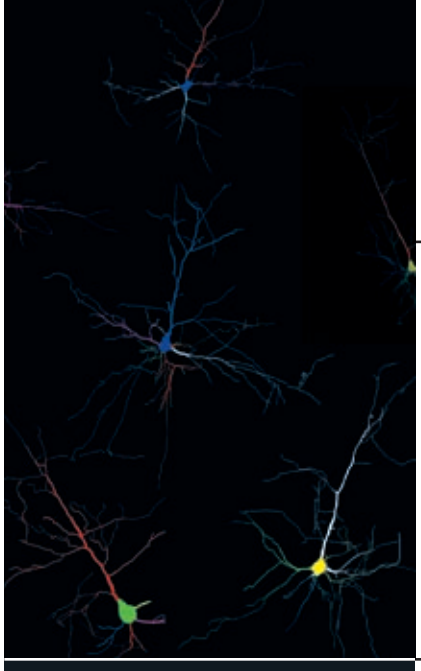


Spatiotemporal Processing and Information Transmission in Brain

Principal Investigator
Prasun Kumar Roy

Research Fellow
Subhadip Paul
Rekha Varrier

Project Assistant
Rajiv Ramaswamy

A decisive challenge in brain research and neuroscience is to decipher how flow occurs, whether that of information, electrical current, drugs, cells or tissue displacement, across the layered brain extent. One needs a quantitative matrix (i.e., tensor) approach that can account for, and furnish a principled description of flow processes and its neuromodulation across brain. We have developed the methodology of dynamic functional tensor neuroimaging and obtained accurate measurement of matrix-tensor maps to describe flow and deformation processes, information flux or connectivity in the brain. The research has considerable potentiality of applications to clinical

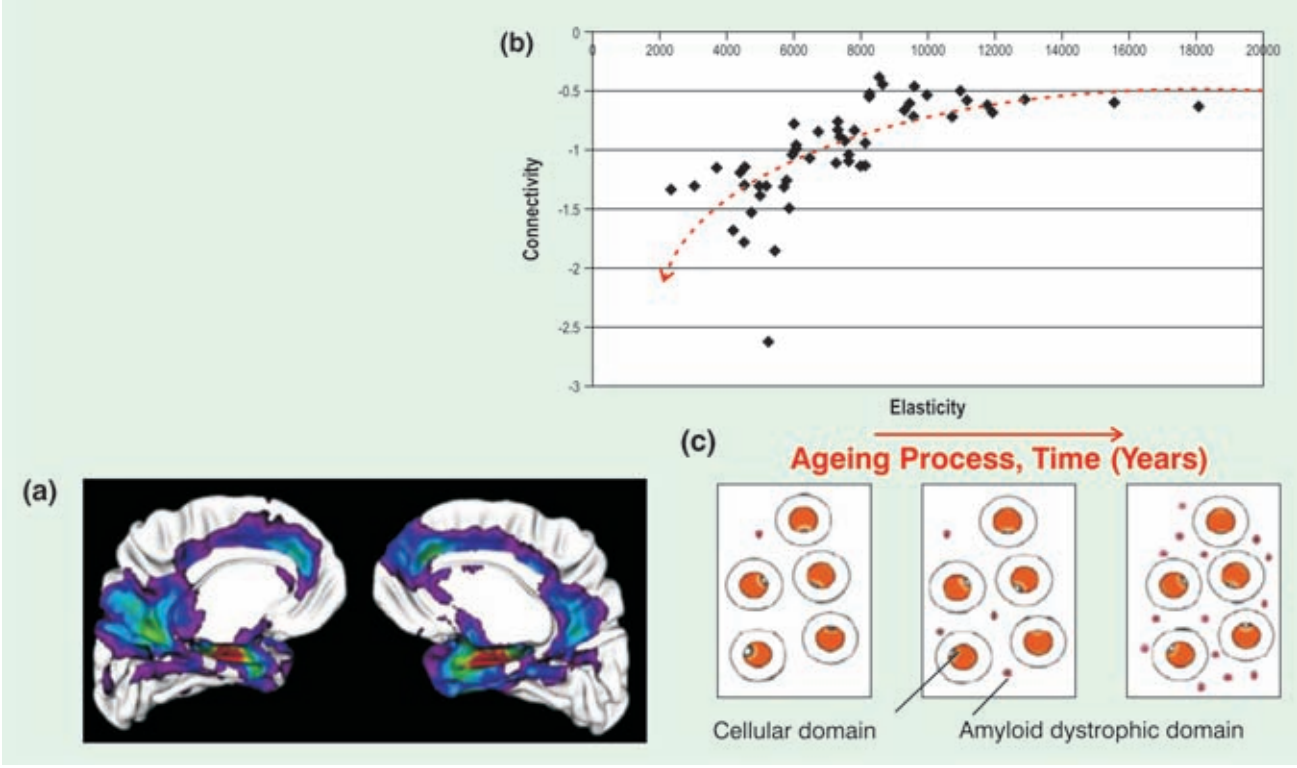
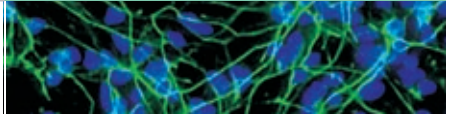


Figure 1. **(a)** Brain tissue displacement as estimated from structural MRI scanning. **(b)** Using MRI Elastometry to find elasticity modulus (in pascals) and connectivity index (log value) from the scan of the individual, the two parameters are respectively plotted along the x-axis. The data of 50 subjects are shown. Note hyperbolic activation pattern of curve, on which is superimposed an increasing stochastic term to account for the increased Brownian dispersion as time elapses (arrow direction). **(c)** The hyperbolic activation pattern can be accounted for using a saturation model of process kinetics, whereby interdomain connectivity saturates as elastic consolidation increases.



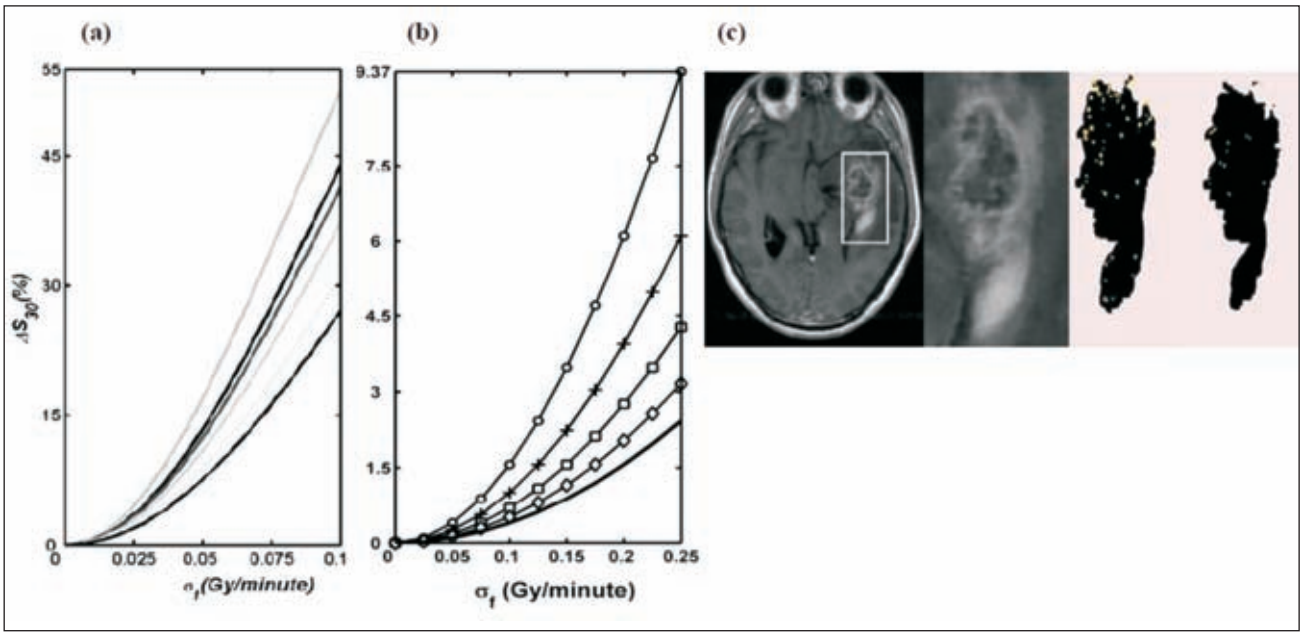


Figure 2.

(a) Enhanced effect of radiotherapy on tumour by increasing the temporal fluctuation level in radiation flux, without increasing the radiation dose administered. The x-axis denotes the fluctuation level in Gray/minute (kilorad/minute), the y-axis is the relative decrease in survival fraction of malignant cells due to stochastic radiation. Fractionated radiotherapy used for 30 days with total dose = 2 Grays. The different curves (top to bottom) denote behaviour of different kinds of tumour tissue: slow and fast growing types of neuroblastoma, adenocarcinoma or infiltratring epithelioma. At 0.1 Gy/min. fluctuation, the enhanced performance of stochastic radiotherapy is 30-55% as per tissue type.

(b) Protection of normal tissue by using conformal multidirectional beamlets, collinear only on tumour tissue, but not on normal tissue. At fluctuation level of 0.1 Gy/minute (x-axis), the relative decrease of survival fraction of normal tissue (y-axis) is negligible, at 0.5-1.5%. The different curves (from top to bottom) are for increasing the number of beamlets, from 4 to 8.

(c) Developing MRI template for stochastic radiotherapy planning of glioma tumour, for optimizing clinical performance of the 30-day treatment protocol. The 4 panels respectively show: Gadolinium ontrast-enhanced MRI scan of tumour; Region-of-interest of the tumour; Response under typical steady-beam radiotherapy; Response under stochastic radio-therapy. Each yellow marker in the last 2 panels denotes thresholds of 100 malignant cells thresholded. Note the prominent enhancement of therapy performance under the stochastic protocol.

medicine as well as to biological engineering, especially for diagnosis, therapy and neurophysiological investigations.

MRI based Elastometry: Reactive Stress/Strain Alteration and Elastic Modulation of Tissue:

There is a critical need of non-invasive determination of the biophysical character of the brain, as elasticity, plasticity and topological connectivity, which can be of considerable help in (i) diagnostic perspective, as delineating the oxidative consolidation stress in tissue under the biological process of neuromechanical alteration, like cortical dysplasia or hippocampal sclerosis as in epilepsy, (ii) therapeutic perspective, as for planning neurosurgical intervention using the data of tissue elasticity or shear. However, the standard methodology of MR-based stress-strain measurements and elastic determination is not readily usable as one needs to administer efficient ultrasonic deformation to the brain tissue through a piezoelectric transducer through the two impervious bony diploic tables of the human skull (thus producing signal weakening), and one needs intricate mechanostriction-based radiofrequency signal-acquisition and processing schemes for the scanner. Thus an alternative MRI approach is readily needed. We have earlier developed the methodology of using the MRI image texture and transport process as tissue displacement/distortion (Figure 1a), and have also obtained biophysical mobility parameters as conductivity and perfusivity.

We have now generalized the method further, to obtain other biophysical mobility parameters as tensile elasticity and contexural connectivity. We have found out these parameters using MRI images of 50 subjects (Figure 1b). The points can be described by a stochastic hyperbolic activation model of process kinetics (Figure 1c), whereby (i) as porous inclusion increases (elasticity decreases), the contexural connectivity diminishes due to consolidation effect, (ii) the superimposed stochastic component is due to increasing fluctuation variance that can be accommodated by the increased porosity space (i.e. decreasing elasticity modulus).

As porosity gradually rises, the connectivity remains constant upto a threshold level following physiological resilience, the elasticity ranges of the brain parenchyma is found by this method to be 8.5 - 12.5 kilopascals. These values are well validated by direct mechanical measurement of elasticity of brain tissue, which is found to be between 8.2 – 12.7 kilopascals. This methodology of MRI elastometry has been communicated for patenting.

MRI-based treatment planning methodology for optimizing radiotherapy performance

Neuroimaging is having a seminal transformation from being merely a diagnostic or anatomy-based modality, and maturing as a therapeutic approach, as neuroimaging - methodologies are being used for maximizing treatment outcome and for enhancing therapeutic efficacy, MRI-based therapy planning and optimization. In clinical situation, there happen to be various competing radiation treatment plans and radio-therapeutic schedules, the most efficacious one is selected by minimizing the tumor control survival fraction formulation. However, the effective utilization of radiotherapy is restricted by the radiation tolerance limit of normal tissues. The total radiation dose often cannot be escalated beyond a prescribed limit; otherwise there are toxicity in normal tissues, which often restrict dose-increase trials, which otherwise could have been eliminated the tumour.

We have developed an analytical framework to study the enhancement of tumour cell elimination, by increasing the stochastic fluctuation in radiation dose-rate, without increasing the dose of radiotherapy. We find that this enhancement can be effected by increasing the fluctuation level, without the need to increase the dose (Figure 2a). Importantly, we show that, the increase in the fluctuation level does not appreciably enhance normal tissue elimination, provided the number of sub-fractions in the multiple-beam radiotherapy is chosen suitably (Figure. 2b). We have developed a patient-specific MRI-based radiotherapy planning methodology for glioma tumours (Figure 2c), which can be used to optimize the performance of the stochastic radiotherapy, so that the tumour survival minimizes.

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ii. P. Roy and S. Pal. Higher-order Electrical Conductivity Tensor Imaging: Implications for clear localization of Epileptogenic source, Utrecht University Medical Centre, Utrecht, Aug. 2011.

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Funding

Ministry of Information Technology, Govt. of India.

Collaborators

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Dr Alan Evans, Montreal Neurological Institute, McGill University
Dr. Manjari Tripathi and **Dr P Sarat Chandra,** All-India Institute of Medical Sciences, Delhi

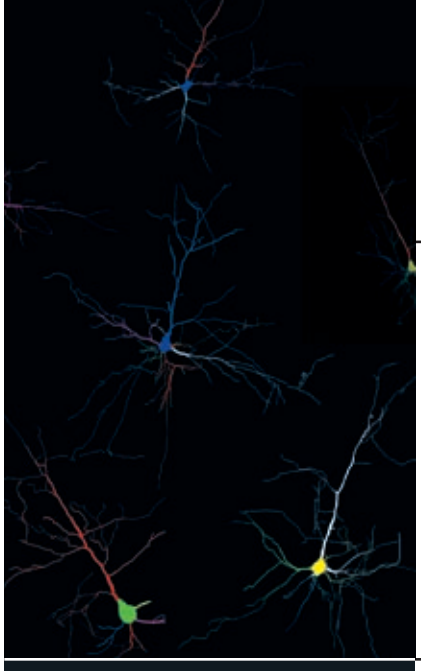
Awards

i. P. Roy. Elected as Fellow of Indian National Academy of Engineering, New Delhi, Sept. 2011.

ii. P. Roy. Visiting Professorship, Division of Radiology, Radiotherapy and Nuclear Medicine, Utrecht University Medical Centre, Utrecht, The Netherlands, June-August, 2011.

M. Tech. thesis

Sharma, H., for the thesis on “Network analysis of brain activations during visuospatial perception task” (University of Rajasthan, Jaipur).



Application of Stochastic Activation and Stability Analysis for Brain Imaging and Therapy

Principal Investigator
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Research Fellow
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VPS Rallabandi

An enduring pursuit in applied neuroscience is the enhancement of the efficiency of clinical output, such as that of neuroimaging processes, whether diagnostic or therapeutic. A tactical perspective is offered by the process of perturbation-induced activation, an emerging research field in computational neuroscience and biomedical engineering. This procedure 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 application of the principle of stochastic facilitation or diffusive activation as a novel technique for electrical or chemical signal enhancement, whether in diagnostic or therapeutic neuroimaging, has not been systematically investigated. Exploring the feasibility of such applications towards clinical medicine is the aim of our program.

MRI-based mobility estimation of endogenous stem cell for optimizing regenerative therapy in cerebral stroke

The study of spatiotemporal mobility of endogenous neural stem cell and reparative neuroblast across the brain, under pharmacological action, is a promising area for regenerative therapy in stroke

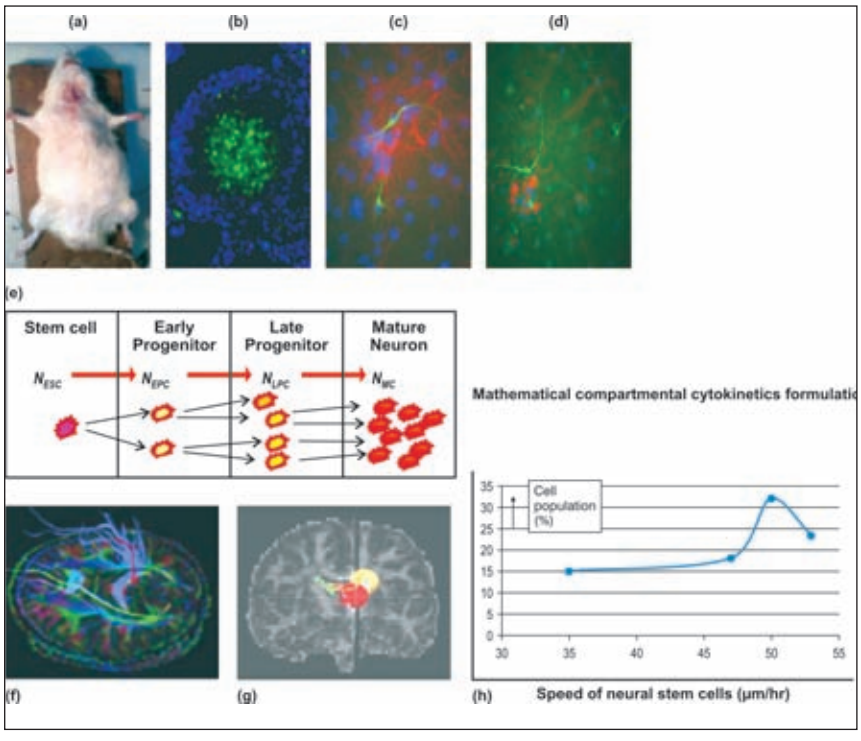
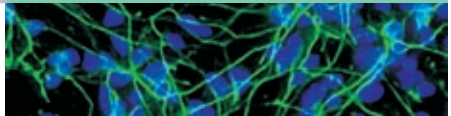


Figure 3.

(a) Preclinical rodent model of neurogenesis and neuroblast migration in cerebral ischemia.
(b-d) Successive cultures from subventricular zone cultures: Neurosphere stained by Nestin; 1st day neurons under BIII & GFAP; 3rd day neurons under NeuN &GFAP.
(e) Successive spatiotemporal compartmental model of neural stem cell cytokinetics.
(f) MRI tractography to show tracts that enable progenitor cell migration to penumbra.
(g) Track geometry mapping, incoming migration site and outgoing migration site shown by red and yellow fields.
(h) Validation of the mathematically calculated neural progenitor cell speed formulation by empirically measured speed distribution.



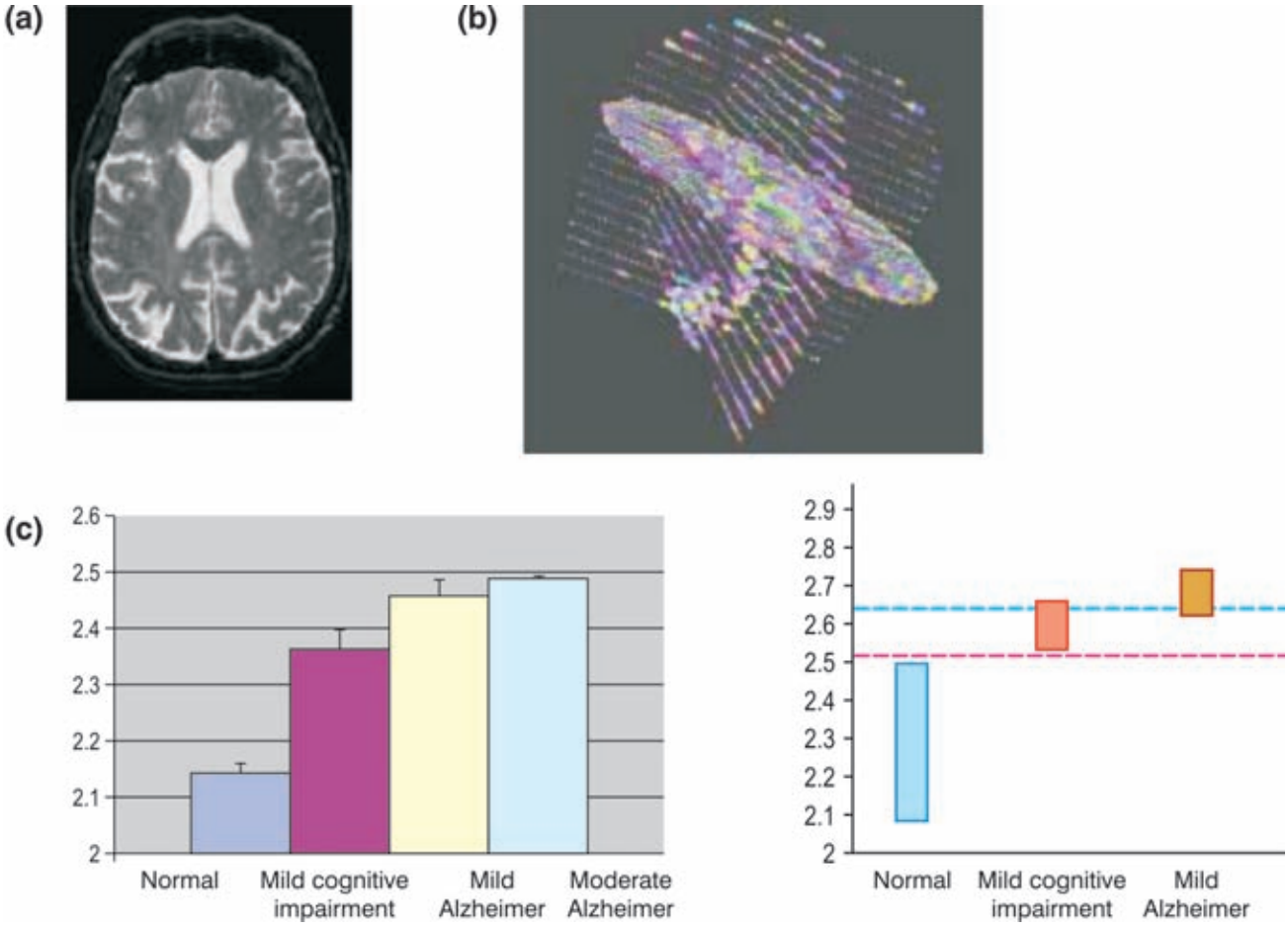


Figure 4.

(a) Transcallosal MRI image of patients of Alzheimer's Disease used for analysis,

(b) Textural displacement analysis of the MRI brain image using specific GUI brain template

(c) Discrimination of algorithm in 204 individuals using scanner/upgrades of single manufactuer: normals, mild cognitive impairment (MCI) and Alzheimer's disease; vertical axis denotes effective contextural index, mean value of index and deviation bars shown. Note wide separation between normals and MCI.

(d) Automated diagnosis in 1,034 individuals using scanner/upgrades of the three major manufacturers and across different populations. The bars denote the full range of values of each stage. Note narrower but sharp separation between normals and MCI.

and vascular dementia, utilizing MRI-based finite element analysis of brain parenchyma. Based on immunohistochemical studies on the rodent model (Figure 3 a - d), we formulated the process kinetics of neural stem cell proliferation and mobilization (Figure 3e). Thence, we upscaled to the human system by means of cytokinetic allometric dynamics, and subsequently elucidated the formulation of neural progenitor cell migration using stochastic transport terms, obtained from MRI. An important aspect of neuroregenerative therapy is to administer the pharmacological agent for synaptogenesis/synaptic stabilization, only at the proper time, namely when the migrating neurons reach the penumbra from the subventicular zone, via the white matter tract.

Only in the latter case, are there fresh migrating neurons in penumbra to initiate and maintain new synapses, and on these neurons the agent can act. We have developed methods to estimate (i) the migration speed of the neuroblasts (ii) the path length required to be traversed by the migrating neuroblasts, using MRI parameters of the patient (Figure. 3f-g). By this information, we can delineate the desired timing of the drug administration for inducing synaptogenesis/synaptic stability, so that optimal recovery occurs in the stroke penumbra zone. The results of the mathematical MRI analysis are validated by data of experimental findings from preclinical model (Figure. 3h). This approach thus deals with a main problem in clinical pharmacological neuroregeneration therapy, that is, efficient synaptotropic conversion of individual neurons to functionally behaving neurons with synaptic/dendritic stabilization. The clinical applicability of the procedure

to optimize regenerative therapy for the stroke penumbra is being now explored with a collaborating medical institute.

Development of Automated diagnosis of dementia across different populations and various scanner types

Based originally on MRI images of dementia patients obtained from Delhi, Bombay, Trivandrum and Calcutta, we developed a textural analysis of scans to diagnose the grade of dementia, by 1st & 2nd order topological metric indices. Thereafter, we constructed a discriminative algorithm to automatedly classify MRI images into normals, MCI, and mild or moderate Alzheimer's disease (AD). We have now heuristically evolved the algorithm and ensured that it is applicable to scanners at different cities and of different manufacturers, in spite of altered radiofrequency jitter and Nyquist noise that varies according to scanner types. Our procedure uses transcallosal MRI slice (Figure 4a), on which textural shear analysis is done using specific GUI brain template [fig. 4(b)]. The earlier results of MR images of 204 individuals, based on scanner of a single manufacturer is shown in Figure 4c; there is perfect discrimination between normals and MCI, while 98.4% discrimination is between MCI and AD, the error being 1.6% (Figure 4c).

Our recent results on 1036 subjects are shown in Figure 4d, and are based on scanners of all three manufacturers (Philips, Siemens, General Electric), scan inputs are from 4 countries (India, Canada, USA, Netherlands), some of the images being obtained courtesy of our collaborators. One sees that, due to multicentric scanner jitter, there is decrease in discriminative separation between Normals and MCI (compare Figure 4c,d), nevertheless there is still perfect separation between the two groups. Whilst, it may be noted that the discriminative separation between MCI and AD decreases, and error is only 4.2%. The most important distinction clinically needed is between normal and MCI, so that disease-modifying measures and life-style inputs could be initiated properly in the MCI subjects. Hence, it is satisfactory that the method can give fully accurate discrimination between normals versus MCI, across scanners, countries and populations.

Publications

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i. P. Roy. Multimodal image transfer from Developing Countries, Roundtable on Datasharing, Workshop on Neuro-Imaging Data Access & Data Sharing, International Neuro-Informatics Coordination Facility (INCF), Quebec City, June 2011.

ii. K. Sripad, K. Kumar, S. Hota and P. Roy. Under-connectivity of Default Mode Network due to Extreme High-altitude Hypoxia in The Himalayas, Int. Conf. On Human Brain Mapping, Quebec City, July 2011.

iii. S. Kapoor, S. Chardrasekhar, V. Subramanyam, R., Padhi and P. Roy. Targeted feedback-control design applied to multimodal therapy for elimination of malignant tumor with normal tissue protection, Int. Conf. on New Horizons in Cancer Research, American Association of Cancer Research, Delhi, Dec. 2011.

iv. V.P. Subramanyam and P. Roy. Hyperthermia and Tumor Regression: A Validated Approach using Systems Pathway Model of Immunodynamic Activation, International Workshop on Mathematical Biology, Indian Institute of Science, Feb. 2012.

Collaborators

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Dr Peter Luijten, Dutch Centre for Translational Molecular Medicine & Utrecht University.
Dr R. K. Padhi, Indian Institute of Science, Bangalore.
Dr Sashi Bala Singh and **Dr Sunil Hota**, Defence Research & Development Organization, Delhi.

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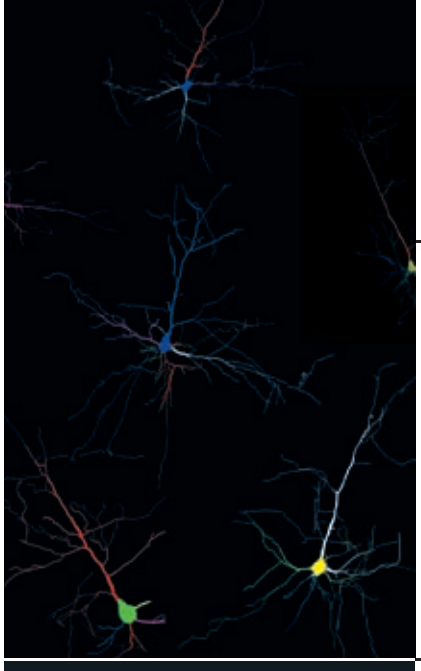
Awards

i. P. Roy. Saxena Award in Bio-Medical Engineering, National Academy of Medical Sciences, New Delhi, Sept. 2011.

ii. P. Roy. Research Presentation Award, Indian Society of Neuro-Radiology, ISNR-2011, Institute of Postgraduate Medical Education & Research, Chandigarh, Oct. 2011.

iii. V.P. Subramanyam, Selected for Young Participant Award, International Workshop on Mathematical Biology, Institute Mathematical Initiative, Indian Institute of Science, Bangalore, Feb. 2012.

iv. V.P. Subramanyam, Selected for Training Fellowship, NIH Advanced Neuroimaging Program, Brain Imaging Centre, University of California, Los Angeles, March, 2012.



Brain Oxidative Stress Mapping using Non-invasive Spectroscopic Techniques

Principal Investigator
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Research Fellows
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Sriya Bhattacharya

Oxidative stress plays an important role in different neurodegenerative disorders, especially AD Glutathione (GSH) serves as an important anti-oxidant in the brain and serves as an indirect indicator of oxidative stress levels within the brain. We have reported the in vivodistribution of GSH in the human brain with respect to gender in cognitively normal subjects, as well as patients with mild cognitive impairment (MCI) and AD. We showed that the mean GSH content is higher in females than males in the left frontal cortex (LFC; $p=0.006$), as well as the left and right parietal cortices (left, $p=0.04$; right, $p=0.01$).

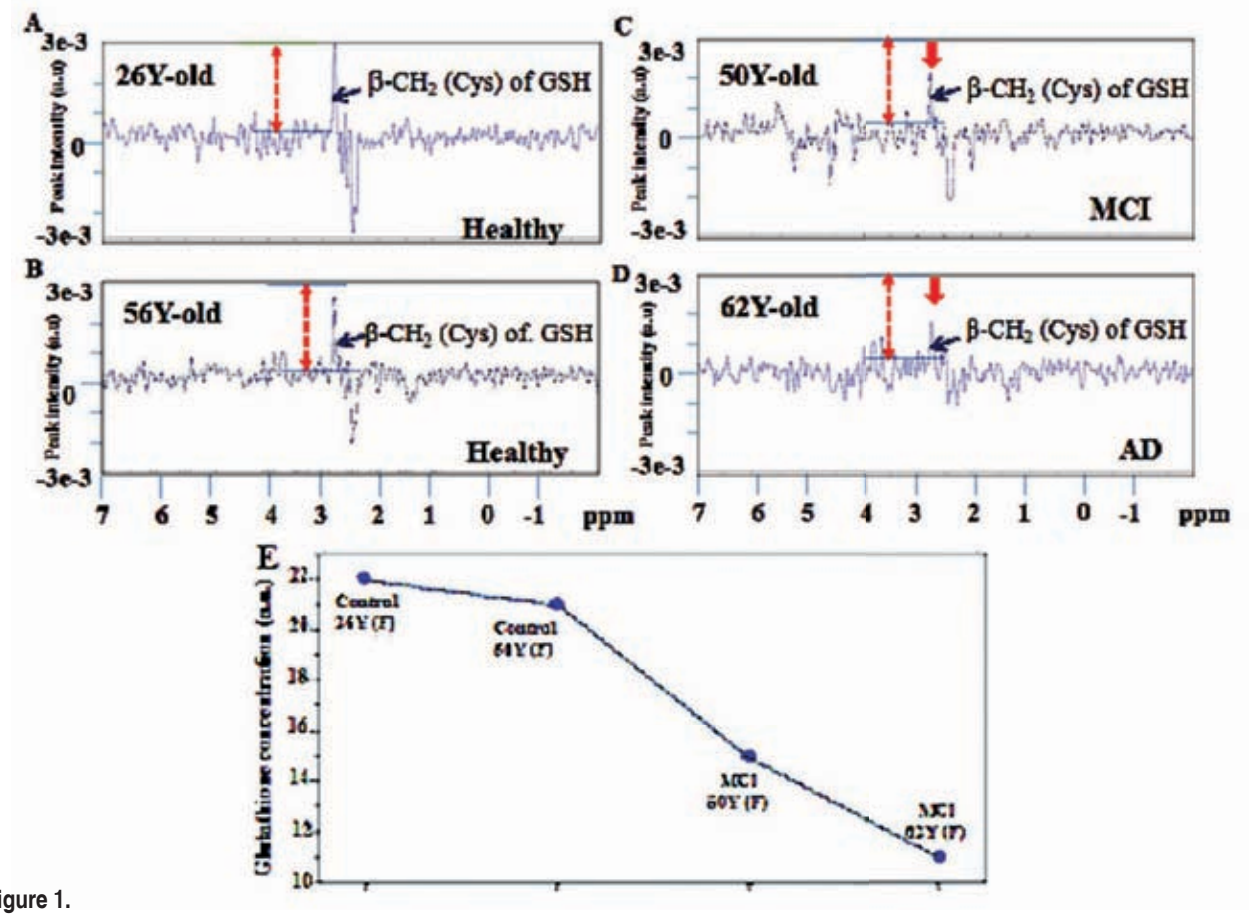
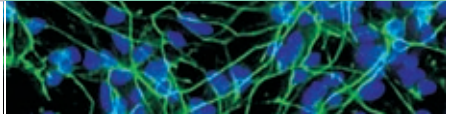


Figure 1.

GSH level in right frontal cortex in various cases: (A) healthy female (26Y old); (B) healthy female (56Y old); (C) MCI female (50Y old) and (D) probable AD female patient (62Y old) using MEGA-PRESS pulse sequence in a 3T MRI scanner. The decrease of GSH content is indicated by red arrow. (E) Quantitative presentation of GSH concentration in four different cases (A–D) as mentioned above.



Further, GSH levels were found to be depleted in AD in a gender-specific manner, with significant reduction of GSH levels in the right frontal cortex of AD female patients ($p=0.003$) and in the (RFC) region of AD male patients ($p=0.05$). This clinical study not only provides novel evidence of gender-dependency in GSH levels within the brain, but also demonstrates that GSH levels are downregulated in a region- and gender-specific manner in AD brains, thereby highlighting GSH as a plausible clinical biomarker for neurodegenrative disorders like AD. We are presently pursing this research and further probing studying the correlation between brain GSH levels and oxidative stress in the brains of male and female subjects. We this unique technique of GSH quantitation as a non-invasive method for mapping stress levels in individuals.

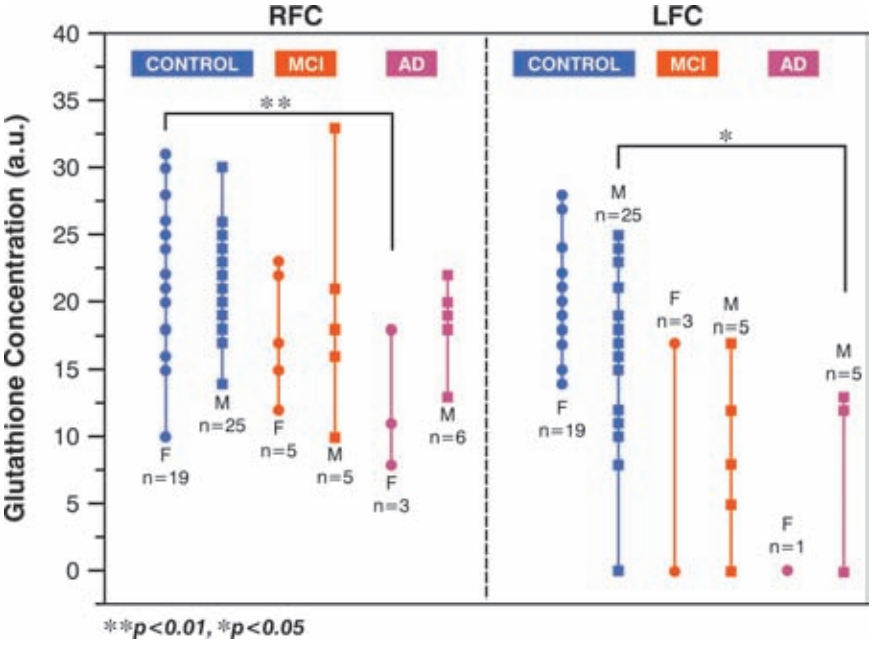


Figure 2.

Quantitative representation of GSH concentration (in a.u) in RFC and LFC regions of healthy young male, healthy young female, MCI (male and female) and AD maleand female patients. M and F symbols refer to male and female subject while sample size is indicated as n. It is clearly evident that GSH level is depleted in male and femaleAD patients as compared to healthy male and female subjects. Depletion of GSH level was statistically significant in RFC region among AD female patients compared tohealthy female subjects and LFC region in male AD patients when compared to healthy male subjects. Although amount of GSH was found to be less in MCI cases than inhealthy subjects, it did not reach significant value.

Publications

1. **P.K. Mandal**., M. Tripathi and S. Sugunan. Brain oxidative stress: Detection and mapping of anti-oxidant marker 'Glutathione' in different brain regions of healthy male/female, MCI and Alzheimer patients using non-invasive magnetic resonance spectroscopy. **Biochemical Biophysical Research Communications**, 417, 43-48 (2012).
2. **P.K. Mandal**. Proton Magnetic Resonance Spectroscopic Signal Processing for the Quantitation of Neurometabolites. **European Journal of Radiology**, 81, 653-664 (2012) (in PRESS in 2011).
3. **P.K. Mandal**. and H.Akolkar. .A new experimental approach and signal processing scheme for the detection and quantitation of 31P brain neurochemicals from in vivo MRS studies. **Biochemical and Biophysical Research communications**, 412, 302-306 (2011).

Funding

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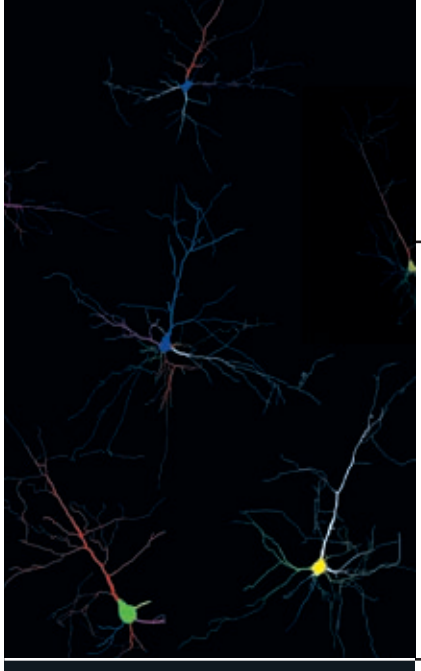


Profile of Hippocampus Neurochemicals and Brain pH using Non-invasive Imaging Technique

Principal Investigator
Pravat Kumar Mandal

Research Fellows
Dr. Sumiti Saharan
Shammi More
Sheenum Marwaha
Himanshu Akolakar

Magnetic resonance spectroscopy (MRS) can provide crucial information about various neuro-chemicals that reflect essential cellular properties such as oxidative stress, intracellular pH, as well as membrane and energy metabolism. Monitoring these cellular properties through neurochemical levels can serve to provide early indication of neurodegenerative pathologies such as (AD). Our laboratory is interested in mapping different brain neurochemicals non-invasively and correlating their levels with MCI and AD. With the help of multi-voxel phosphorous (31P) MRS imaging, we have reported changes in key neurochemical levels as well as pH levels of both hippocampal areas of MCI and AD subjects as compared to cognitive normal subjects. We observed a significant increase in phosphodiester (PDE), a membrane breakdown product, and a corresponding decrease in phosphomonoester (PME), the building block of neuronal membrane, in the left (PDE $p<0.001$; PME $p=0.005$) as well as the right (PDE $p<0.001$; PME $p=0.008$) hippocampal regions of AD patients. These changes are a characteristic signatre of membrane degradation and can serve to indicate onset of neurodegenrative pathology associated with AD. We also showed significant changes in the energy metabolism of AD subjects, with significant increase in ψ-ATP ($p=0.008$), and PCr ($p = 0.001$) levels in the left hippocampus of AD patients as compared to thecontrol subjects. In addition, the pH levels in the left hippocampus showed an interesting, though non-significant, inversal; while the left hippocampi of MCI patients had an acidic pH relative to controls, the pH in AD patients showed a slight trend towards alkaline range. The pH (left hippocampus) in AD was found to be negatively correlated ($r = -0.829$, $p = 0.042$) with PCr level (left hippocampus) in AD subjects.

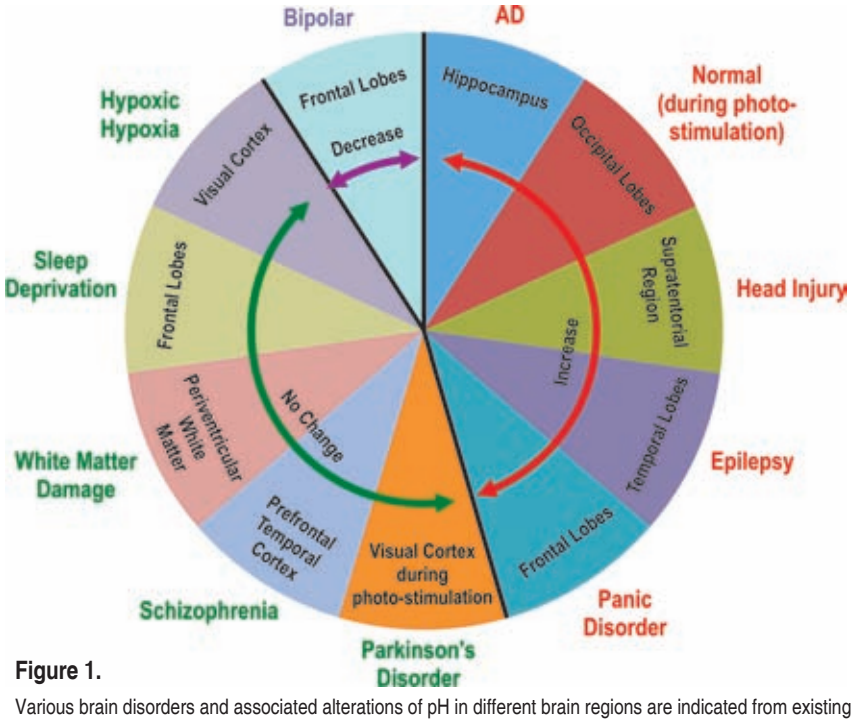
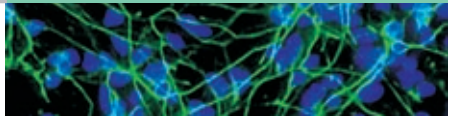


Figure 1.
Various brain disorders and associated alterations of pH in different brain regions are indicated from existing literature. The pH is increased in epilepsy (region: temporal lobes), in panic disorder (region: frontal lobes), and in Alzheimer's disease (region: hippocampus area) and decreased in bipolar disorder (region: frontal lobes). There is no change in pH in Parkinson's disease patients (during visual-stimulation), white matter damage, schizophrenia, sleep deprivation, or hypoxic hypoxia cases.



The statistically significant changes in membrane and energy metabolism observed in AD subjects can provide extremelycrucial clinical information, which can be used as a reliable biomarker for AD and potentially aid in the diagnos is. Further, al though non-significant, the observed trend of inversal of pH levels, from acidic in MCI patients to alkaline in AD patients suggests that monitoring of pH levels might provide an excellent indicator of the converting MCI-to-AD population. Given the above findings and their clinical significance, we are currently characterizing the changes in pH and neurometabolite levels in other brain regions of MCI and AD patients, as compared to healthy controls. This novel methodology is also being extended to other brain disorders.

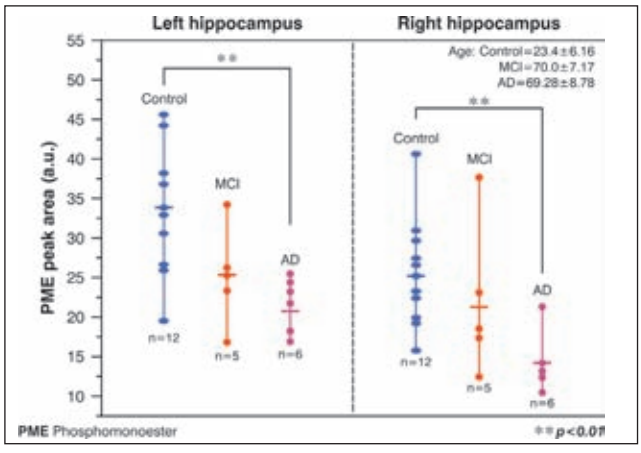


Figure 2.

Estimated PME values in the left and right hippocampi for control, MCI, and AD subjects. PME has been found to significantly decrease in both hippocampal areas of AD subjects as compared to young control subjects. PME is also found to decreasein the case of left and right hippocampi of MCI subjects, but it isnot statistically significant. Mean PME for each case is indicated asa bar.

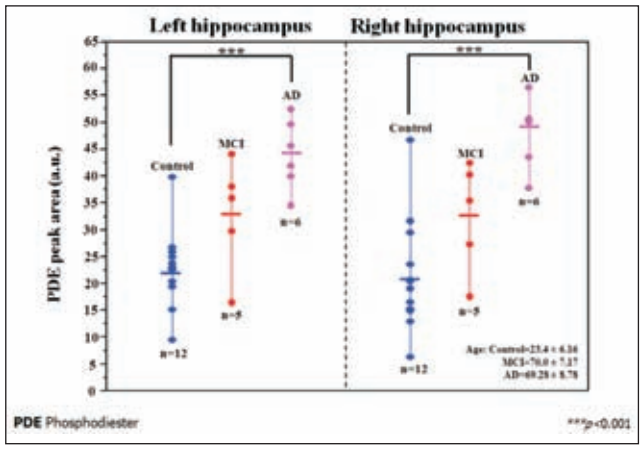


Figure 3.

Estimated PDE values in the left and right hippocampi of control, MCI, and AD subjects. PDE has been found to significantly increase areas of AD subjects as compared to young control subjects. PDE is also found to increasein the case of left and right hippocampi of MCI subjects, but it is not statistically significant. Mean PDE for each case is indicated as a bar.

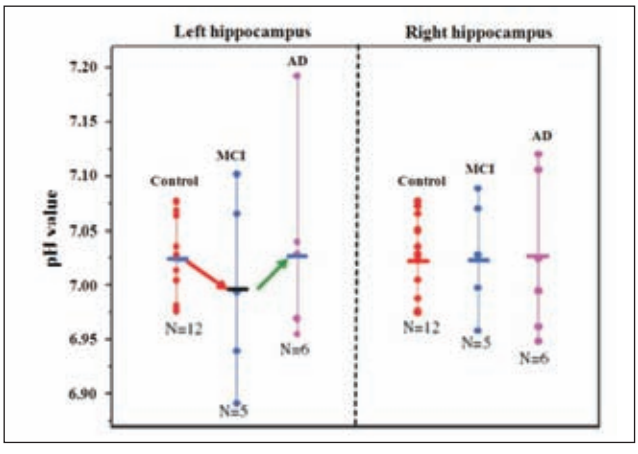


Figure 4.

Calculated pH values in the left and the right hippocampus for control, MCI and AD subjects. Increase in pH has been found inthe case of AD and MCI with respect to the young control subjects but statistical significant level was not reached. The pH is decreased toward the acidic region in normal healthy aging process, but in AD brain, the pH increases toward the alkaline range as compared to MCI subjects. Mean pH for each case is indicated as a bar.

Publications

1. P.K. Mandal, H. Akolkar, and M. Tripathi. (2012) "Mapping of Hippocampal pH and Neurochemicals from in vivo Multi-Voxel 31P Study in Healthy Normal Young Male/Female, Mild Cognitive Impairment, and Alzheimer's Disease." Journal of Alzheimer's Disease, DOI:10.3233/JAD-2012-120166.

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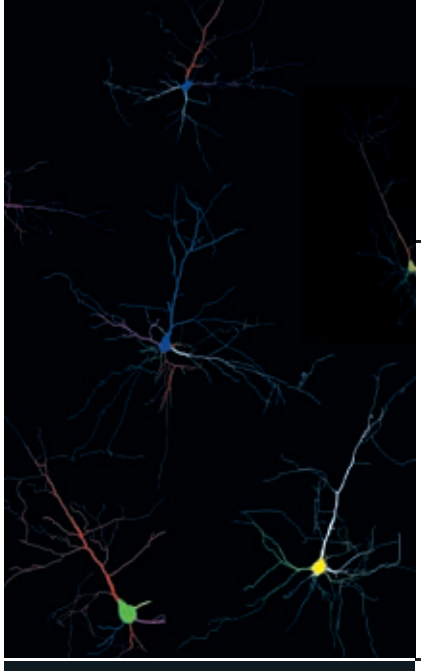

Visuospatial Performance and Memory Network impairment for Alzheimer's disease using Functional MRI (fMRI) studies

Principal Investigator
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Research Fellows
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Dr. Sumiti Saharan
Suvarnalata Xanthate
Monika Grewal

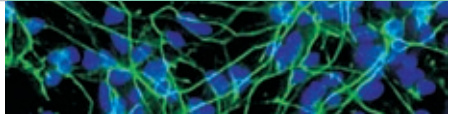
In recent years, the focus of Alzheimer's research has shifted towards finding reliable diagnostic biomarkers that enable accurate detection of AD. Functional magnetic resonance imaging (fMRI) has the potential to identify functional changes in the preclinical stages of AD. Both, memory deficits, as well as deficits in visuospatial cognition, are pervasive in AD. Our lab aims to identify the early functional brain network changes associated with these deficits in the preclinical stages of AD.

Memory deficits are the cardinal symptom of AD. Our lab is presently working on identifying the functional network changes

Brain regions		Clinical Status			
		fMRI		PET/SPECT	
		MCI	AD	MCI	AD
Parietal	Precuneus	↑ [67, 114]	↓ [129]	↓ [171] ↓ [172, 173]*	↓ [115, 174, 175] ↓ [176]*
	IPL	↑ [114, 177]	↓ [129] ↑ [117]		↓ [115, 175] ↓ [178]*
	SPL	↑ [67]	↓ [11, 117]		↓ [115, 174, 175] ↓ [178]*
Temporoparietal	-	-	-	↓ [144, 176]	-
Temporal	ITG	-	↓ [117, 129]	-	↓ [178]*
	MTG	↑ [114]	↑ ↓ [129] ↓ [117]	-	↓ [174] ↓ [178]*
	STG	-	↑ [119]	-	↓ [175] ↓ [178]*
Frontal	IFG	↑ [125]	↓ [129] ↑ [119]	↑ [173]*	-
	MFG		↓ [117, 129]	-	-
Posterior Cingulate	-	-	↓ [117]	-	↓ [176, 178]*

Functional neuroimaging of VSP in AD Existing literature with VSP studies on MCI and AD using fMRI and PET/SPECT has been summarized. For fMRI studies, only VSP task-related studies, which report significant functional activation changes during VSP task are reported. For PET/SPECT studies, only the studies which show significant correlation between functional metabolic findings and VSP task performance are included (except for the studies marked with #. Please see below). The hyper (I) or hypo (II) activation in respective brain areas are compared to age-matched cognitively normal control subjects. (III) refers to inconclusive results from different laboratories; (-) refers to no available data.

These studies showed significant changes in both PET/SPECT metabolic data and VSP task performance, but did not run correlational analysis between them.



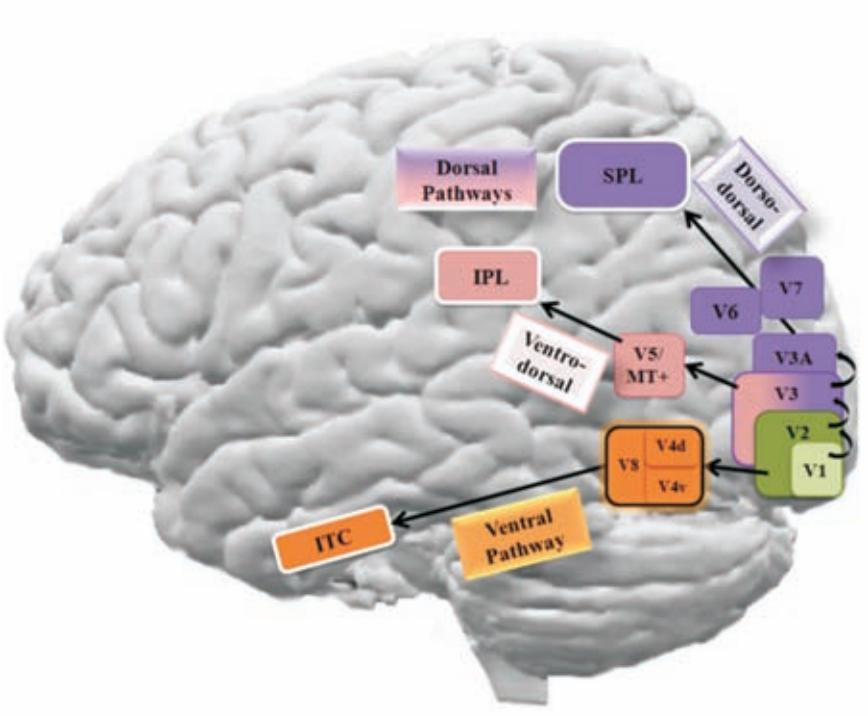


Figure.

Visual processing: Dorsal (where) and ventral (what) cortical pathways. This schematic represents the two major cortical pathways engaged in visual perception- the dorsal ('where') and the ventral ('what') pathway. The dorsal pathway segregates from V3 into two streams, i.e. the ventro-dorsal stream (shown in pink) containing the V5/MT+ and IPL; and the dorso-dorsal stream (shown in purple) that contains V3A, V6, V7 and SPL. These streams together are responsible for motion and spatial perception. On the other hand, the ventral pathway (shown in orange) projects from V2 to V4 (dorsal: V4d, ventral: V4v), V8, and ITG. This pathway is responsible for form, color and object perception. IPL Inferior parietal lobe; ITC Inferior temporal cortex; MT+ Middle temporal and medial superior temporal cortex; SPL Superior parietal lobe.

associated with specific aspects of associative memory in MCI. Recent neurophysiological and imaging studies have revealed that changes in visuospatial perception (VSP) functions can also be detected in the early stages of AD. We have authored a comprehensive review that probes the diagnostic potential of monitoring functional network alterations related to visuospatial perception deficits in AD. This manuscript highlights the scope of monitoring VSP functional brain networks as a biomarker for early detection of AD. Given the vital need of AD biomarkers that can facilitate early diagnosis and clinical trials, investigating the functional reorganization of VSP networks in association with AD pathology is likely to have significant impact on AD diagnostics. Our lab has designed specific VSP paradigms and is actively working to identify the functional changes associated with specific aspects of VSP in early AD.

Publications

1. **P.K. Mandal**., J. Joshi and S. Saharan. Visuospatial Perception: An Emerging Biomarker for Alzheimer's Disease. **Journal of Alzheimer's Disease**, 33, DOI: 10.3233/JAD-2012-120901 (In Press)
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Funding

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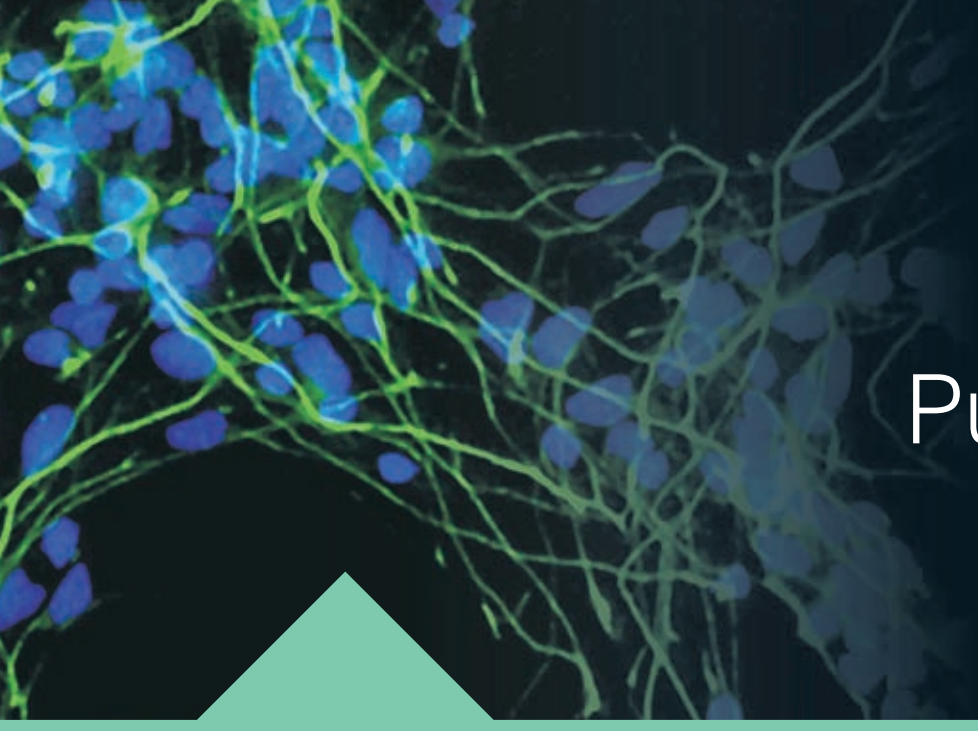

Publications

National Brain Research Centre

NBRC

Publications

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5. J. Sharma, S. Mulherkar, D. Mukherjee and **N.R. Jana**. Malin regulates Wnt signaling pathway through degradation of Dishevelled 2. **Journal of Biological Chemistry,** 287, 6830-6839, 2012.
6. J. Sharma, S. N. Rao, S. K. Shankar, P. Satishchandra, and **N. R. Jana.** Lafora disease ubiquitin ligase malin promotes proteasomal degradation of neuronatin and regulates glycogen synthesis. **Neurobiology of Disease.** 44, 133-141, 2011.
7. V. Chennupati, D. Datta, M.R. Subba Rao, N. Boddapati, M. Kayasani, R. Sankaranarayanan, M. Mishra, **P. Seth,** C. Mani, and S. Mahalingam (2011). Signals and Pathways Regulating Nucleolar Retention of Novel Putative Nucleolar GTPase NGP-1(GNL-2). **Biochemistry** 50 (21): 4521-4536.
8. L. Durgadoss, P. Nidadavolu, K.R. Valli, U. Saeed, M. Mishra, **P. Seth,** and V. Ravindranath (2012). Redox modification of Akt mediated by the dopaminergic neurotoxin MPTP, in mouse midbrain, leads to down-regulation of pAkt. **FASEB J** 26(4): 1473-1483.
9. M. Pant, P. Garg and **P. Seth** (2012). Central Nervous System Infection by HIV-1: Special Emphasis to NeuroAIDS in India. **Proceedings of National Academy of Science, (India)** 82 (1):81–94.
10. D. Dixit, V. Sharma, S. Ghosh, V.S. Mehta and **E. Sen.** Inhibition of Casein Kinase 2 induces p53 dependent cell cycle arrest and sensitizes glioblastoma cells to Tumor Necrosis factor (TNFα) induced apoptosis through SIRT1 inhibition. **Cell Death and Disease;**3:e271. doi: 10.1038/cddis.2012.10.
11. R. Tewari, S. Roychoudhury, S. Ghosh, V.S. Mehta and **E. Sen** (2012). Involvement of TNFα induced TLR4-NFκB and TLR4-HIF-1α feed-forward loops in the regulation of inflammatory responses in glioma". **Journal of Molecular Medicine**; 90(1):67-80
12. S. Sinha, N. Koul, D. Dixit, V. Sharma and **E. Sen** (2011). IGF-1 induced HIF-1a-TLR9 cross talk regulates inflammatory responses in glioma. **Cellular Signaling**. 23 (11):1869-1875.04
13. V. Sharma, D. Dixit, S. Ghosh and **E. Sen.** (2011). COX-2 regulates the proliferation of glioma stem like cells. **Neurochemistry International**; 59(5):567-71.
14. N. Sehgal, K.L. Kumawat, **A. Basu** and V. Ravindranath (2012) Fenofibrate reduces mortality and precludes neurological deficits in survivors in murine model of Japanese encephalitis viral infection. **PLoS One** 7(4): e35427
15. A. Nazmi, R. Mukhopadhyay, K. Dutta, and **A. Basu** (2012) STING mediates neuronal innate immune response following Japanese encephalitis virus infection. **Scientific Reports**, 2:347

16. D.K. Kaushik, R. Mukhopadhyay, K.L. Kumawat, M. Gupta and **A. Basu** (2012) Therapeutic targeting of Kruppel like factor 4 abrogates microglial activation. **Journal of Neuroinflammation** 9(1), 2012:57

17. D.K. Kaushik, M Gupta, K.L. Kumawat, and **A. Basu** (2012) NLRP3 inflammasome: Key mediator of neuroinflammation in murine Japanese Encephalitis. **PLoS One** 7(2); 2012:e32270.

18. A. Nazmi, K. Dutta, and **A. Basu** (2011) RIG-I Mediates Innate Immune Response in Mouse Neurons Following Japanese Encephalitis Virus Infection. **PLoS One** 6(6):e21761

19. A. Nazmi, K. Dutta, S. Das, and **A. Basu** (2011) Japanese Encephalitis Virus Infected Macrophages Induces Neuronal Death **J Neuroimmuno Pharmacology** 6(3):420-33

20. **N. Jain** and S. Tandon (2011). Plasticity of the somatosensory system following spinal and peripheral injuries. In **Expanding Horizons of the Mind Sciences** (Eds. Tandon PN, Tripathi RC and Srinivasan N, Eds). Nova Science Pub, NY. pp 93-104.

21. AS. Pundir, L.S. Hameed, P.C. Dikshit, P. Kumar, S. Mohan, B. Radotra, S.K. Shankar, A. Mahadevan, **S. Iyengar (2011).** Expression of Medium and Heavy Chain Neurofilaments in the Developing Human Auditory Cortex. **Brain Structure and Function** 217 (2); 303-321.

22. P. Haldipur, U. Bharti, S. Govindan, S. Sarkar, **S. Iyengar,** P. Gressens, S. Mani **(2011)**. Expression of sonic hedgehog during cell proliferation in the human cerebellum. **Stem Cells and Development,** 21(7):1059-1068.

23. P. Haldipur, U. Bharti, C. Alberti, C. Sarkar, G. Gulati, **S. Iyengar**, P. Gressens, S. Mani **(2011)**. Preterm Delivery Disrupts the Developmental Program of the Cerebellum. **PloS ONE**; 6(8).

24. V. Jain, E. Ravindran, **N.K. Dhingra** (2012) Differential expression of Brn3 transcription factors in intrinsically-photosensitive retinal ganglion cells in mouse. **J Comparative Neurology** 520:742-755.

25. **N. C. Singh** (2012) The developing biliterate brain. **ISSBD Bulletin** 1(61), 22 – 26.

26. M. Sharda and **N. C. Singh** (2012) Auditory Perception of Natural Sound Categories – An fMRI Study. **Neuroscience,** 214 49–58

27. A. Chakraborty, T. A. Sumathi, V. S. Mehta and **N. C. Singh**. Picture-naming in patients with left frontal lobe tumor – a functional neuroimaging study, **Brain Imaging and Behavior** DOI 10.1007/s11682-012-9165-4

28. C. Rao, S. Soni and **N.C. Singh**. The Case of the Neglected Alphasyllabary: Orthographic Processing in Devanagari, Peer Commentary in **Brain and Behavioural Sciences** (In press)

29. T. Das, R.S. Bapi, P. Padakannaya and **N.C. Singh** (2011) Cortical network for reading linear words in an alphasyllabary **Reading and Writing**, 24:697–707

30. S. Pal and **P. Roy**. The effect of stochastic fluctuation in radiation dose-rate on cell survival following fractionated radiotherapy, **Physics in Medicine and Biology,** 57, 1561-1570, 2012.

31. S. Chandrasekha, S. Kapoor, S. Rallabandi, R. Padhi and **P. Roy** (2012). Automated Treatment of Melanoma with Chemoimmunotherapy using Optimal Dynamic Inversion, **Advances in Control and Optimization of Dynamical Systems,** vol. 2, 930-935.

32. P. Raghunathan and **P. Roy.** (2012) Neuroimaging Studies of Human Cognition: Measurement Techniques and Recent Developments, Tripathi, R (ed). Expanding Horizons of the Mind Sciences, **Nova Science Publishers,** New York, 33-47.

33. V.P. Subramanyam and **P. Roy.** (2011). From Particle Mechanics to Pixel Dynamics: Using Stochastic Resonance Principle for Biomedical Image Enhancement, **Thermodynamics,** vol. 4, 215-228.(reported as 'accepted' last year).

34. **P.K. Mandal,** M. Tripathi and S. Sugunan. (2012) Brain oxidative stress: Detection and mapping of anti-oxidant marker 'Glutathione' in different brain regions of healthy male/female, MCI and Alzheimer patients using non-invasive magnetic resonance spectroscopy" **Biochemical Biophysical Research Communications,** 417, 43-48.

35. **P.K. Mandal.** (2012) Proton Magnetic Resonance Spectroscopic Signal Processing for the Quantitation of Neurometabolites. **European Journal of Radiology** (2012) (in PRESS in 2011).

36. **P.K. Mandal** and Himanshu Akolkar (2012) A new experimental approach and signal processing scheme for the detection and quantitation of 31P brain neurochemicals from in vivo MRS studies. **Biochemical and Biophysical Research communications,** Vol 412, Pages 302-306 (2011)(In PRESS in 2011)

37. **P.K. Mandal,** H. Akolkar, and M. Tripathi (2012) Mapping of Hippocampal pH and Neurochemicals from in vivo Multi-Voxel 31P Study in Healthy Normal Young Male/Female, Mild Cognitive Impairment, and Alzheimer's Disease. **Journal of Alzheimer's Disease,** DOI:10.3233/JAD-2012-120166.

38. **P.K. Mandal,** J. Joshi and S. Saharan (2012). Visuospatial Perception: An Emerging Biomarker for Alzheimer's Disease. **Journal of Alzheimer's Disease,** 33, DOI: 10.3233/JAD-2012-120901 (In Press)

39. **P.K. Mandal,** R. Mahajan and I.D. Dinov (2012.) Structural Brain Atlases: Design, Rationale and Applications in Normal and Pathological Cohorts. **Journal of Alzheimer's Disease,** 33, DOI: 10.3233/JAD-2012-120412 (In Press)

40. **E. Sen** (2011). Targeting inflammation induced transcription factor activation: An open frontier for glioma therapy. Invited Review in **Drug Discovery Today**. 16(23-24):1044-51.

41. S.M. Shukla and **S.K. Sharma** (2011) Sinomenine inhibits microglial activation by Aβ and confers neuroprotection. **Journal of Neuroinflammation** 8:117.

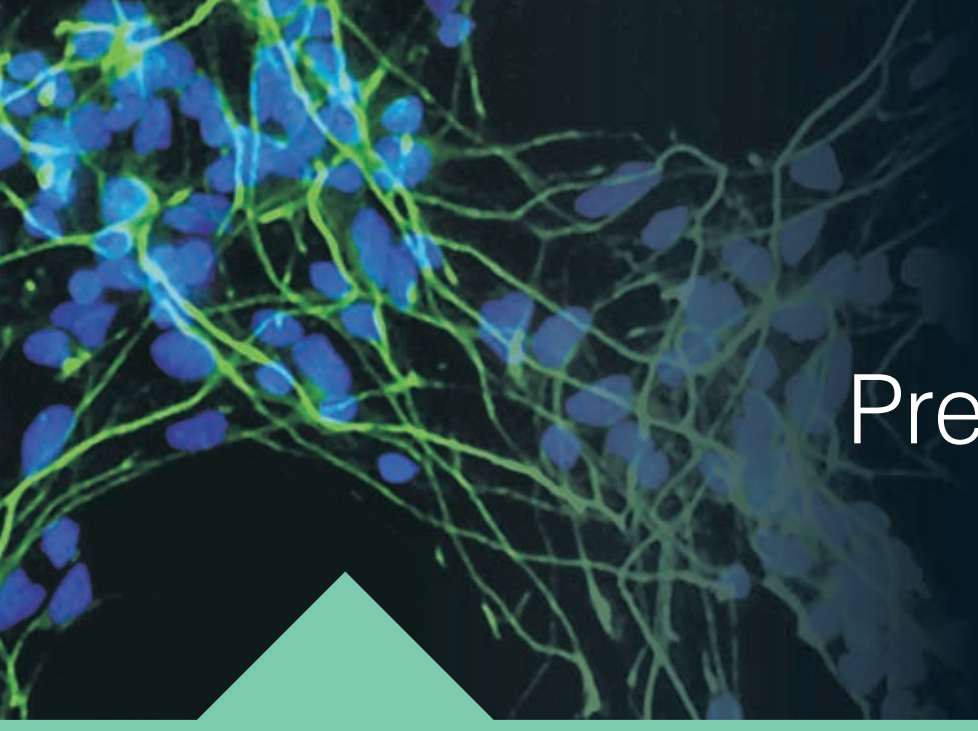
42. S. Ghosh and **A. Basu** (2012) Network Medicine in Drug Design: Implications for Neuroinflammation. **Drug Discovery Today** 17(11-12):600-7

43. I.M. Ariff, A. Mitra and **A. Basu** (2012) Epigenetic regulation of self-renewal and fate determination in neural stem cells. **Journal of Neurosci Research** 90(3):529-39 (Cover photo)

Book Chapter

1. M. Mishra and P. Seth. Cellular and Molecular Basis of Neurocognitive Deficits in HIV/AIDS. In: Expanding Horizons of Mind Science(s). Publishers - Nova Science Publishers, Inc, NY, USA, Chapter 21, Pages 383-405, 2012.

* Shown in Press last year



Presentations

National Brain Research Centre

NBRC

Presentations

National

1. N. R. Jana. Understanding the pathogenesis of Angelman syndrome. Department of Physiology, Calcutta University, 2011.
2. N. R. Jana. Understanding the pathogenesis of Lafora's Progressive Myoclonus Epilepsy. Department of Physiology, Calcutta University, 2011.
3. P.Seth. HIV-1 finds a New Hiding Place, the Brain. Brain Awareness Program at Government Girls College, Gurgaon, India. September 8, 2011. Guest Speaker.
4. P. Seth and M. Mishra. Neural Progenitor Cells in Management of Alzheimer 's disease. Alzheimer's Disease Symposia, Department of Neurology, King George's Medical College, Lucknow, Dec 3, 2011. Invited Speaker.
5. P. Seth and S. Malik. HIV-1 and Drugs of Abuse - it takes two to tango. At Applied Physiologist and Pharmacologists of India, at All India Institute of Medical Sciences, New Delhi, Dec 15, 2011 Invited Speaker.
6. P. Seth and S. Malik. Free Radicals in HIV-1 Neuropathogenesis. National Seminar on Reactive Oxygen Species, Department of Biochemistry, Lucknow University, Lucknow, Dec 24, 2011. Invited Speaker.
7. P. Seth. NeuroAIDS: Past, Present and Possible Future. Indian Institute of Science Education and Research, IISER-Kolkata, Feb 8th, 2012 Guest Faculty.
8. P. Seth, S. Malik, P. Garg, M. Pant and M. Fatima. Understanding NeuroAIDS Using Cellular and Molecular Approaches Golden Jubilee Symposium, Department of Biochemistry, Panjab University, Chandigarh, February 10-11, 2012. Invited Speaker
9. P. Seth and S. Malik. HIV-1 and Drugs of Abuse - Implications in NeuroAIDS. Pankaj Seth and Shaily Malik. 5th Symposium on Molecular Medicine at Special Centre for Molecular Medicine, Jawaharlal Nehru University, New Delhi Feb 17-18, 2012. Invited Speaker.
10. S. Malik, R. Saha and P. Seth. Role of forkhead box transcription factors in human immunodeficiency virus protein-Tat and illicit drug exposure induced neuronal apoptosis. XXIX Annual Conference of Indian Academy of Neurosciences, October 30 - November 1, 2011 at DIPAS, New Delhi, India.
11. P. Garg, M. Pant and P. Seth. Novel Insights into Neuron-glia Communication in NeuroAIDS. XXIX Annual Conference of Indian Academy of Neurosciences, October 30 - November 1, 2011 at DIPAS, New Delhi, India.
12. E. Sen. The T-L-R connection. National Conference on CME in Immunology, WBSU, 4th Nov 2011
13. E. Sen. The NFkB B-p53-SIRT1 nexus in glioma: More than meets the eye??? 5th Symposium on "Frontiers in Molecular Medicine" Special Centre for Molecular Medicine , JNU, 18th February 2012
14. E. Sen. Inflammation and tumorigenesis : An evolving concept "Bioepoch" School of Biotechnology, JNU, 24th February 2012
15. E. Sen, S. Ghosh and A. Paul. Role of Cofilin in Modulating Apoptotic Signals in Glioblastoma Multiforme. Recent Advances in Chemical and Physical Biology, SINP, Kolkata, 5th -7th March, 2012
16. A. Nazmi and A. Basu (2012) MPYS (STING) mediates neuronal innate immune response following Japanese encephalitis virus infection. 5th Congress of the Federation of Immunological Societies of Asia Oceania; 14th -17th March 2012, New Delhi, India.
17. A. Basu (2012) Microglia; A friend in need may not be a friend indeed.BIOSPARKS 2012, School of Life Sciences, JNU, New Delhi, 14-15th March, 2012.

18. A. Basu (2012) Modulation of neural stem cell fate following Japanese encephalitis virus infection. Biotech 2012, Annual Conference "Current Advances in Biotechnology and Medicine", Institute of Liver and Biliary Sciences, New Delhi 24th-25th February, 2012

19. I.M. Ariff, S. Das, and A. Basu (2012) Japanese Encephalitis virus infection and Neural stem/progenitor fate determination. 19th Biennial meeting of the International Society of Developmental Neuroscience; 11th - 14th January 2012, Tata Institute of Fundamental Research, Mumbai, India.

20. A. Basu (2011) Nervous about immunity: neuronal signals control innate immune response.CME in Immunology, Organized by West Bengal State University, 4-5th November,

21. A. Basu (2011) Transcriptional Regulation of Microglial activation: Inflammation in Hypoxia. XXIX Annual Meeting of Indian Academy of Neurosciences, New Delhi, 30th Oct- 1st Nov. 2011

22. A. Basu (2011) JE Virus infects brain: Murder in triplicate NERVE 2011, Haffkine Institute, Mumbai, 27-28th September, 2011..

23. A. Basu (2011) Evaluation of Minocycline as a therapy in an experimental model of Japanese Encephalitis. Department of Pediatrics, CSM Medical University, Lucknow, 13th June, 2011.

24. K. Dutta, M.K. Mishra, S. Das and A. Basu (2011) Therapeutic implications in Japanese encephalitis- taking Minocycline from the bench to the bedside. 2nd Molecular Virology meeting, 29th-30th April 2011, Indian Institute of Science, Bengaluru, India

25. D. Adhya, K. Dutta, and A. Basu (2012) Immune evasion by Japanese encephalitis virus – a novel strategy for persistent peripheral infection. 2nd Molecular Virology meeting, 29th-30th April 2011, Indian Institute of Science, Bengaluru, India.

26. A. Basu (2011) Inflammation and neuro-genesis in Japanese Encephalitis.2nd Molecular Virology Forum meeting, IISC, Bangalore, 29-30th April, 2011.

27. P.S. Ghate and R.K. Giri. Neurosphere culture as a novel In vitro model for Alzheimer's Disease. Annual Meeting of Indian Academy of Neuroscience, New Delhi, India, 2011. Best Research Paper Award

28. S. Iyengar: Song Learning in Birds. Brain and Cognition Workshop (sponsored by DST and IUSSTF), IISc, Bengaluru, July, 2011.

29. S. Iyengar: BirdSong and Learning. Fifth DST-SERC school in Neuroscience (Learning and Memory), NIMHANS, Bangalore, Manesar, February, 2011.

30. D. Yoganarasimha: Invited lecture on "Spatial Memory and Navigation" at International Brain and Cognition Workshop (5 July to 14 July 2011), Centre for Neuroscience, Indian Institute of Science, Bangalore, India.

31. N.C. Singh - Word processing in a non-linear alphasyllabary – the reading network for Devanagari, Invited talk at the symposium entitled Language, Literacy and Cognitive Development: current issues for a science of education' 15-17the December 2011, Bangalore, India.

32. N.C. Singh - "Brain and Behaviour: How do they correlate during reading scripts", Invited talk at 'Chaperons', the Annual Festival of Ambedkar Centre for Biomedical research, Delhi University, Delhi, 19th March 2012.

33. R. Varrier, S. Kondra and P. Roy. Distinct Bimodal Information Processing Pathways in Brain Activated during Interpretation of Projective Perceptual Field, National Conference on Neuropsychology and Cognitive Neuroscience, NIMHANS, Bangalore, Nov. 2011.

34. S. Pal, D. Polders, V. Mehta, P. Luijten, H. Hoogduin and P. Roy. The Tumorigenic Field Model of Neoplastic Growth with application to Neuro-oncology: Elucidating the cytoproliferative contour using MR imaging, Recent Trends in Neurosciences, Indian Academy of Neurosciences, New Delhi, Oct. 2011.

35. S. Kapoor, S. Chardrasekhar, V. Subramanyam, R. Padhi and P. Roy. Targeted feedback-control design applied to multimodal therapy for elimination of malignant tumor with normal tissue protection, Int. Conf. on New Horizons in Cancer Research, American Association of Cancer Research, Delhi, Dec. 2011.

36. V.P. Subramanyam and P. Roy. Hyperthermia and Tumor Regression: A Validated Approach using Systems Pathway Model of Immunodynamic Activation, International Workshop on Mathematical Biology, IISc, Feb. 2012.

37. R. Ramaswamy, R. Khanna and P. Roy. Topological Connectivity and Elastic Response of the Human Brain: A window to the Alzheimer-type Neurodegenerative process, Int. Conf. on New Developments in NMR and MRI, Indian Institute of Science, Bangalore, March 2012.

International

1. N. R. Jana, S. K. Godavarthi, P. Dey and M. Maheshwari. Hyperactivity of HPA axis and enhanced anxiety in a mouse model of Angelman syndrome. Annual meeting of Society for Neuroscience, Washington DC, 2011.

2. N. R. Jana. Understanding the physiological function of Ube3a and pathogenesis of Angelman syndrome. India Brazil workshop on biomedical sciences, Rio de Janeiro, 2011.

3. N.R. Jana. Neuronatin in Lafora disease pathogenesis. RIKEN Brain Science Institute, Japan, 2012

4. P. Seth and P. Garg. Neuron-Glia Crosstalk in HIV-1 Neuropathogenesis. Symposium on The Consequences if substance abuse and HIV on Stem Cell Biology at 17th Society of Neuro Immune Pharmacology Scientific Conference, April 9, 2011, Clearwaters, Florida, USA. Invited Speaker.

5. P. Seth, S. Malik and H. Khalique PDGF Attenuates HIV-1 Tat & Morphine Induced Damage to Human Neurons. Department of Neuroscience, School of Medicine, Temple University, Philadelphia, USA, April 12, 2011. Invited Speaker.

6. P. Seth and P. Garg. Neuron-Glia Interactions in NeuroAIDS. Children's Hospital of Philadelphia, Philadelphia, USA, April 13, 2011. Invited Speaker.

7. R. Tewari, S. Roychoudhury, S. Ghosh, V.S. Mehta and E. Sen. Involvement of TNFα induced TLR4-NFβB and TLR4-HIF-1α feed-forward loops in the regulation of inflammatory responses in glioma". Shanghai Symposium: Signaling, Inflammation and Cancer, Shanghai 25-28 July, 2011.

8. E. Sen and D. Dixit. Role of Casein Kinase 2 (CK2) in resistance of Glioma cells towards TNFα mediated apoptosis. 19th Euroconference on Apoptosis, Stockholm,14-17 September, 2011.

9. S. Ghosh and E. Sen. Role of β-catenin mediated chromatin remodeling in TNFα induced transcriptional regulation of MHC Class I genes. Spetses Summer School on Chromatin and Systems Biology, Greece 17-23 September, 2011.

10. D. Dixt and E. Sen. Role of Casein Kinase 2 (CK2) in resistance of Glioma cells towards TNFα mediated apoptosis. Society for Neurochemistry. 12-16th November 2011

11. K. Dutta, A Nazmi, R Mukhopadhyay and A Basu (2012) Involvement of the RLR pathway in neuronal immunity following Japanese encephalitis virus infection. 43rd Annual meeting of the American Society for Neurochemistry; 3rd –7th March 2012, Baltimore, USA.

12. D.K. Kaushik, and A. Basu (2012) Therapeutic targeting of Krüppel like factor 4 abrogates neuro-inflammation. 43rd Annual meeting of the American Society for Neurochemistry; 3rd –7th March 2012, Baltimore, USA

13. D.K. Kaushik, and A. Basu (2012) Kureppel like factor 4, a zinc finger transcription factor is associated with microglial activation and subsequent neuro-inflammation. 41st Annual meeting of Society for Neuroscience; 12th-16th November 2011, Washington DC, USA.

14. D.K. Kaushik and A. Basu (2011). Upregulation of Krueppel like factor 4 in microglia is associated with its activation and successive neuro-inflammation. 23rd Biennial ISN-ESN meeting, 28th August-1st September 2011, Athens, Greece.

15. R.K. Giri and P.S. Ghate. Utilization of neurosphere cultures to model Alzheimer's disease in vitro. Annual Meeting of Society for Neuroscience, Washington DC, USA, 2011.

16. R.K. Giri. Utilization of Neurosphere Culture in the Development of a Novel in vitro model of Alzheimer's Disease, McLaughlin Research Institute, Great Falls, Montana, USA, 2012.
17. S. Sen, L.S. Hameed, N Ramanathan and S. Iyengar (2012) Role of the Endogenous Opioid System in modulating Adult Neurogenesis in Zebra Finches (Taenopygia guttata). Poster presented at the 19th Biennial Meeting of the International Society for Developmental Neuroscience, Mumbai, India. Theme: Neurodevelopment and Neurological diseases, January, 2011.
18. A. Dutta, N. Kambi, P.Raghunathan, S. Khushu and N. Jain (2011). Functional magnetic resonance imaging (fMRI) of the normal somatosensory cortex in adult macaque monkeys and its reorganization following spinal cord injuries. Neuroscience 2011, Annual Meeting of the Society for Neuroscience, USA. Nov 12-16, Washington, DC, USA.
19. N Ramanathan and S. Iyengar: Role of δ-opioid receptors on female directed song and other behaviours in male zebra finches. Poster presented at the 8th Horizons in Molecular Biology International PhD Student Symposium, Göttingen, Germany, September, 2011.
20. N.K. Dhingra, V. Jain, R. Guruswamy: M1 type of intrinsically-photosensitive retinal ganglion cells express Brn3 transcription factors in rd1 mouse. ARVO, Fort Lauderdale (USA). May, 2011 (poster).
21. N.C. Singh. On the read to being a biliterate – cortical reading networks in children learning two scrips, British Dyslexia Association, Harrogate, UK, June 2011
22. B. Khundrakpam and P. Roy. Planning Hypothermic Therapy in Neonatal Stroke using Energy Flow Mapping and Heat Conduction Imaging, Brain Connectivity Workshop, University of Montreal, Montreal, June 2011.
23. P. Roy. Multimodal image transfer from Developing Countries, Roundtable on Datasharing, Workshop on Neuro-Imaging Data Access & Data Sharing, International Neuro-Informatics Coordination Facility (INCF), Quebec City, June 2011.
24. K. Sripad, K. Kumar, S. Hota and P. Roy. Under-connectivity of Default Mode Network due to Extreme High-altitude Hypoxia in The Himalayas, Int. Conf. On Human Brain Mapping, Quebec City, July 2011.
25. P. Roy and S. Pal. Higher-order Electrical Conductivity Tensor Imaging: Implications for clear localization of Epileptogenic source, Utrecht University Medical Centre, Utrecht, Aug. 2011.

Distinctions, Honours & Awards

National Brain Research Centre

NBRC

Distinctions, Honours & Awards

Details of Ph.D. students who have obtained Degree along with Title of Thesis

S. No.	Name of candidate	Date of Award of Degree	Enrolment No.	Title of the thesis
1.	Dr. Varsha Agarwal (2003)	3/5/2011	0018	Identification and functional characterization of brain specific cytochrome P450 enzymes
2.	Dr. Manisha Chugh (2003)	18/07/2011	0015	Influence of lesions of motor cortex on somatosensory function
3.	Dr. Ziauddin (2002)	25/07/2011	0012	Influence of cortical injuries on somatosensory function
4.	Dr. Shalaka Ajit Mulherkar (2004)	1/8/2011	0032	Characterization of Motor Deficits in a mouse model of angelman syndrome:
5.	Dr. Nitin Koul (2005)	25/08/2011	0042	Understanding the implications of insulin-like growth factor (IGF-1) induced signaling in Glioblastoma
6.	Dr. Tanusree Das (2005)	27/09/2011	0040	Cortical Reading Networks in Hindi-English Biscriptals
7.	Dr. Richa Tewari (2005)	15/11/2011	0039	Study of aberrant, pro-survival cellular signaling cascades in glioblastoma: implications in therapeutics
8.	Dr. Arjun R (2004)	24/02/2012	0026	Voluntary control of saccadic eye movement planning

Dr. Ellora Sen

Prof. BK Bachawat Travel Grant for Young Scientists (2012) to Ellora Sen by Christian Medical College, Vellore

Dr. Anirban Basu

Elected as a Fellow of the National Academy of Sciences, India.

Prof. Prasun Kumar Roy

Elected as Fellow of Indian National Academy of Engineering, New Delhi, Sept. 2011.

Saxena Award in Bio-Medical Engineering, National Academy of Medical Sciences, New Delhi, Sept. 2011.

Research Presentation Award, Indian Society of Neuro-Radiology, ISNR-2011, Institute of Postgraduate Medical Education & Research, Chandigarh, Oct. 2011.

Visiting Professorship, Division of Radiology, Radiotherapy and Nuclear Medicine, Utrecht University Medical Centre, Utrecht, The Netherlands, June-August, 2011.

Students Awards

i. Deobrat Dixit was awarded an IBRO international travel grant in 2011 for attending SFN, 2011

ii. Deepak Kumar Kaushik was awarded an ISN Travel Award, to attend 23rd Biennial Meeting of ISN-ESN, Athens, 2011.

iii. Deepak Kumar Kaushik was awarded a DST Travel Award, to attend Society for Neuroscience meeting, Washington DC, 2011.

iv. Dr Kallol Dutta, IBRO and DST Travel Award, to attend 43rd Annual meeting of American Society for Neurochemistry, 3-7th March, Baltimore.

v. V.P. Subramanyam. Selected for Young Participant Award, International Workshop on Mathematical Biology, Institute Mathematical Initiative, Indian Institute of Science, Bangalore, Feb. 2012.

vi. V.P. Subramanyam. Selected for Training Fellowship, NIH Advanced Neuroimaging Program, Brain Imaging Centre, University of California, Los Angeles, March, 2012.

vii. Sarika Cherodath, Integrated Ph.D. 2008 student was awarded a travel grant by DBT to attend a Conference in BDA, Yorkshine, UK from 02nd to 04th June 2011.

viii. Ms. Megha Sharda, Integrated Ph.D. 2007 student was awarded a travel grant by NBRC for attending the Annual Meeting of the International Society of Neuroimaging in Psychiatry 2011, Heidelberg, Germany from 07th – 10th September 2011.

ix. Mr. Sadashib Ghosh, Integrated Ph.D. 2007 student was awarded a travel grant by NBRC for attending the Spetses Summer School on Chromatin and System Biology in Anargyrios and Korgialenios School in Spetses, Greece from 17th – 23rd September 2011.

x. Mr. Niranjan A.Kambi, Ph.D. 2004 student was awarded a travel grant by NBRC for attending the Neuroscience Conference in Tuebingen, Germany from 12th – 14th March 2012.

Course-Work

Mr. Atesh Koul (a Ph.D. student), has been awarded first rank upon completion of course work during the year 2011.

Mr. Vaibhav Tyagi (a Ph.D. student), has been awarded second rank upon completion of course work during the year 2011.

Mr. Priyabrata Halder (an Integrated Ph.D. student), has been awarded first rank upon completion of course work during the year 2011.

Ms. Imran Jamal (an Integrated Ph.D. student), has been awarded second rank upon completion of course work during the year 2011.

Ms. Mahar Fatima (Ph.D.) and Mr. Imran Jamal for Integrated Ph.D. were awarded for the best performance in the Comprehensive Viva at the end of the first year course work (2011).

Externally Funded Research Projects

National Brain Research Centre

NBRC

Externally Funded Research Projects

Prof. Subrata Sinha

i. Centre for research in epilepsy (R&D Project). Funded by DBT, India dated from 11.02.2011 to 10.02.2016 (Budget ₹3344.17 Lakh)

Dr. Nihar Ranjan Jana

i. Understanding the role of ubiquitin-proteasome system dysfunction in the pathogenesis of Huntington's disease: Indo-Japan cooperative science program. Funded by DBT, India dated from 16.09.2009 to 31.03.2012 (Budget ₹2.29 Lakh).

ii. Study of Neuroprotective role of ubiquitin ligase, E6-AP in the transgenic mice model of Huntington's disease: National Bioscience Awardee. Funded by DBT, India dated from 11.05.2012 to 10.05.2013. (Budget ₹ 9.00 Lakh).

iii. Study the defects in Neurogenesis and intial synapse formation in mouse model of Angelman mental retardation syndrome. Funded by CSIR, India dated from 25.06.2012 to 24.06.2013 (Budget ₹ 5.72 Lakh).

iv. Understanding the Physiological function of malin a ubiquitin ligase mutated in lafora's progressive myoclonus epilepsy. Funded by DBT, India dated from 17.09.2012 to 16.09.2013 (Budget ₹ 42.11 Lakh).

Dr. Pankaj Seth

i. Characterization of Human Fetal Brain Derived Neural Stem Cells as a Model for Studying Neurodegenerative Diseases.Grant number: BT/PR6615/MED/14/857/2005. Grant award date: Dec 2006 (Ended Dec 2011). Department of Biotechnology, Ministry of Science & Technology, Govt. of India.

ii. Role on CNS Opportunistic infection in subsequent development of HIV dementia. Funded by RO1, NIH, USA dated from 01.07.2009 to 30.06.2014 (Budget USD 104,000).

iii. Role of human umbilucal cord blood stem and neural stem and neural stem cell in neuronal regeneration and functional restoration. Funded by DBT, India dated from 28.06.2011 to 27.06.2014 (Budget ₹ 9.00 Lakh)

iv. Molecular mechanism & therapy for cocaine abuse in HIV associated neurocognitive disorder (HAND), Funded by ICMR, India dated from (Budget ₹ 21.76 Lakh)

v. Understanding Neuro-Glia Crosstalk in HIV Neuropathogenesis (National Initiative on Glial Cell Research in Health and Disease). Funded by DBT, India dated from 22.03.2012 to 21.03.2015 (Budget ₹ 35.14 Lakh)

Dr. Ellora Sen

i. Oligodendrocyte Differentiation from Neural Stem Cells - Implication in CNS repair. Funded by DBT, Govt. of India. BT/PR6615/MED/14/857/2005.

ii. Understanding signalling circuitaries involved in transcriptional regulation of genes associated with survival and immune response in an inflammatory environment: Implication in glioblastoma progression. Funded by DBT, India dated from 20.04.2012 to 19.04.2013 (Budget ₹ 66.02 Lakh)

Dr. Shiv Kumar Sharma

i. Effect of amyloid beta on Growth factor signaling the hippocampus: Implication for the Alzheimer Disease. Funded by CSIR, India dated from 01.03.2009 to 28.02.2012

ii. Effects of an alkaloid on amyloid beta-induced changes in astrocytes: implications for Alzheimer's disease (National Initiative on Glial Cell Research in Health and Disease. Funded by DBT, India dated 27.03.2012 to 26.03.2015 (Budget ₹31.64 Lakh)

Dr. Anirban Basu

i. To Elucidate the role of inflammasomes and other molecular events leading to hypoxia induced neuro inflammation. Funded by DRDO, India dated from 02.08.2010 to 01.08.2013 (Budget ₹ 21.01 Lakh)

ii. To study the role of neuronal innate immune response in Japanese Encycphalitis virus infection Funded by CSIR India dated from 28.12.2010 to 27.12.2013 (Budget ₹ 7.15 Lakh)

iii. HOST- Directed Drug Targeting: Implication of suppressors of cytokine signaling (SOCS) in the pathogenesis of Japanese Encephalitis. Funded by DBT, India dated from 29.07.2011 to 28.07.2014 (Budget ₹ 9.00 Lakh)

Dr. Ranjit Kumar Giri

i. The study of Molecular and cellular events in mouse CNS stem cell cultures replicating mouse prions, development of a novel in vitro of prion pathology. Funded by DBT, India dated from 7.12.2009 to 6.12.2012 (Budget ₹ 48.55 Lakh)

Prof. Neeraj Jain

i. The uses of stem cells in treating cases of spinal injury: Basic biology of stem cells grant. Funded by DBT, India dated from December 2007 to December 2010.

ii. Perception Engineering Programme. Funded by DIT, India dated from 22.02.2011 to 21.02.2012 (Budget ₹ 19.00 Lakh)

Dr. Soumya Iyengar

i. Effects of altering the level of neuronal proliferation on the learning and production of behavior in male Zebra finches: Basic biology of stem cells grant awarded in 2007. Funded by DBT India dated from December 2007 to December 2010. (Budget ₹ 31.41 lakh).

ii. Opioid modualation of motivated behaviours in male zebra finches. Funded by DST, India dated from 10.06.2010 to 9.06.2013. (Budget ₹ 37.2 Lakh)

iii. Neurobiology and understanding circadian system linkage of cognitive performance in an avian model system. Funded by DST, India dated 20.07.2011 to 19.07.2014 (Budget ₹ 25.8 Lakh)

Dr. Narender K. Dhingra

Transplantation of stem cells in Degenerating retina - A study on formation of Functional synapses between stem cells and host retinal Neurons in vivo and in vitro: Basic biology of stem cells grant Funded by DBT, India dated December 2007 to December 2010. (Budget ₹ 42.4 lakh).

Dr. Yoganarasimha Doreswamy

i. Neural network mechanisms in subicular complex neurons during spatial navigation and learning in awake behaving rats. Funded by DBT, India dated from 21.01.2011 to 20.01.2014 (Budget ₹ 97.42 Lakh).

Dr. Nandini C. Singh

i. A multi-disciplinary, system-level investigation into neurobiology of Parkinson's disease. Funded by DBT, India dated from 22.03.2010 to 21.03.2013 (Budget ₹ 16.87 Lakh)

ii. A functional imaging study of dyslexia in biscriptal Indian children. Funded by DBT, India dated from 22.09.2010 to 21.09.2013 (Budget ₹ 30.65 Lakh)

iii. Perception Engineering Programme. Funded by DIT, India dated from 22.02.2011 to 21.02.2012 (Budget ₹19.2 Lakh)

iv. Language and brain organization in normative multilingualism. Funded by DST, India dated 01.02.2012 (Budget ₹ 4.37 Lakh)

v. Speech and music processing in Autism Spectrum Disorder - A functional neuroimaging study. Funded by DST, India dated 20.03.2012 to 19.03.2015 (Budget ₹ 27.12 Lakh)

Prof. Prasun Kumar Roy

i. Collabotation for translational and clinical research between Translational Health Science and Technology Institute, NBRC, RCB & CGH Gurgaon. Funded by DBT, India dated 6.10.2010 to 5.10.2015 (Budget ₹ 234.22 Lakh)

ii. Perception Engineering Programme. Funded by DIT, India dated from 22.02.2011 to 21.02.2013 (Budget ₹ 23.9372 Lakh)

iii. Indian Integration with global imaging system via McGill Linkage. Funded by NICSI, India dated from 30.06.2011 to 29.06.2016 (Budget ₹ 89.89 Lakh)

iv. Using stereo X-Ray image to develop a ready automated method for screening of Alzheimer-type mild cognitive impairment from normal ageing in a resource constrained setting. Funded by DBT, India dated from 04.05.2012 to 03.05.2015 (Budget ₹ 22.2 Lakh)

Dr. Pravat Kumar Mandal

i. Perception Engineering Programme. Funded by DIT, India dated from 22.02.2011 to 21.02.2012 (Budget ₹ 20.00 Lakh)

ii. Pulse sequence (in vivo) and processing scheme development for anesthetics and amyloid beta peptide interactions using 19F MRS. Funded by DBT, India dated from 29.03.2012 (Budget ₹ 18 Lakh)

iii. Characterization of the molecular interactions of anaesthetics with the beta amyloid. Funded by IMUR, Italy dated from 22.09.2008 (Budget ₹ 14 Lakh)

iv. Brain chemical analysis using non-invasive MRS spectroscopy. Funded by DBT, India from 15. 10. 2009 (Budget ₹ 38 lakhs).

Dr. Sayali Ranade

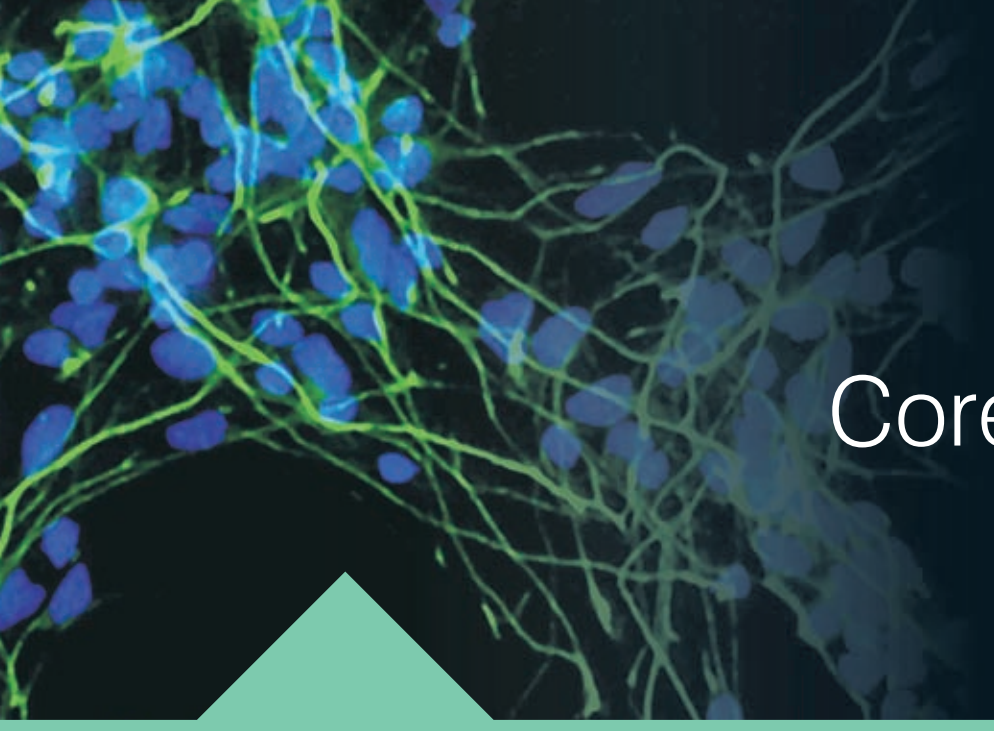
i. Iron Deficiency memory dysfunction hippocampal development and defects: Women Scientist Awardee. Funded by DST, India dated from 01.07.2009 to 30.06.2012 (Budget ₹ 19.53 Lakh)

Dr. Chaitra Rao

i. Investigation of the relationship between literacy instuction and metalinguistic awareness in adults. Funded by DST, India dated from 02.02.2012 to 01.02.2014 (Budget ₹ 12.48 Lakh)

Dr. D. Subhashree

i. Identification of associations between genetic variants in the neuronal migration pathway and behavioral correlates of dyslexia-linking genes and behavior using familial and sporadic cases. Funded by DST, India dated from 07.03.2012 to 06.03.2014 (Budget ₹ 12.48 Lakh)



Core Facilities

Distributed Information Centre (DIC)
Animal Facility
Digital Library

National Brain Research Centre
NBRC

Distributed Information Centre

The Distributed Information Centre is the computer centre of the Institute. The centre manages the complete computing and networking infrastructure of the institute thus aiding in the academic and research prospective apart from facilitating e-Governance support for digital library and other administrative activities. The centre also provides technical support to users and researchers and participates in research activities particularly those connected with computational aspects of neurosciences.

The Core IT infrastructure of the centre is listed as under

- Campus wide managed LAN with 10 Gbps fiber backbone and redundant paths.
- Campus wide Wi-Fi zone covering most of the institute including hostel and residential areas provides secure and authenticated network access.
- The center is linked with National Knowledge Network (NKN) over a gigabit fiber link for aiding teaching and research activities with other institutes, it also has a redundant 10 Mbps Radio link for maintaining essential services.
- The institute has a secure Firewall setup for intrusion detection and prevention apart from enforcing IT Policy including detailed auditing and logging. It also provided VPN services to users for secure access of NBRC IT resources from remote locations.
- The centre also houses a managed mini-datacenter where all the central servers, storage servers and core networking components are located and this forms the core of the IT facility.
- The centre has in-house management and hosting of institutes e-mail services and web services. Apart from this, the websites of the Indian Academy of Neurosciences and the Society of Neurochemistry, India are also hosted and maintained at the facility.
- The centre also hosts and maintains a pool of application servers running on windows and Linux server operating systems which are used by the researchers from different laboratories of the institute.
- The centre also hosts a video-conferencing facility for collaboration with fellow researchers across the globe.

Upcoming and Ongoing Activities

- The centre is taking the initiative for total IPv6 compliance of IT infrastructure as per Government of India directions.
- The expansion of the campus wide LAN and Wi-Fi areas is being planned for the upcoming institutional building.
- The centre is also working on integration of Voice and Data networks and potentially switching to VoIP PBX in coming days to provide better and additional collaboration services to researchers.
- The planning of an active-active DR Datacenter in the campus is also under process apart from upgrading the existing datacenter.

Animal Facility

NBRC is an autonomous institute created by the Department of Biotechnology, Govt. of India, with the mandate of carrying out frontline research to understand the neurobiology of brain disorders. As part of the infrastructure, NBRC has a state of art animal facility to meet the requirements of the scientists for advanced neuroscience research. The Institute recognizes that the use of laboratory animals in research is an important privilege accompanied with great ethical responsibility to ensure the 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 the peer-reviewed evaluation of all activities prior to the 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. The Animal Facility is registered with the National 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/a/CPCSEA, dated 24/08/2001. All activities of the Laboratory 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 records of the animals as per the statutory requirement of CPCSEA.

The main activity of Animal Facility is 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. The animal facility staff ensures humane and appropriate animal care. 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 rabbit and monkey cages. The staff are required to take showers and changing to work-overalls before entering the animal rooms, and again in the evening after finishing their work. All users wear facemasks and gloves before handling animals.

All animal species are housed in species appropriate cages, which are designed as per CPCSEA guidelines. The outdoor play area for non-human primates has six large interconnected enclosures that provide a flexible layout for optimising enrichment and social interactions. The transgenic, knock out and mutant mice are housed under germ-free conditions in filter top cages and individually ventilated cages (IVC). Such animals are handled in laminar hoods, and then moved to fresh cages in the cage-changing station under hepa-filtered air.

The animals are maintained under controlled environmental conditions as specified in CPCSEA guidelines, with temperature maintained between 22 ± 2^{0}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. 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.

All animals are procured as per CPCSEA guidelines. A health surveillance program for screening incoming animals should be carried out to assess animal quality. Animals procured from other palaces would be kept in quarantine. An effective quarantine minimizes risk for introduction of infection in the established colonies.

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 animal carcasses.

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 are screened for tuberculosis. Everyone handling non-human primates is trained in the procedures for the first-aid in case of an injury from an animal bite or scratch.

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

The Veterinary staff of Animal Facility also conducts short term training programmes for Int- Phd, Phd students and Project assistants in the field of laboratory animal science covering the ethical guidelines on the regulation of scientific experiments on animals, general biology and reproduction of 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

Nude Mice Transgenic Mice

- B6C3-Tg (APP695)85DboTg(PSEN1)85Dbo (Alzheimer disease model)
- UBC-GFP (Green fluorescent protein)
- B6CBA-Tg (Hdexon1) 62Gpb/3J (Huntington disease model)
- B6.Cg–Mapttm1 (EGFP)KltTg(MAPT)8cPdav/J (Alzheimer disease model)
- B6.129P2-Gsk3btm1Dgen/J (Alzheimer disease model)

Knock Out Mice

- GAP-43 knockout mice,
- UBE3A null mice (Angelman syndrome model)

Mutant Mice

- CBA/J mice (Retinal degeneration model)

Rat Strains

- Long Evans
- Sprague Dawley

Rabbits

- New Zealand white

Guinea Pigs

- Duncan Hartley

Non-human primates

- Rhesus Monkeys (Macaca mulata)
- Boneet Monkeys (Macaca radiata)

Birds

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

All the mice strains are maintained by inbreeding and the rat strains by out breeding. Guinea pig and 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 the presence or absence of the gene of interest.

Digital Library

The NBRC Library plays a vital role in the collection, development and dissemination of scientific and technical information to meet the present and future needs of the centre and also provides facilities and support to the scientists, researchers, students, staff and NBRC's networked centers.

The NBRC library has a large collection of Journals and 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 16 journals, and also subscribes to 917 online journals through the DBT e-Library Consortium (DeLCON). 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 IBM PC-Pentium-IV Computers with ISDN 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 within the campus portal.

The Library provides access to the most current reference sources available in order to assure the accuracy of information. The Library has been providing electronic access to the subscribed journals within the campus portal. It also maintains digital archives and news clips about the centre.

A total of 105 registered users including scientists, researchers, students and other staff used the NBRC library facilities in the past year. 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 Sh. D. D. Lal (ddlal@nbrc.ac.in) which are then downloaded and sent to them free of cost. The library entertains an average of approximately 440 requests for articles and this number is increasing every year.

The NBRC Library regularly evaluates its information services to ensure that the Institution's requirements are met. It promotes resource sharing and cooperation activities among libraries by providing an efficient and reliable means of resource sharing, that is, the inter library loan for the maximum use of resources, by providing copies of documents which are not available to researchers at centres outside the institute.

Main Activities of NBRC Library

1. Book Acquisition
2. Periodical 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 and maintains, stores and retrieves information and data keeping in view the evolving needs of its researchers
11. Help to Network Centres.

A separate two-storied library building is under construction, which will have provision for a reading room, reference room, video conferencing, online journal access facility, book section, Internet access facility, 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.

DBT's Electronic Library Consortium (DeLCON)

National Brain Research Centre

NBRC

DBT's Electronic Library Consortium (DeLCON)

The 'DeLCON Consortium' (Department of Biotechnology's Electronic Library Consortium) is a major national initiative of the DBT to promote the use of electronic databases and full text access to journals amongst the research and academic community in the country. Launched in January, 2009 with the 10 DBT member Institutions (including DBT H.Q. & ICGEB), this consortium provides access to scholarly electronic resources including full-text and bibliographic databases in various life science subjects to the DBT institutional community to improve teaching, learning and research. The subjects covered by DeLCON include 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 and Systems Neuroscience.

The DeLCON Consortium provides current as well as archival access to more than 917 core and peer-reviewed journals and one bibliographic database (SCOPUS Database) in different disciplines from 20 foreign publishers and aggregators. Access to all major e-resources was given to 10 institutions in the beginning of the year 2009. It has been extended to 17 institutions in the year 2010 and 7 others in the beginning of year 2011.

Currently, DeLCON comprises the following member institutions:

DeLCON MEMBERS (2009) PHASE-I

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

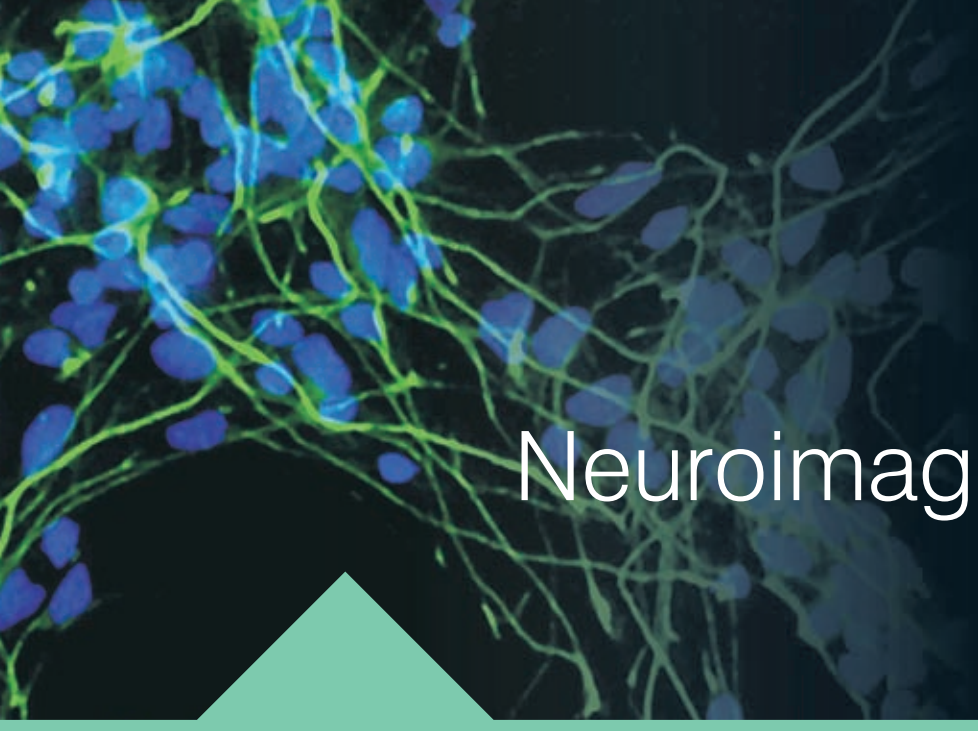
- Indian Institute of Technology Guwahati (IITG), Guwahati, Assam
- National Agri-Food Biotechnology Institute (NABI), Mohali, Punjab
- National Institute of Biomedical Genomics (NIBHG), Kalyani, Kolkata
- Regional Centre for Biotechnology (RCB), Gurgaon
- Tezpur University (TU), Tezpur, Sonitpur, Assam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

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 the DBT, over a period of time.

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

Appendix I

1	American Association for Advancement of Science	http://www.sciencemag.org	(3 Journals)
2	American Association for Cancer Research (AACR)	http://www.aacr.org	(8 Journals)
3	American Chemical Society (ACS)	http://pubs.acs.org	(37 Journals)
4	Annual Reviews	http://www.annualreviews.org	(23 Journals)
5	American Society for Biochemistry and		
	Molecular Biology	http:///www.jbc.org	(2 Journals)
6	American Society For Microbiology	http://www.asm.org/	(12 Journals)
7	Cold Spring Harbor Laboratory Press Journals	http://www.cshl.edu	(4 Journals)
8	Informa Healthcare / Taylor and Francis	http://www.informaworld.com	(7 Journals)
9	Lippincott William and Wilkins (LWW)/ Walter and Kluwer/OVID	http://ovidsp.ovid.com	(11 Journals)
10	Mary ANN Liebert	http://www.liebertonline.com	(7 Journals)
11	Nature Publications	http://www.nature.com	(40 Journals)
12	Oxford University Press (OUP)	http://www.oxfordjournals.org	(18 Journals)
13	Springer India	http://www.springerlink.com	(237 Journals)
14	Society for General Microbiology	http://mic.sgmjournals.org	(3 Journals)
15	Society for Hematology	http://bloodjournals.hematologylibrary.org	(1 Journal)
16	Wiley-Blackwell	http://www3.interscience.wiley.com/cgi-bin/home	(86 Journals)
17	Elsevier Science (ScienceDirect)	http://www.sciencedirect.com	(415 Journals)
18	American Society of Plant Biologist	http://www.aspb.org/	(2 Journals)
19	American Association of Immunologist	http://www.aai.org/	(1 Journal)
20	Scopus Database	http://www.scopus.com	(1 Database)



National Neuroimaging Facility

National Brain Research Centre

NBRC

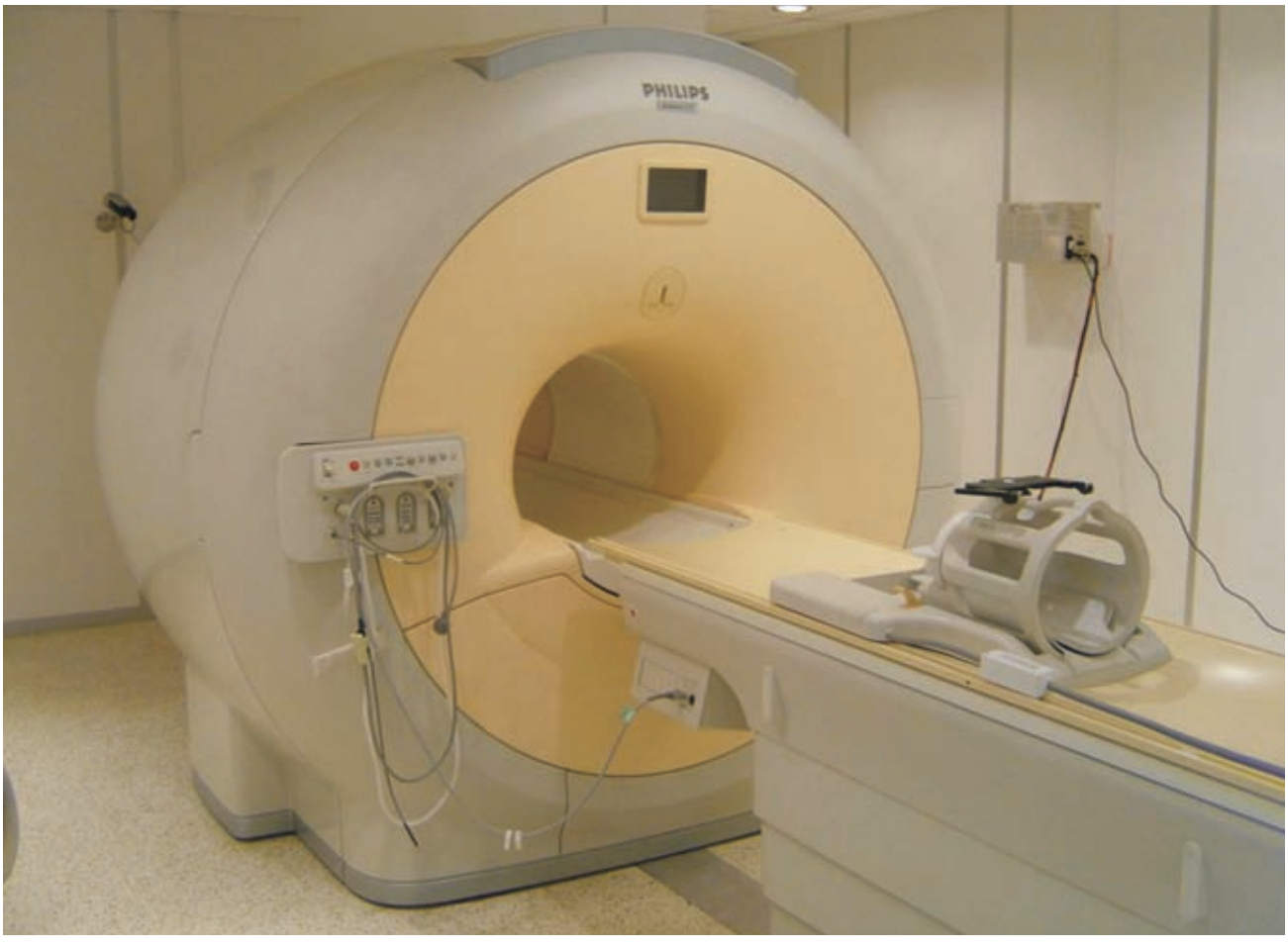
National Neuroimaging Facility

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

3T Magnetic Resonance Imaging (MRI) Scanner

The 3Tesla Phillips whole body MRI scanner at our Facility is equipped with state-of-the-art hardware (head coil, spine coil; neck coil, knee coil), 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 closely interacts with leading imaging centers within the country and across the globe.

This center is being used extensively for clinical studies for patients involving Alzheimer's and Parkinson's disease, autism, epilepsy, depression, brain tumour, as well as for monitoring the brain for healthy aging.



Translational Research: Clinical Unit

National Brain Research Centre

NBRC

Translational Research : Clinical Unit

Consultant Clinical Professor: Dr. V. S. Mehta

Consultant Clinical Assistant Professor: Dr Kapil Agarwal

Consultant Clinical Assistant Professor: Dr Rajnish Kumar

Clinical Neuropsychologist: Dr Krishan Kumar (till Sept. 2011), Dr Preeti Singh (from Oct. 2011)

Clinic Assistant: Hanuman Singh and Pawan Kumar

The unit is located at the Government General Hospital, Civil Lines, Gurgaon, 122001.

Investigation facilities:

The following facilities are available to the patients of the unit through the hospital/clinics at concessional rates:

MRI system: Siemens Magnetom 1.5 Tesla scanner with various investigation protocols

CT system

Ultrasonography

Neurophysiology: EEG and Evoked response.

X-Ray and Contrast imaging.

Wetlab facilities:

Biochemistry, Microbiology, Haematology, Pathology and Immunology.

Translational research aims to connect basic research to patient care: “From the Bench lab to the Bedside patient”. The Clinical Research Unit of NBRC covers the full spectrum of clinical neuroscience: neurology, neurosurgery, neuropsychology, neuropsychiatry, behavioral therapy, and psychometry. The unit has a morning outpatient facility, at the Government General Hospital four days a week, each of the consultant clinical faculty is available on one of the designated days. The NBRC Unit has integrated well with the Civil Hospital medical team and there are 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 internal medicine specialists of the General Hospital, the patient is taken care of. The out-patient facility is busy, and on some days, attendance can exceed forty patients. About 65% to 70% of the patients suffer from headache or seizure disorder, 5% have neuroses/psychoses and the remaining belong to a miscellany group of peripheral neuropathies, Bell’s palsy, sciatica, trigeminal neuralgia, old stroke, mental retardation and other common neurological disorders.

The follow up by the patients is about 90%. 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 patients attending, and movement disorders are an important cause of attendance. Patients attending the OPD at the Civil Hospital come from old Gurgaon township and the villages and towns in the surrounding districts of Haryana, while some come from neighbouring states Rajasthan, Uttarkhand, Delhi and Uttar Pradesh.

Patients requiring advanced specialist neurology in-patient care are referred to All-India Institute of Medical Sciences (AIIMS), 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. As part of the major plans for renovation of Civil Hospital, the Neurology OP rooms have been refurbished.

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 the Distributed Information Centre of NBRC. We have decided to prospectively enter all the medical data of new patients and to create a comprehensive computer database with relevant patient data along with any planned neuroimaging/molecular/systems 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 protocol has been formulated jointly with the Government General Hospital/ Government of Haryana.

The association of NBRC with Alzheimer's & Related Disorders Society of India (ARDSI) which has been going on from 2005, has been further fostered. This interaction promises to grow to the mutual benefit of both institutions concerned primarily with the common goal of the care of elders in its varied aspects. Besides medical and neurological health conditions, one is exposed to the psychosocial and public health problems of the ageing populace in their home environment.

Further expansion of the electrophysiological facility is underway, with procurement of 64-channel high density EEG/Evoked potential response analysis, Electrical dipole source mapping, Electromyography (EMG) and Neurophysiological studies as Nerve Conduction velocity system and neurometry.

For proper functioning and further clinical support, the Unit receives the fullest cooperation of the Ministry of Health - Government of Haryana, and the Deputy Commissioner - Gurgaon, as well as from the Civil Surgeon and the Principal Medical Officer of the Hospital.

Meeting & Workshops

Prof. Ramamurthi Memorial Lecture

National Brain Research Centre

NBRC

Meeting & Workshops

The late Dr. B. Ramamurthi Memorial Lecture

The seventh late Dr. B. Ramamurthi Memorial Lecture was delivered by Prof. Obaid Siddiqi, Senior Scientist and Founder-Director, NCBS, Bangalore on 20th April 2012, at the National Brain Research Centre in Manesar. Initiated in 2006, this lecture series commemorates Professor Ramamurthi's immense contribution role in setting up NBRC. Prof. Subrata Sinha, Director, NBRC, talked about Prof. Ramamurthi's contributions to Neuroscience and reminded the gathering about his role in the setting up of a centre devoted to research in Neuroscience. Prof. Siddiqi's scientific oration was entitled 'Learning and Memory in Drosophila'. The lecture was followed by interactions between Prof. Siddiqi, NBRC students and faculty.

International Collaborations & Networking

International Collaborations
Networking

National Brain Research Centre
NBRC

International Collaborations

International collaborations aimed at promoting neuroscience enabling the Centre to evolve cross border relationship between Indian Neuroscientists and the international neuroscience community through such exchange programs. Towards this endeavour of excellence in a very short span of time, NBRC has made great strides in establishing such collaborations with various prestigious neuroscience institutions in different countries around the world. Following are a few notable collaborative arrangements:

United States

NIH-RO1 grant has been awarded to Dr. Pankaj Seth in collaboration with Prof. A.Nath of the Johns Hopkins University. This NIH-RO1 grant proposes to study the "Role of CNS opportunistic infections in subsequent development of HIV dementia".

Japan

Dr. Nobuyuki Nukina and Dr. Nihar Ranjan Jana have been awarded a JSPS-DST collaborative grant to study the role of ubiquitin-proteasome system dysfunction in the pathogenesis of Huntington's disease.

Italy

The Italian Ministry for University and Research funded a project to Dr.Pravat K.Mandal, NBRC in collaboration with Prof.Vincenzo Fodale of University of Messina, Italy to study "Characterization of the molecular interactions of anesthetics with the beta-amyloid".

The Ministry of Education & Research, Italian Govt. under program of European Commission, has funded a project for collaboration between Prof Prasun Roy and Prof. Patrizia Baraldi, University of Modena & Reggio Emilia, for functional and tensorial neuroimaging approach to cortical information transmission (training project).

The Netherlands

Prof Prasun Roy and Prof. Peter Luijten, Utrecht Medical Centre are working together on developing high field neuroimaging methodology which has been sponsored by The Utrecht University Foundation & Philips Research.

Canada

A neuroinformatics project on imaging systems & networks has been initiated by Prof. Prasun Roy and Prof. Alan Evans, Montreal Neurological Institute, McGill University.

Networking

A major goal of NBRC is to network the existing neuroscience groups/ institutions in the country and promote multidisciplinary research in neuroscience. This is aimed to prevent unnecessary duplication of the work and facilities already existing. It also facilitates sharing of expertise and available infrastructure for mutual benefit. Networking also helps to bring together researchers from varying backgrounds to pursue common objectives that may be beyond the capacity of an individual investigator, group or institution. This is important because major achievements in neuroscience are being made through a multidisciplinary approach by bringing together scientists working in different disciplines into the main stream of neuroscience and brain research activity. The networking is possible by information sharing through electronic network and identifying "Collaborating" centres for mutual interaction. Currently 48 centres throughout India are networked to NBRC. The following institutions/universities are member of our network activities

List of Network Centres

1. All India Institute of Medical Sciences (AIIMS), New Delhi.
2. Banaras Hindu University (BHU), Varanasi.
3. Bangur Institute of Neurology, Kolkata.
4. Centre for Behavioural and Cognitive Sciences (CBCS), University of Allahabad, Allahabad.
5. Centre for Cellular & Molecular Biology (CCMB), Hyderabad.
6. Central Drug Research Institute (CDRI), Lucknow.
7. Centre for DNA Fingerprinting and Diagnostic, Hyderabad.
8. Central Food and Technological Research Institute (CFTRI), Mysore.
9. Cochin University of Science and Technology, Cochin.
10. Department of Biotechnology. New Delhi.
11. Delhi University, South Campus, Delhi.
12. Dr. A. L. Neurosurgical Centre, Chennai.
13. Indo American Hospital Brain and Spine Center, Kerala.
14. Institute of Cybernetics, Systems and Information Technology, Kolkata.
15. International Centre for Genetic Engineering and Biotechnology (ICGEB), New Delhi.
16. Institute of Genomics and Integrative Biology (IGIB), Delhi.
17. Institute of Human Behaviour & Allied Sciences (IHBAS), Delhi.
18. Indian Institute of Information Technology (IIIT), Allahabad.
19. Indian Institute of Technology (IIT), Mumbai.
20. Indian Institute of Technology (IIT), Delhi.
21. Indian Institute of Technology (IIT), Kanpur.
22. Indian Institute of Science (IIS), Bangalore.
23. Indian Institute of Chemical Biology (IICB), Kolkata.
24. Institute of Nuclear Medicine and Allied Sciences (INMAS), New Delhi.
25. Industrial Toxicology Research Centre (ITRC), Lucknow.

26. Indian Statistical Institute, Kolkata.
27. International School of Photomics, Cochin.
28. Jagadguru Sri Shivarathreeshwara Medical College, Mysore
29. Jawaharlal Nehru University (JNU), New Delhi.
30. Jawaharlal Nehru Centre for Advance Scientific Research (JNCASR), Bangalore.
31. Jiwaji University, Gwalior.
32. M.S. University of Baroda (Dept. of Microbiology and Biotechnology Centre), Baroda.
33. National Centre for Biological Sciences (NCBS), Bangalore.
34. National Informatics Centre (Medical Informatics and Telemedicine Division), (NIC) New Delhi.
35. National Institute of Mental Health & Neuroscience (NIMHANS), Bangalore.
36. Nizam's Institute for Medical Sciences (NIMS), Hyderabad.
37. Rajiv Gandhi Centre for Biotechnology, Trivandrum.
38. National Neuroscience Centre (NNC), Kolkata.
39. Sanjay Gandhi Post-Graduate Institute of Medical Sciences (SGPGIMS), Lucknow.
40. School of Information Technology, West Bengal University.
41. Shree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvanthapuram.
42. Sri Venkateswara Institute of Medical Sciences, Tirupati.
43. Tata Institute of Fundamental Research (TIFR), Mumbai.
44. University College of Medical Sciences (UCMS), Delhi.
45. University of Hyderabad, Hyderabad.
46. University of Calcutta, Kolkata.
47. Vidyasagar Institute of Mental Health and Neuroscience (VIMHANS), New Delhi.
48. Vision Research Foundation, Chennai

Invited Lectures

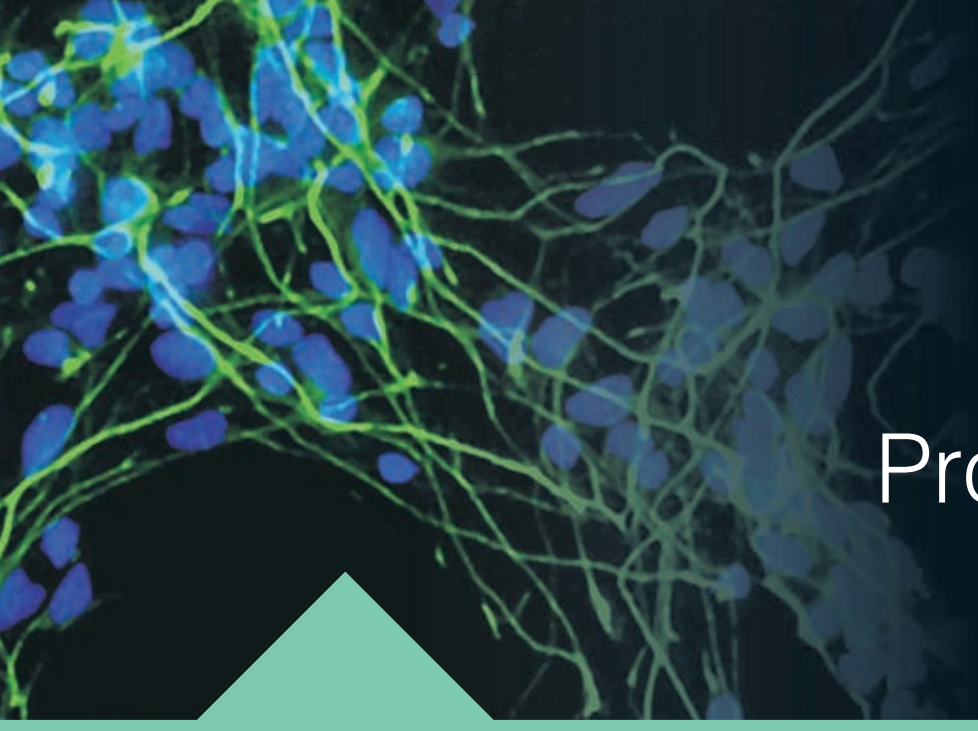
National Brain Research Centre

NBRC

Invited Speaker

Sr. No.	Name of the Speaker	Title of the Lecture	Date
1.	Dr. Baroness Susan Greenfield, Professor of Pharmacology at Lincoln College, Oxford University	'Can neuroscience help us understand consciousness?	April 4, 2011
2.	Dr Shilpee Dutt Assistant Professor ACTREC/ Tata Memorial Center	Understanding molecular mechanism of axon guidance: A step towards repairing nerve injuries	April 7, 2011
3.	Dr. Arvind Caprihan The Mind Research Network Albuquerque, New Mexico, USA	Brain Connectivity Measurements by Magnetic Resonance Imaging (MRI)	April 15, 2011
4.	Dr Jitendra Dave Division of Psychiatry and Neuroscience Walter Reed Army Institute of Research Silver Spring, MD 20910-7500 USA	'Molecular and Physiological Events after Experimental Penetrating Brain Injury'	April 25, 2011
5.	Dr Mehdi Hayat Shahi Department of Pharmacology School of Medicine University of California, Davis California, USA	Role of Sonic Hedgehog Signaling Pathway in Brain Tumor Development	April 26, 2011
6.	Dr. S. Senthil Kumaran, Associate Professor, Department of NMR & MRI Facility, All India Institute of Medical Sciences, New Delhi	Functional MRI and Clinical Application	April 28, 2011
7.	Dr. Aubrata Ghosh, Centre for Multimodal Neuroimaging INRIA-INSERM Unit Sophia-Antipolis, Nice, France	Higher Order Approaches to Diffusion MRI and Applications	May 5, 2011
8.	Dr. Mahak Sharma, Postdoctoral Fellow, Brigham and Women's Hospital, Harvard Medical School	Uncovering the molecular mechanisms regulating protein sorting in the endosomal /lysosomal system	May 20, 2011
9.	Dr. Gunjan Dhawan Dept. of Pharmacology, Physiology and Therapeutics, University of North Dakota School of Medicine Grand Forks, ND-58203	Role of non-receptor tyrosine kinase in amyloid-dependant microgliosis in Alzheimer's Disease	June 8, 2011
10.	Dr. Girish Rachakonda Research Instructor, Department of Radiation Oncology, Vanderbilt University Medical Center, Nashville, Tenesse, USA	Role of NRF2 in radiation resistance & neuroendocrine differentiation	July 5, 2011
11.	Prof. Andrew Schwartz Professor of Neurobiology University of Pittsburgh Pittsburgh, USA	Recent progress with high-performance brain-controlled interfaces	July 11, 2011
12.	Dr. Jeff Krichmar Department of Cognitive Sciences University of California at Irvine, USA	Computational Approaches in Cognitive Neuroscience: Case studies in neurobotics and large-scale cortical modeling	July 18, 2011
13.	Pratik Mutha, PhD. New Mexico VA Healthcare System 1501 San Pedro Dr SE, Albuquerque, NM 87108	Critical neural substrates for correcting unexpected Trajectory errors and learning from them	July 19, 2011
14.	Prof. Tom Albright Salk Institute USA	Neuronal foundations of visual perception and memory	July 21, 2012

15.	Mr Raghav Singh, Scientist, Cognitive Computing Project, IBM Research India	Network architecture of the long-distance pathways in the macaque brain	September 14, 2011
16.	Dr Sagnik Bhattacharyya Consultant Psychiatrist Psychosis Clinical Academic Group King's Health Partners Academic Health Sciences CentreDepartment of Psychosis Studies Institute of Psychiatry King's College London De Crespigny Park, London	Investigating the neurobiology of psychosis: pharmacological challenge, imaging genomics and translational potential	October 14, 2011
17.	Dr. Rajan Gogna Dorothy. M. Davis Heart and Lung Research Institute Ohio State University	Role of Oxygen and Flower Code in Cancer and Cardiovascular Diseases	October 27, 2011
18.	Dr Yuri Nikolsky, Vice-President (Research & Development) Thomson Reuters (Gene-Go Group) Philadephia.	Functional analysis of disease expression data of Huntington's Disease using MetaMiner platform	November 15, 2011
19.	Prof. Jürgen Wolfrum, Professor (em.) for Physical Chemistry & Founding Director BioQuant, Ruprecht-Karls- University Heidelberg	Systems Biology – a new quantitative approach in life sciences and medicine	November 17, 2011
20.	Dr. Sarojini Cruz-Sengpta	ADHD: A pharmaco-behavioural-genetic approach to fine map the disorder	December 13, 2011
21.	Dr. Naihe Jing, Professor & Executive Director Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, CHINA	BMP signaling and neurogenesis of developing spinal cord	January 16, 2012
22.	Anirban Dutta, Dept. of Clinical Neurophysiology, University of Medicine, Gottingen, Germany.	Neuromodulation Therapies for Movement Rehabilitation	January 24, 2012
23.	Suruchi Utreja Ph.D. Candidate Dept Dept of Biology and Biotechnology, College of Arts and Sciences Drexe Drexel University	Role of Calcineurin In Alzheimer's Disease In-vitro/ In-vivo Studies	February 1, 2012
24.	Dr. Santanu Banerjee, PhD Postdoctoral Researcher Department of Cell and Developmental Biology University of Pennsylvania, School of Medicine Philadelphia,	Genetic dissection of neural crest cell migration	February 6, 2012
25.	Dr. Rajesh Kana University of Alabama at Birmingham	The Functional Architecture of Brain Connectivity in Autism	February 9, 2012
26.	Prof. Sidhartha Tan, University of Chicago	Oxidative stress markers and MR Imaging in the study of Cerebral Palsy	February 29, 2012
27.	Dr. Partha Pratim Bose West Bengal University of Technology, Saltlake, Calcutta	Peptidomimetics in drug development against Alzheimer's Disease	March 13, 2012
28.	Subhash Bhatnagar Department of Speech Pathology and Audiology from Marquette University	A clinical study of Hindi speaking stroke patients with aphasia	March 19, 2012



Academic Programmes

Ph.D. in Neuroscience
Intergrated Ph.D. in Neuroscience
Summer Training & Short term Programmes

National Brain Research Centre
NBRC

Academic Programmes

Deemed University Status

NBRC was awarded Deemed University status (de-novo category) in 2002 under the 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 Institute among the Institutes of the Department of Biotechnology to attain this status.

On completion of 5 years period from the time NBRC has been given de-novo deemed University status, a Committee [duly constituted by the University Grants Commission (UGC)] visited NBRC for reviewing the 'Deemed to be University' status and recommended a further extension. The deemed university status has also been reviewed by an independent Committee constituted by Ministry of Human Resource & Development. The Committee placed this University / Institute under category "A".

As a Deemed University, NBRC has completed 10 years in May 2012. As on 31st March 2012, 31 students were awarded the degree of Doctor of Philosophy by the institute.

Courses Offered:

Ph.D. in Neuroscience

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

NBRC inducts students for its Ph.D. programme from diverse backgrounds including a 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.

The fellowship for Junior Research Fellows is ₹ 16,000/- per month and for Senior Research Fellows it is ₹ 18,000/-

Integrated-Ph.D. in Neuroscience

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

NBRC inducts students for its Integrated Ph.D. programme from diverse backgrounds including Bachelor's degree in any branch related to Neurosciences, M.B.B.S., B.E., B. Tech. or Psychology. NBRC recognizes that understanding brain functions requires a fusion of knowledge from multiple disciplines.

Integrated Ph.D. Students are provided a fellowship of ₹ 5000/- per month for the first two years. From the third year onwards, they are paid a fellowship on par with Ph.D. students. After completing the Integrated Ph.D. programme, students will be awarded a dual degree (M.Sc. and Ph.D.). NBRC is one of the first Institutes in the country to develop an integrated multidisciplinary teaching programme in Life Sciences.

NBRC offers certain benefits to its students in the form of fellowships, hostel accommodation, transportation facility and medical reimbursement to its students.

Summer Training and Short-term Programmes

NBRC conducted a Summer Training Programme 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, for a period of 8 weeks. The Trainees selected for this programme were provided with shared accommodation in the NBRC Hostel during their training period. Summer trainees were encouraged to attend seminars and journal clubs organized at the Institute.

The summer training projects give students an exposure to Neuroscience and encourage them to consider it as a future career option.

NBRC celebrated its 8th Foundation Day on 16th December 2011. Five schools from Gurgaon / Manesar participated in the open exhibition and quiz held at NBRC in connection with the Foundation Day celebrations. The participants visited various Laboratories at NBRC, attended a poster session, a lecture on the functions of the brain in the Seminar Hall (presented by senior students) and took part in a Quiz.

On the occasion of the National Science Day (28th February, 2012), Ph.D. students, Integrated Ph.D. students, post-doctoral Fellows and project employees of NBRC participated in a presentation at Kendriya Vidhyalaya, NSG, Manesar, Govt. Girls Higher Secondary School, Manesar, Govt. Senior Secondary School, Pachgaon and Govt. College, Sidhrawali.

General & Academic Administration

National Brain Research Centre

NBRC

General & Academic Administration – A Profile

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

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

During the year under review, the Administration achieved excellence in execution of following activities at NBRC:

- The annual cultural festival of NBRC, 'TANTRIKA 2011' was organized within the campus which included a variety of cultural and sports events. Students, officers, and staff of NBRC participated in the event.
- Provided necessary logistics in conducting international and national conferences/seminars organized in the campus as well outside of the campus.
- Made major imports from different countries in terms of equipments and other consumables with meticulous planning and adhered to a precise schedule.
- The 8th Foundation Day of NBRC was held on 16th day of December, 2011. On this occasion, several programmes were organized within and outside the campus. The daylong celebrations included the poster presentations on ongoing research activities of NBRC. Students from various schools were invited to interact with NBRC scientists and they visited the laboratories. A quiz programme for students from local schools was also organized on this occasion. On this august occasion, Prof. Avindra Nath, MD, Clinical Director, NINDS, NIH, USA delivered the Foundation Day lecture to the students and scientific community at Indian National Science Academy, New Delhi.
- During the year under review, Prof. Mriganka Sur, Professor, Massachusetts Institute of Technology (MIT) took over as Distinguished Biotechnology Chair at NBRC on 1st January, 2011.
- The process of recruiting two scientists, that is, Dr. Sourav Banerjee and Dr. Sharba Bandyopadhyay was completed during 2011. While Dr. Banerjee's research focuses on the molecular control of synapse formation by non-coding RNAs and the ubiquitin proteasome system, Dr. Bandyopadhyay's research focuses on imaging technology and the auditory cortex (ACX).
- The process of recruiting Mr. N. Subramanian as the Chief Administrative Officer was completed during 2011.
- The faculty, students and staff were administered a solemn pledge to work in harmony and emotional oneness of all people regardless of region, caste, religion or language on the occasion of the Sadbhavana Diwas.

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. NBRC Administration received a letter of appreciation from the Ministry of Home Affairs, Regional Implementation Office, Ghaziabad towards implementation of Hindi in day to day official work during the year. The Rajbhasha Sansthan, New Delhi, awarded NBRC with a shield in recognition of its efforts made towards the implementation of Hindi as the official language.

RTI Act

The provisions of RTI Act are being followed at NBRC in letter and in spirit. All RTI applications seeking information on various matters concerning NBRC are being provided the requisite information.

Women Empowerment

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

Reservations and concessions in Employment & Admissions of Students

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

Vigilance

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

Institutional Governance Structure & People at NBRC

NBRC Society
Governing Council
Finance Committee
Scientific Advisory Committee
Research Area Panel
Building Committee
Academic Council
Board of Studies
M.Sc. Neuroscience Co-ordination Committee
Scientific Staff
Other Staff

National Brain Research Centre
NBRC

Members of the NBRC Society

1	Prof. P.N. Tandon (President) No. 1, Jagriti Enclave, Vikas Marg, New Delhi	2	Dr. M.K. Bhan Secretary Department of Biotechnology, New Delhi
3	Dr. T. Ramasami Secretary Department of Science & Technology, New Delhi	4	Dr. V.M.Katoch Director-General Indian Council of Medical Research, New Delhi
5	Dr. Sandip K. Basu Professor of Eminence, National Institute of Immunology, New Delhi	6	Dr. K. Vijayaraghavan Director National Centre for Biological Sciences, Bangalore, Karnataka
7	Prof. Samir K. Brahmachari Director General CSIR Institute of Genomics & Integrative Biology, Mall Road, Delhi	8	Ms.Vandana Srivastava, IDAS JS&FA, Department of Biotechnology, New Delhi
9	Dr. Gourie Devi Director (Retd.), Flat –9, Doctors Apartments, Vasundhara Enclave, Delhi	10	Dr. L.M. Patnaik CSA Department Indian Institute of Science Bangalore
11	Prof. Kalluri Subba Rao Hon. Professor. & INSA-Senior Scientist Centre for Biotechnology, (IST) Jawaharlal Nehru Technological University Hyderabad , Andhra Pradesh	12	Prof. Gomathy Gopinath Flat #001, Kanchanjunga Apartments, 122/2, Nagavarapalaya, Varthur Road, Bangalore, Karnataka
13	Dr. T.S. Rao Advisor, Department of Biotechnology, New Delhi		

Members of the Governing Council

1	Dr. M.K. Bhan (Chairperson) Secretary Department of Biotechnology New Delhi	2	Prof. P.N. Tandon No. 1, Jagriti Enclave, Vikas Marg, New Delhi
3	Dr. T. Ramasami Secretary Department. of Science & Technology New Delhi	4	Ms. Anuradha Mitra,IDAS JS & FA Department of Biotechnology New Delhi
5	Prof. Seyed E.Hasnain Kusuma School of Biological Sciences Indian Institute of Technology Delhi, New Delhi	6	Dr. Sanjeev Jain Professor & Head NIMHANS, Bangalore, Karnataka
7	Prof. Upinder S.Bhalla NCBS Tata Institute of Fundamental Research Bangalore	8	Prof. Dinakar M. Salunke Executive Director Regional Centre for Biotechnology Gurgaon, Haryana
9	Prof. G. Mehta, FNA, FRS School of Chemistry, University of Hyderabad, Hyderabad, Andhra Pradesh	10	Dr. A.K. Agarwal Dean Maulana Azad Medical College, New Delhi
11	Prof. Chitra Sarkar Professor of Pathology AIIMS, New Delhi	12	Dr. V. M. Katoch Director-General, ICMR New Delhi
13	Dr. T.S. Rao Advisor Department of Biotechnology, New Delhi	14	Prof. Subrata Sinha (Member Secretary) Director National Brain Research Centre Manesar, Haryana

Members of the Building Committee

1	Dr. T.S. Rao (Chairman) Adviser, DBT, New Delhi	2	Dr. Satish Gupta (Member) Deputy Director, NII, New Delhi
3	Dr. Siddharth Satpathy (Member) Professor, Deptt of Hospital Administration, AIIMS, New Delhi	4	Mr. Nand Kishor (Member) Deputy Secretary, DBT, New Delhi
5	Mr. M. K. Gupta (Member) Engineer-in-charge, IURC	6	Prof. Subrata Sinha (Convener) Director, NBRC, Manesar

Members of the M.Sc. Neuroscience Co-ordination Committee

Prof. Subrata Sinha (Chairman) Director National Brain Research Centre, Manesar, Haryana	Dr. Nihar Ranjan Jana National Brain Research Centre Manesar, Haryana
Prof. K.Muralidhar Head Dept. of Zoology, University of Delhi, Delhi-110 007	Dr. Pankaj Seth National Brain Research Centre, Manesar, Haryana
Dr. Jaya Tyagi Dept. of Biotechnology, AIIMS New Delhi	Prof. Prasun Kumar Roy National Brain Research Centre, Manesar, Haryana
Dr. Arjun Surya Chembiotech Research International Block No:BN-Plot-7, Sector-5, Salt Lake, Kolkata	Dr. Pravat K. Mandal National Brain Research Centre, Manesar, Haryana
Dr.(Mrs.) Suman Govil Advisor Department of Biotechnology, C.G.O. Complex, New Delhi	Dr. Ranjit Giri National Brain Research Centre, Manesar, Haryana
Dr. Anirban Basu National Brain Research Centre Manesar, Haryana	Dr. Shiv K. Sharma National Brain Research Centre Manesar, Haryana
Dr. Ellora Sen National Brain Research Centre, Manesar, Haryana	Dr. Soumya Iyengar National Brain Research Centre, Manesar, Haryana
Dr. Nandini Singh National Brain Research Centre, Manesar, Haryana	Dr. Yoganarasimha Doreswamy National Brain Research Centre, Manesar, Haryana
Dr. Narender K. Dhingra National Brain Research Centre, Manesar, Haryana	Mr. K.V.S. Kameswara Rao National Brain Research Centre, Manesar, Haryana
Prof. Neeraj Jain National Brain Research Centre, Manesar, Haryana	

Technical Staff

Scientists

1 Prof. Subrata Sinha (Director)
2 Prof. Prasun Kumar Roy
3 Prof. Neeraj Jain
4 Dr. Nihar Ranjan Jana
5 Dr. Pravat Kumar Mandal
6 Dr. Pankaj Seth
7 Dr. Narender K. Dhingra
8 Dr. Shiv Kumar Sharma
9 Dr. Ranjit Kumar Giri
10 Dr. Nandini C. Singh
11 Dr. Soumya Iyengar
12 Dr. Anirban Basu
13 Dr. Yoganarasimha Doreswamy
14 Dr. Ellora Sen
15 Dr. Rema Velayudhan

Consultant

1 Prof. Partha Raghunathan

Research Scientist

2 Dr. Tora Mitra Ganguli

Scientist (WOS-A)

3 Dr. Sayali C. Ranade (DST Project)

Research Associate

1 Dr.Chaitra Rao (Innovation Clusters Scheme - DST)
2 Dr.Shripad Arun Kondra
3 Dr.Kallol Dutta (DBT Project)
4 Dr.Arkadeb Dutta (DBT Project)
5 Dr.Sanchari Sinha
6 Dr.Rupanjan Mukhopadhyay (Till 11/01/12)
7 Dr.Supriya Bhavnani
8 Dr.Prem Chand
9 Dr.Pratima Pandey (Till 22-06-11)
10 Dr. D.Subhashree
11 Dr. Vidhata Dixit
12 Dr. Atish Kumar Prakash (Till 25-07-11)
13 Dr. Amar Nath Maurya
14 Dr. T. Mrudula (DBT Project)

Members of the Academic Council

Prof. Subrata Sinha (Chairman) Director National Brain Research Centre, Manesar, Haryana	Dr. Nihar Ranjan Jana National Brain Research Centre Manesar, Haryana
Prof. Basabi Bhaumik Department of Electrical Engineering Indian Institute of Technology, New Delhi	Dr. Pankaj Seth National Brain Research Centre, Manesar, Haryana
Dr. V. S. Mehta Paras Hospital, Gurgaon, Haryana	Prof. Prasun Kumar Roy, National Brain Research Centre, Manesar, Haryana
Prof. K. Muralidhar Head, Dept. of Zoology, University of Delhi, Delhi	Dr. Pravat K. Mandal National Brain Research Centre, Manesar, Haryana
Dr. Anirban Basu National Brain Research Centre, Manesar, Haryana	Dr. Ranjit Giri National Brain Research Centre, Manesar, Haryana
Dr. Ellora Sen National Brain Research Centre, Manesar, Haryana	Dr. Shiv K. Sharma National Brain Research Centre, Manesar, Haryana
Dr. Nandini Singh National Brain Research Centre, Manesar, Haryana	Dr. Soumya Iyengar National Brain Research Centre, Manesar, Haryana
Dr. Narender K. Dhingra National Brain Research Centre, Manesar, Haryana	Dr. Yoganarasimha Doreswamy National Brain Research Centre, Manesar, Haryana
Prof. Neeraj Jain National Brain Research Centre, Manesar, Haryana	Mr. K.V.S. Kameswara Rao National Brain Research Centre, Manesar, Haryana

Members of the Board of Studies

Prof. Subrata Sinha (Chairman) Director, National Brain Research Centre, Manesar, Haryana	Dr. Pankaj Seth National Brain Research Centre Manesar, Haryana
Prof. D. N. Rao Indian Institute of Sciences, Bangalore, Karnataka	Prof. Prasun Kumar Roy National Brain Research Centre, Manesar, Haryana
Prof. Rohit Manchanda Indian Institute of Technology, Mumbai, Maharashtra	Dr. Pravat K. Mandal National Brain Research Centre, Manesar, Haryana
Dr. Anirban Basu National Brain Research Centre, Manesar, Haryana	Dr. Ranjit Giri National Brain Research Centre, Manesar, Haryana
Dr. Ellora Sen National Brain Research Centre, Manesar, Haryana	Dr. Shiv K. Sharma National Brain Research Centre, Manesar, Haryana
Dr. Nandini Singh National Brain Research Centre, Manesar, Haryana	Dr. Soumya Iyengar National Brain Research Centre, Manesar, Haryana
Dr. Narender K. Dhingra National Brain Research Centre, Manesar, Haryana	Dr. Yoganarasimha Doreswamy National Brain Research Centre, Manesar, Haryana
Prof. Neeraj Jain National Brain Research Centre, Manesar, Haryana	Mr. K.V.S. Kameswara Rao National Brain Research Centre, Manesar, Haryana
Dr. Nihar Ranjan Jana National Brain Research Centre, Manesar, Haryana	

Members of the Building Committee

1	Dr. T.S. Rao (Chairperson) Advisor Department of Biotechnology, New Delhi	2	Dr. Satish Gupta Scientist National Institute of Immunology, New Delhi
3	Prof. Subrata Sinha Director National Brain Research Centre Manesar, Haryana	4	Shri B. Bose Senior Consultant National Institute of Immunology, New Delhi
5	Mr. K.V.S.Kameswara Rao Registrar National Brain Research Centre, Manesar, Haryana	6	Mr. Kannan Kasturi N.S (Member Secretary) Offg.Chief Administrative Officer National Brain Research Centre, Manesar, Haryana

Members of the M.Sc. Neuroscience Co-ordination Committee

Prof. Subrata Sinha (Chairman) Director National Brain Research Centre, Manesar, Haryana	Dr. Nihar Ranjan Jana National Brain Research Centre Manesar, Haryana
Prof. K.Muralidhar Head Dept. of Zoology, University of Delhi, Delhi-110 007	Dr. Pankaj Seth National Brain Research Centre, Manesar, Haryana
Dr. Jaya Tyagi Dept. of Biotechnology, AIIMS New Delhi	Prof. Prasun Kumar Roy National Brain Research Centre, Manesar, Haryana
Dr. Arjun Surya Chembiotech Research International Block No:BN-Plot-7, Sector-5, Salt Lake, Kolkata	Dr. Pravat K. Mandal National Brain Research Centre, Manesar, Haryana
Dr.(Mrs.) Suman Govil Advisor Department of Biotechnology, C.G.O. Complex, New Delhi	Dr. Ranjit Giri National Brain Research Centre, Manesar, Haryana
Dr. Anirban Basu National Brain Research Centre Manesar, Haryana	Dr. Shiv K. Sharma National Brain Research Centre Manesar, Haryana
Dr. Ellora Sen National Brain Research Centre, Manesar, Haryana	Dr. Soumya Iyengar National Brain Research Centre, Manesar, Haryana
Dr. Nandini Singh National Brain Research Centre, Manesar, Haryana	Dr. Yoganarasimha Doreswamy National Brain Research Centre, Manesar, Haryana
Dr. Narender K. Dhingra National Brain Research Centre, Manesar, Haryana	Mr. K.V.S. Kameswara Rao National Brain Research Centre, Manesar, Haryana
Prof. Neeraj Jain National Brain Research Centre, Manesar, Haryana	

Technical Staff

Scientists

1 Prof. Subrata Sinha (Director)
2 Prof. Prasun Kumar Roy
3 Prof. Neeraj Jain
4 Dr. Nihar Ranjan Jana
5 Dr. Pravat Kumar Mandal
6 Dr. Pankaj Seth
7 Dr. Narender K. Dhingra
8 Dr. Shiv Kumar Sharma
9 Dr. Ranjit Kumar Giri
10 Dr. Nandini C. Singh
11 Dr. Soumya Iyengar
12 Dr. Anirban Basu
13 Dr. Yoganarasimha Doreswamy
14 Dr. Ellora Sen
15 Dr. Rema Velayudhan

Consultant

1 Prof. Partha Raghunathan

Research Scientist

2 Dr. Tora Mitra Ganguli

Scientist (WOS-A)

3 Dr. Sayali C. Ranade (DST Project)

Research Associate

1 Dr.Chaitra Rao (Innovation Clusters Scheme - DST)
2 Dr.Shripad Arun Kondra
3 Dr.Kallol Dutta (DBT Project)
4 Dr.Arkadeb Dutta (DBT Project)
5 Dr.Sanchari Sinha
6 Dr.Rupanjan Mukhopadhyay (Till 11/01/12)
7 Dr.Supriya Bhavnani
8 Dr.Prem Chand
9 Dr.Pratima Pandey (Till 22-06-11)
10 Dr. D.Subhashree
11 Dr. Vidhata Dixit
12 Dr. Atish Kumar Prakash (Till 25-07-11)
13 Dr. Amar Nath Maurya
14 Dr. T. Mrudula (DBT Project)

Senior R&D Engineer / Sr. Scientific Officer

1 Mr.V.P.Subramanyam Rallabandi (DRDO Project)

R&D Engineer

1 Mr. Himanshu Akolkar (Till 25-01-12)
2 Mr. Komal Janghel (Till 30-06-11)
3 Ms.Gargi Mishra (Till 30-06-11)
4 Mr. Ashish Chittora (Till 08-08-11)
5 Mr. S.A.Manigandan (Till 09-11-11)
6 Ms. Rashima Mahajan (Till 29-02-12)
7 Ms. Sweta Chander (Till 30-11-11)
8 Mr. Rajdeep Singh Rathore
9 Ms. Tejaswini Adikane

Junior R&D Engineer

1 Mr. Amit Lal (Till 12-07-11)
2 Ms. Manisha Ahuja (Till 15-06-11)
3 Mr. Sudip Chatterjee (Till 08-12-11)
4 Mr. Joshi Jitesh Narendra

Psychologist

1 Ms.Rashi Midha (DBT Project)

SRF

1 Mr. Mohd Sikender

JRF (Project)

1 Ms. Aditi Arora (Till 28-09-11)
2 Mr. Sourav Ghosh (Till 04-11-11)
3 Mr. Rahul V.V.
4 Mr. Ashwat Nagarajan

Research Assistant

1 Mr. Sukhvir Pundir (DBT Project)

Technical Assistant

1 Ms. T.A.Sumathi

Programmer

1 Mr. Tanmay Nath

Statistician

1 Mr. Arnab Chakrabarti

Ph.D. Students

1 Ms. Chinmoyee Maharana
2 Mr. Leslee Lazar
3 Mr. Arjun R
4 Mr. Niranjan A. Kambi
5 Mr. Jaiprakash Sharma
6 Ms. Neha Sahgal
7 Mohd. Hisham P.M
8 Ms.Rupali Srivastava
9 Ms. Richa Tiwari (Till 01-07-11)
10 Ms. Radhika Rajan
11 Ms. Shilpa Mishra
12 Mr. Subhadip Paul
13 Mr. Parthiv Haldipur (Till 02-03-12)
14 Mr. Nitin Koul (Till 01-01-11)
15 Ms. Tanushree Das (Till 29-04-11)
16 Mr. Kaushik Pramod Sharma
17 Ms. Neha Bhutani
18 Ms. K.M.Sharika
19 Mr. Sudheendra Rao
20 Mr. Rahul Chaudhary
21 Mr. Pankaj S Ghate
22 Mr. Deepak Kr Kaushik
23 Mr. Deobrat Dixit
24 Ms. Kiran
25 Mr. Arshed Nazmi
26 Mr. Apoorv Sharma
27 Ms. Pretty Garg
28 Ms. Manju Tewari
29 Mr. I Mohd Ariff
30 Mr. Dharam Pal (Till 05-08-11)
31 Mr.Sandeep Kumar
32 Mr.Vaibhav Tyagi
33 Mr.Sourish Ghosh
34 Mr.Bharat Prajapati
35 Ms.Mehar Fatima
36 Mr.Vasav J.Arora
37 Mr.Atesh Koul
38 Ms. Tripti Rai (Till 04-11-11)
39 Ms. Neelam Singh (Till 17-02-12)
40 Mr. Brijesh Kumar Singh
41 Mr. John Thomas
42 Mr. Arghya Dutta Choudhury
43 Mr. Kautuk Kamboj

Integrated Ph.D. Students

1 Ms. Swetha Kameswari
2 Ms. Varsha Jain
3 Mr. Ajit Ray
4 Ms. Shaily Malik
5 Mr. Sadashib Ghosh
6 Ms. Megha Maheswari
7 Mr. Deepak Poria
8 Mr. Manvi Goel
9 Mr. Pavan Kumar R.
10 Mr. Atul Gopal PA
11 Ms. Megha Sharda
12 Ms. Suhela Kapoor
13 Ms. Guncha Bhasin
14 Ms. Sarika Cherodath
15 Ms. Himakshi
16 Ms. Ruchi Ghildiyal
17 Ms.Piyushi Gupta
18 Ms. Avantika Mathur
19 Ms. Shankhamala Sen
20 Mr.Priyabrata Halder
21 Mr.Imran Jamal
22 Mr.Fahim Ahmad
23 Ms.Manika Arora
24 Ms.Uzma Din
25 Ms.Rekha S.Varrier
26 Ms. Chitra Mohinder Singh Singhal
27 Ms. Utkarsha A.Singh
28 Ms. Kirti Snigdha (Till 26-08-11)
29 Ms. Pooja Parishar
30 Mr. Apurva Agarwal
31 Mr. Atanu Datta

Project Assistants

1 Mr.R.Ethiraj
2 Mr.Saurav Roy Choudhury (Till 08-11-11)
3 Mr. L.Shahul Hameed (Till 01-07-11)

4 Ms.Kanchan Bisht
5 Ms.Malvika Gupta (Till 02-12-12)
6 Ms.Ananya Samanta
7 Mr.Diptendu Mukherjee
8 Mr.Dwaipayan Adhya
9 Ms.Anya Chakraborty
10 Ms.G.Revathy
11 Ms.Neethu Michael
12 Mr.Sourav Ghosh
13 Mr.Jeet Bahadur Singh (Till 23-11-11)
14 Mr.N.Ramanathan
15 Mr.G.Naga Rajesh
16 Mr. Nikhil Ahuja
17 Mr. Sabyasachi Das
18 Mr. Darpan Chakraborty
19 Mr. Rajeev Ramaswamy
20 Ms.Sashirekha Sahoo
21 Ms.Panghki Medhi
22 Ms.Sushma
23 Ms. Rinki Saha
24 Mr.Arinjay Mitra
25 Mr. Kaushik Kumar Deka
26 Ms. Saba Parween
27 Mr. Bandhan Mukherjee
28 Mr. Abhinaba Ghosh
29 Ms.Upasana Sahu (Till 30-06-11)
30 Mr. Nilabh Anand
31 Mr. Aniruddha Das
32 Mr. Rajarshi Mukherjee
33 Mr.Rakesh Kr. Ruhela
34 Ms. Arti Kumari (Till 09-11-11)
35 Ms. Manisha Ahuja (Till 03-05-11)
36 Mr. Saurabh Ghosh
37 Mr. Partha Narayan Dey (Till 28-04-11)
38 Ms. Pangkhi Medhi
39 Mr. Kaushik Kumar Deka
40 Ms. Saba Parween
41 Mr. Bandhan Mukherjee
42 Mr. Abhinaba Ghosh
43 Mr. Aniruddha Das
44 Mr. Rajarshi Mukherjee
45 Mr. Manu Verma (Till 12-08-11)
46 Mr. Shubhranshu Shekhar Jena (Till 15-02-12)
47 Ms. Aparna Ghildiyal (Till 02-12-12)
48 Ms. Teesta Naskar
49 Mr. Tanveer Verma
50 Mr. Arkoprovo Paul
51 Ms. Sriya Bhattacharya
52 Mr. Kiran Kundu
53 Mr. Himanshu (Till 30-11-11)
54 Mr. Anshu Khandelwal
55 Mr. Namit Bharija
56 Mr. Kuldeep Tripathi
57 Mr. Nikhil Anto P.
58 Ms. Gitanjali Nanda (Till 13-02-12)
59 Ms. Jyothirmayi Vadlamudi
60 Ms. Avipsa Mohanty
61 Ms. Snigdha Kundu (Roy)
62 Ms. Patel Varsha Atulbhai
63 Ms. Ankita Srivastava
64 Ms. Nidhi Chandra

Other Staff

Technical Staff

1 Mr. Rajbir Singh
2 Mr. Sanjeev K. Choudhary
3 Mr. Dev Das Lal
4 Mr. Mahender Kumar Singh
5 Dr. Suresh Kumar (till 29.8.2011)
6 Mr. Jitender Ahlawat
7 Mr. Arvind Singh Pundir
8 Mr. Kanhaiya Lal Kumawat
9 Mr. Kedar Singh Bajetha
10 Mr. Shankar Dutt Joshi
11 Mr. Sumit Kumar Sinha Mahapatra
12 Mr. D. Narender
13 Mr. Sanjay Kumar
14 Mr. Mithlesh Kumar Singh
15 Mr. Ankit Sharma
16 Mr. Sanjeev Bhardwaj
17 Mr. Yunis Khan
18 Mr. Durgalal Meena
19 Mr. Irshad Alam
20 Mr. P. Manish
21 Mr. Dil Bahadur Karki
22 Mr. Rammehar
23 Mr. Manish Kumar
24 Mr. Hari Shankar
25 Mr. Mahendra Singh
26 Mr. Sanjay Kumar Singh

Administrative Staff

1 Mr. K.V.S. Kameswara Rao
2 Mr. Kannan Kasturi N. S. (till 5.3.2012)
3 Mr. Santosh Kumar Choudhary
4 Mr. Debashish Bhattacharjee
5 Mr. Ravinder Pal
6 Mr. Sunil Kumar Dwivedi (from 15.11.2011)
7 Ms. Pooja Gosain
8 Mr. Sanjay Kumar Gupta
9 Mr. Shiv Kumar
10 Mr. Rajbir Singh
11 Mr. Surender Kumar
12 Mr. Bhupender Pal Sharma
13 Mr. Satish Kumar

DIC Staff

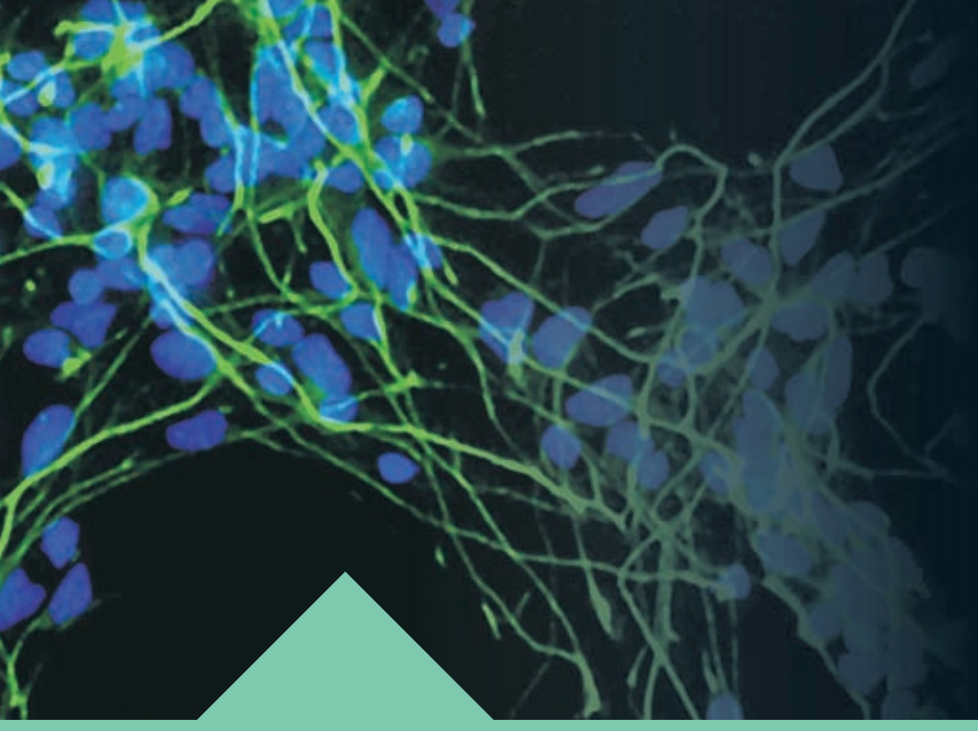
1 Mr. Jibananda Chhotaray
2 Ms. Reema Saxena
3 Mr. Amit Kumar
4 Ms. Sunita
5 Mr. R. Ganesh Gurumoorthy

NBRC Construction Project Staff

1 Mr. Shailender Singh
2 Mr. Anil Kumar Yadav
3 Mr. Bhupender Singh
4 Mr. Subhashji Roy

Contractual Staff

1 Dr. Inderjeet Yadav
2 Mukesh Chauhan
3 Mukesh Kumar Pandey
4 Shweta Mishra



Budget

National Brain Research Centre

NBRC

Auditor's Report

To,
The Members of
M/s National Brain Research Centre
NH-8, Nainwal More, Manesar
Gurgaon (Haryana)

We have audited the attached Balance Sheet of M/s National Brain Research Centre, Nainwal More, Near NSG Campus, Manesar, Gurgaon as at 31st March 2012 and the related statements for the period ended on that date, annexed thereto. These financial statements are the responsibility of the centre's management. Our responsibility is to express an opinion on these financial statements based on our audit.

1. We conducted our audit in accordance with auditing standards generally accepted in India. These standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement(s). An audit includes examining, on test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principals used and significant estimates made by the management, as well as evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis of our opinion.

2. Further to our comments subject to Notes on Accounts as per Schedule-16, we report that:

   2.1 We have obtained all the information and explanation, which to the best of our knowledge and belief were necessary for the purpose of our audit.

   2.2 In our opinion, proper books of accounts, as required by law, have been kept by the centre so far as appears from our examination of these books.

   2.3 The Balance Sheet dealt with by this report is in agreement with the books of accounts.

   2.4 Subject to Significant Accounting Policies and notes on accounts thereon and in our opinion to the best of our information and according to the explanations given to us, the said Income & Expenditure & Balance Sheet comply with the Accounting Standards issued by the Institute of Chartered Accountants of India

   2.5 In our opinion and to the best of our information and according to the explanations given to us, the said accounts read together with the notes thereon, give the information required in the manner so required and give a true and fair view:

   2.5.1 In case of Balance Sheet, of the state of affairs of the centre as at 31st March 2012;

   2.5.2 In the case of the Income & Expenditure, of the Surplus of the centre for the period ended on that date.

For **A. K. WADHWA & ASSOCIATES**
Chartered Accountants

Place: Gurgaon
Dated: 28th June, 2012

(ATUL KUMAR WADHWA)
Partner/Proprietor
M.No. 088237

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

BALANCE SHEET AS AT 31st MARCH 2012

	SCHEDULE	CURRENT YEAR	PREVIOUS YEAR
CORPUS / CAPITAL FUND AND LIABILITIES			
CORPUS/ CAPITAL FUND	**1**	1,131,074,000.00	961,074,000.00
RESERVE AND SURPLUS	**2**	178,875,603.57	178,220,600.33
EARMARKED/ ENDOWMENT FUNDS	**3**	754,162,690.90	743,457,520.70
CURRENT LIABILITIES AND PROVISIONS	**4**	24,610,969.72	31,918,980.72
TOTAL		**2,088,723,264.19**	**1,914,671,101.75**
ASSETS			
FIXED ASSETS	**5**	969,879,087.96	944,742,482.33
INVESTMENTS - CPF FUND	**6**	13,386,646.81	21,912,285.16
CURRENT ASSETS, LOANS, ADVANCES ETC.	**7**	1,105,457,529.42	948,016,334.26
TOTAL		**2,088,723,264.19**	**1,914,671,101.75**
NOTES ON ACCOUNTS	**16**		

SANTOSH K CHOUDHARY
DY. FINANCE OFFICER

PROF. SUBRATA SINHA
DIRECTOR

FOR A.K WADHWA & ASSOCIATES
CHARTERED ACCOUNTANTS

A.K WADHWA
PROPRIETOR
MEMBER SHIPNO.088237

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

INCOME AND EXPENDITURE ACCOUNT FOR THE YEAR ENDED 31.03.2012

	SCHEDULE	CURRENT YEAR	PREVIOUS YEAR
INCOME			
Grants/ Subsidies		**108,569,000.00**	147,477,000.00
Fees/Subscriptions	**8**	**2,327,266.25**	2,631,130.50
Interest Earned	**9**	**53,630,656.90**	35,741,318.58
Other Income	**10**	**968,690.00**	991,372.00
TOTAL (A)		**165,495,613.15**	**186,840,821.08**
EXPENDITURE			
Establishment Expenses	**11**	52,045,081.00	43,168,291.00
Other Administrative/Lab Expenses etc.	**12**	13,336,663.74	11,855,404.13
Repair & Maintenance	**13**	39,483,489.56	35,053,733.00
Training and Networking Expenses	**14**	16,087,189.46	14,274,080.00
Laboratory and Animal house consumables	**15**	34,675,789.15	31,027,736.51
Depreciation	**5**	9,212,397.00	8,374,460.00
TOTAL (B)		**164,840,609.91**	**143,753,704.64**
BALANCE BEING SURPLUS/(DEFECIT) CARRIED TO RESERVE & SURPLUS (A-B)		**655,003.24**	**43,087,116.44**

SANTOSH K CHOUDHARY
DY. FINANCE OFFICER

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DIRECTOR

FOR A.K WADHWA & ASSOCIATES
CHARTERED ACCOUNTANTS

A.K WADHWA
PROPRIETOR
MEMBER SHIPNO.088237

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

RECEIPTS AND PAYMENTS OF FOR THE YEAR ENDED 31.03.2012

	RECEIPT	CURRENT YEAR	PREVIOUS YEAR		PAYMENT	CURRENT YEAR	PREVIOUS YEAR
I.	**Opening Balances**			I.	**Expences**		
a)	Cash in Hand	120,239.00	180,029.00	i)	Establishment Expenses (Corresponding to Schedule 11)	4,521,750.00	4,378,268.00
b)	Bank Balances			ii)	Administrative Expenses (Corresponding to Schedule 12-15)	4,008,758.74	3,580,951.13
i)	In Deposit Accounts	929,923,832.32	444,971,497.69				
ii)	Saving Accounts	4,828,412.16	25,515,149.00	II.	**Payment made against funds for various projects**		
iii)	CPF Investments	21,091,183.00	19,356,198.00		Capital Expenditure	4,686,280.84	2,664,711.00
					Recurring expenditure	8,590,643.52	6,992,637.00
II.	**Grants Received**						
a)	From Government of India			III.	**Maintenance Cost**		
	PLAN			i)	Lab Maintenance Expenses	34,562,596.07	29,470,614.00
i)	Recurring Expenditure	108,569,000.00	101,523,000.00	ii)	Office Maintenance	18,876,463.00	15,084,771.00
ii)	Non-Recurring Expenditure	170,000,000.00	147,477,000.00	iii)	Vehicle Running & Maintenance	145,817.00	184,287.00
	NON PLAN (Recurring)						
b)	Fellowship Grant	1,139,359.00	977,414.00	III.	**Investment and deposit made**		
c)	Delcon Projects	164,988,146.00	107,662,902.00	i)	Out of Earkmark/Endowment funds	189597704.44	139,072,497.00
				ii)	Out of Own Funds (Investments-Others)	-	-
III.	**Receipt made against funds for various projects**						
i)	Capital Receipt			IV.	**Expenditure of Fixed Assets & Capital Work-in-progress (see sch-5)**		
ii)	Recurring Receipt	40,532,584.78	415,474,027.00	i)	Purchase of Fixed Asstts	25,289,199.47	28,932,354.00
				ii)	Expenditure on Capital Work-in-Progress		
IV.	**Interest Received(See Sch-9)**						
i)	On Bank deposits	63,460,886.25	33,206,304.42	V.	Training Expenses	2,171,536.46	3,351,053.00
ii)	Savings Account	1,758,250.00	1,305,557.00				
iii)	On CPF Fund	1,015,711.00	469,175.81	VI.	Other Payments(Specify)		
iv)	Other Interest	4,111.00	-	i)	Advance to Supplier	16,478,804.66	6,798,845.81
				ii)	Advance to staff	6,418,437.16	3,847,756.00

V.	**Any other receipt (As per Schedule-8 to10)**			iii)	Leave Encashment/ Gratuity/ Bonus	820,093.00	359,004.00
	Indirect Income			iv)	Securiety deposit received(paid)	831,772.00	944,946.00
i)	Advance to Supplier received	364,053.18	101,632.00	v)	EMD Refunded	389,400.00	1,307,900.00
ii)	Advance to Staff received	791,953.00	426,871.00	vi)	TDS Payable	3,714,052.00	2,063,915.00
iii)	Sale of tender documents	26,000.00	21,000.00	vii)	Imperest	146,602.00	192,867.00
iv)	Misc.Receipts (Application fee,etc)	849,545.25	1,080,274.50	viii)	Prepaid Insurance Charge	578,219.00	934,344.00
v)	Earnest Deposit Money received	2,668,600.00	1,035,200.00	ix)	TDS Deducted	52,220.00	
vi)	Sale of Scrap	136,600.00	3,500.00	x)	Medical Contribution recovery	1,760.00	-
vii)	Security Deposit received	21,539.55	818,540.00	xi)	Payment Of Current Liabilities.	99,226,554.00	100,642,286.00
viii)	Annual Fees(M.Sc,Ph.D)/ Transcript fee	52,917.00	438,530.00				
ix)	Hostel Deposit	252,000.00	173,000.00	**VII**	**Closing balances**		
x)	CPF Fund received	3,239,747.00	3,876,463.00	a)	Cash in Hand	194,153.00	120,239.00
xi)	Library Deposit	68,000.00	44,000.00	b)	Bank Balance		
xii)	Current Liabilities rec.	251,690.00	449,123.00	i)	In Deposit Accounts	1,054,275,015.52	929,923,832.32
xiii)	Licence Fee Recovery	-	2,040.00	ii)	Saving Accounts	30,576,527.61	4,828,412.16
xiv)	Donation	-	179,246.00	iii)	CPF Investments	10,000,000.00	21,091,183.00
	TOTAL	**1,516,154,359.49**	**1,306,767,673.42**		**TOTAL**	**1,516,154,359.49**	**1,306,767,673.42**

SANTOSH K CHOUDHARY
DY. FINANCE OFFICER

PROF. SUBRATA SINHA
DIRECTOR

FOR A.K WADHWA & ASSOCIATES
CHARTERED ACCOUNTANTS

A.K WADHWA
PROPRIETOR
MEMBER SHIPNO.088237

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

SCHEDULE FORMING PART OF BALANCE SHEET AS AT 31.03.12

	AMOUNT IN (RS)			
SCHEDULE 1-CORPUS/CAPITAL FUND:	**CURRENT YEAR**		**PREVIOUS YEAR**	
1. Grant-in-Aid - Balance as at the beginning of the year		961,074,000.00		859,551,000.00
Add: Contribution towards Corpus/ Capital Fund	170,000,000.00		101,523,000.00	
		170,000,000.00		101,523,000.00
Balance as at the Year - End		**1,131,074,000.00**		**961,074,000.00**

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

SCHEDULE FORMING PART OF BALANCE SHEET AS AT 31.03.12

	AMOUNT IN (RS)			
SCHEDULE 2 - RESERVES AND SURPLUS:	**CURRENT YEAR**		**PREVIOUS YEAR**	
1. GENERAL RESERVE				
As per last Account	178,220,600.33		135,133,483.89	
Addition during the Year	655,003.24		43,087,116.44	
Less : Deductions during the year (deficit)		178,875,603.57		178,220,600.33
Total		**178,875,603.57**		**178,220,600.33**

SANTOSH K CHOUDHARY
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DIRECTOR

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CHARTERED ACCOUNTANTS

A.K WADHWA
PROPRIETOR
MEMBER SHIPNO.088237

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

SCHEDULE FORMING PART OF BALANCE SHEET AS AT 31.03.12

SCHEDULE 3 - EARMARKED / ENDOWMENT FUNDS		AMOUNT IN (RS)			
		CURRENT YEAR		PREVIOUS YEAR	
	(Refer Annexures I - LXXII)				
A.	**Opening Balance of Project Fund**	395,921,628.78		1,135,509.08	
	Add : Grants Received during the year	55,644,630.78		409,501,539.00	
	Less : Grants Refunded During the year	-692,386.00		(330,093.00)	
	Any other addition during the year	0.00	450,873,873.56	5,898,691.00	416,205,646.08
	Less: Utilization / Expenditure towards objectives of funds				
	a) Capital Expenditure				
	Fixed Assets	6,076,730.22		2,928,565.00	
	Others				
	b) Revenue Expenditure				
	Salaries and wages and	6,752,342.00		4,343,634.00	
	Other Administrative Expenses	8,694,098.14		13,011,818.30	
			21,523,170.36		20,284,017.30
	Total (a)		**429,350,703.20**		**395,921,628.78**
B.	**Opening Balance of Fixed Asset Fund (Project)**	172,427,058.92		179,827,069.33	
	Add: Addition During the year	7,840,386.22		1,164,909.00	
	Less:Depreciation for the period 2011-12	8,485,452.00		8,564,919.41	
	Total (b)		**171,781,993.14**		**172,427,058.92**
C.	**Opening balance of Donation received**	2,631,788.00		2,452,542.00	
	Add: Additions during the year	0.00	**2,631,788.00**	179,246.00	**2,631,788.00**
D.	**Endowment fund created for Buildings Opening Balance**	81,284,807.00		81,284,807.00	
	Add: Additions / (Paymnet) during the year	0.00	**81,284,807.00**	0.00	**81,284,807.00**
E.	**Contributory Provident Fund**	10,827,274.00	**10,827,274.00**	20,321,935.00	**20,321,935.00**
F.	**DeLcon E-library Consortium**				
	Opening balance of Consortium	13,344,303.00		43,417,568.00	
	Add : Grants Received during the year	164,988,146.00		107,303,000.00	
	Less: Utilization / Expenditure towards objectives of funds	177,572,323.44		137,376,265.00	
			760,125.56		**13,344,303.00**
G.	**Escrow Account-DBT**				
	Opening balance	57,526,000.00		57,526,000.00	
	Add: Grant Received During the Year	0.00	**57,526,000.00**	0.00	**57,526,000.00**
	Grand total (A+B+C+D+E+F+G)		**754,162,690.90**		**743,457,520.70**

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SCHEDULE FORMING PART OF BALANCE SHEET AS AT 31.03.12

SCHEDULE-4 CURRENT LIABILITIES AND PROVISIONS	AMOUNT IN (RS)			
	CURRENT YEAR		PREVIOUS YEAR	
A. CURRENT LIABILITIES				
1 Sundry Creditors	697,159.00		4,067,549.00	
2 Advances Received (Security deposit)	1,550,751.00		2,249,341.00	
3 Other Liabilities-TDS Payable	95,435.00		134,633.00	
4 Earnest Money Deposit	3,509,609.00		1,255,409.00	
5 Hostel Deposit	552,000.00		465,000.00	
6 Library Deposit	138,000.00		106,000.00	
7 Expenses Payable	782,969.92		6,154,925.92	
8 CPF Payable	296,571.00		172,419.00	
9 GIS Payable	10,294.00		3,034.00	
10 Salary Payable	4,825,903.00		4,799,531.00	
11 NPS(Employees Subscription)	10,297.00		0.00	
12 Prime Minister's Relief Fund	22,567.00	12,491,555.92	22,567.00	19,430,408.92
TOTAL (A)		**12,491,555.92**		**19,430,408.92**
B. PROVISIONS				
1 Gratuity	7,967,087.00		7,965,448.00	
2 Accumulated Leave Encashment	4,152,326.80		4,523,123.80	
		12,119,413.80		12,488,571.80
TOTAL (B)		**12,119,413.80**		**12,488,571.80**
TOTAL (A+B)		**24,610,969.72**		**31,918,980.72**

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SCHEDULE FORMING PART OF BALANCE SHEET AS AT 31.03.12

SCHEDULE 5 - FIXED ASSETS/ DEPRECIATON		GROSS BLOCK				DEPRICIATION				NET BLOCK	
		Cost /valuation As at beginning of the Year	Additions during the Year	Deduc-tions during the Year	Cost /valuation As at end of the Year	As at the beginning of the Year	Depreciation for current year	On Deduc-tions during the Year	Total Depn. Upto 31.03.12	As at Current year-end	As at Previous year-end
A.	FIXED ASSETS										
1	BUILDING	33,979,299.00	20,314,257.00	0.00	54,293,556.00	732,068.86	723630.00	0.00	1,455,698.86	52,837,857.14	33,247,230.14
2	PLANT & MACHINERY AND EQUIPMENT	173,007,656.00	11,670,418.41	0.00	184,678,074.41	38,722,340.54	6,678,279.00	0.00	45,400,619.54	139,277,454.87	134,285,315.46
3	VEHICLES	1,467,305.00	0.00	0.00	1,467,305.00	909,464.48	52,995.00	0.00	962,459.48	504,845.52	557,840.52
4	FURNITURE & FIXTURES	25,035,014.00	204,057.00	0.00	25,239,071.00	8,963,260.32	1,023,322.00	0.00	9,986,582.32	15,252,488.68	16,071,753.68
5	OFFICE EQUIPMENT	19,290,410.00	1,250,706.00	0.00	20,541,116.00	4,409,595.12	734,171.00	0.00	5,143,766.12	15,397,349.88	14,880,814.88
	TOTAL OF THE CURRENT YEAR	**252,779,684.00**	**33,439,438.41**	**0.00**	**286,219,122.41**	**53,736,729.32**	**9,212,397.00**	**0.00**	**62,949,126.32**	**223,269,996.09**	**199,042,954.68**
B.	**FIXED ASSETS (PROJECTS)**										
1	PROJECT EQUIPMENTS	229,493,020.00	7,840,386.22	0.00	237,333,406.22	57,065,961.08	8,485,452.00	0.00	65,551,413.08	171,781,993.14	172,427,058.92
	TOTAL OF THE CURRENT YEAR(A+B)	**482,272,704.00**	**41,279,824.63**	**0.00**	**523,552,528.63**	**110,802,690.40**	**17,697,849.00**	**0.00**	**128,500,539.40**	**395,051,989.23**	**371,470,013.60**
	PREVIOUS YEAR	**438,627,008.00**	**43,645,696.00**	**0.00**	**482,272,704.00**	**93,863,310.99**	**16,939,379.41**	**0.00**	**110,802,690.40**	**371,470,013.60**	**344,763,697.01**
C.	**CAPITAL WORK IN PROGRESS**										
1	**BUILDINGS**										
	Capital work-in-progress including advances,	573,044,168.73	0.00	0.00	573,044,168.73	0.00	0.00	0.00	0.00	573,044,168.73	573,044,168.73
	construction materials and building under										
	construction (net of recovery)										
2	Patent and Copy Right (Application Fee)	228,300.00	1,554,630.00	0.00	1,782,930.00	0.00	0.00	0.00	0.00	1,782,930.00	228,300.00
	TOTAL (A + B+C)	**1,055,545,172.73**	**42,834,454.63**	**0.00**	**1,098,379,627.36**	**110,802,690.40**	**17,697,849.00**	**0.00**	**128,500,539.40**	**969,879,087.96**	**944,742,482.33**

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SCHEDULE FORMING PART OF BALANCE SHEET AS AT 31.03.12

SCHEDULE 6- INVESTMENTS - CPF FUND	AMOUNT IN (RS)	
	CURRENT YEAR	PREVIOUS YEAR
1. FDR In scheduled Banks	**10,000,000.00**	21,686,141.35
2. Balance with Savings Bank Account	**3,386,646.81**	226,143.81
	13,386,646.81	**21,912,285.16**

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SCHEDULE 7 - CURRENT ASSETS, LOANS, ADVANCES ETC.	AMOUNT IN (RS)			
	CURRENT YEAR		PREVIOUS YEAR	
A CURRENT ASSETS				
1 Cash Balances in hand (Including Cheques / Drafts)		194,153.00		120,239.00
2 Bank Balances:				
a) With Schduled Banks:				
-In Deposit Account	684,550,470.52		564,923,832.32	
-In Saving Accounts	27,189,880.80		4,602,268.35	
-In Saving Accounts (Escrow Account)	57,526,000.00		57,526,000.00	
-In Deposit Against various Project Assets	312,198,545.00	1,081,464,896.32	307,474,000.00	934,526,100.67
TOTAL (A)		**1,081,659,049.32**		**934,646,339.67**
B LOANS, ADVANCES AND OTHER ASETS				
1 Advances and other amounts receivable in cash or in kind or for value to be received				
a) Staff	4,339,605.16		1,931,302.00	
b) Prepayments (Advance to NIMHANS)	0.00		1,200,000.00	
c) Advance to Parties	13,438,004.90		4,439,193.00	
d) Others(Security & other Deposits)	413,922.45		435,462.00	
e) TDS Receivable	4,481,913.59		4,429,693.59	
f) Prepaid Insurance	1,125,034.00		934,344.00	
		23,798,480.10		13,369,994.59
TOTAL (B)		**23,798,480.10**		**13,369,994.59**
TOTAL (A + B)		**1,105,457,529.42**		**948,016,334.26**

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SCHEDULE FORMING PART OF INCOME AND EXPENDITURE FOR THE YEAR ENDED 31.03.2012

SCHEDULE 8 - FEES/ SUBSCRIPTIONS	AMOUNT IN (RS)	
	CURRENT YEAR	PREVIOUS YEAR
1. Application Fees (Net)	844,990.25	557,530.00
2. Annual Fees/ Subscription to Journals	342,917.00	1,096,186.50
3. Others (Specify)-Fellowship Grants	1,139,359.00	977,414.00
TOTAL	**2,327,266.25**	**2,631,130.50**

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SCHEDULE 9 - INTEREST EARNED	AMOUNT IN (RS)	
	CURRENT YEAR	PREVIOUS YEAR
1) On Term Deposits:		
a) With Scheduled Banks	51,856,028.90	34,435,761.58
2) On Savings Accounts:		
a) With Scheduled Banks	1,758,250.00	1,305,557.00
3) On Advances:	16,378.00	0.00
TOTAL	**53,630,656.90**	**35,741,318.58**

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SCHEDULE 10-OTHER INCOME	AMOUNT IN (RS)	
	CURRENT YEAR	PREVIOUS YEAR
1. Projects Receipts	0.00	100,000.00
2. Tender Form	26,000.00	21,000.00
3. Overhead charges	195,400.00	142,120.00
4. Miscellaneous (Scrap)	136,600.00	3,500.00
5. Delcon operational income	274,599.00	724,752.00
6. Medical Contribution Recovery	170,460.00	0.00
7. Licence Fee Recovery	165,631.00	0.00
TOTAL	**968,690.00**	**991,372.00**

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SCHEDULE FORMING PART OF INCOME AND EXPENDITURE FOR THE YEAR ENDED 31.03.2012

SCHEDULE 11 - ESTABLISHMENT EXPENSES	AMOUNT IN (RS)	
	CURRENT YEAR	PREVIOUS YEAR
1 Salaries and Wages and allowances	39,556,755.00	32,400,131.00
2 Bonus	146,508.00	138,448.00
3 Contribution to Pension Scheme	1,207,864.00	1,702,759.00
4 Staff Welfare Expenses	106,322.00	66,684.00
5 Children Education Reimbursement	669,464.00	594,382.00
6 Leave Encashment	115,440.00	131,602.00
7 LTC Expenses	646369.00	463146.00
8 Medical Expenses	851,629.00	549,577.00
9 NPS(Employers Subscription)	595,530.00	0.00
Overtime Allowance	26,837.00	40,130.00
Rent for Residence	665,838.00	555,430.00
Honorarium	174,000.00	184,000.00
Skilled Manpower	6,382,000.00	4,976,893.00
Transfer Grant	33,888.00	40,000.00
Computational Neuroscience Expenses	0.00	591,851.00
Medical Insurance	866,637.00	733,258.00
TOTAL	**52,045,081.00**	**43,168,291.00**

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SCHEDULE FORMING PART OF INCOME AND EXPENDITURE FOR THE YEAR ENDED 31.03.2012

SCHEDULE 12 - OTHER ADMINISTRATIVE EXPENSES	AMOUNT IN (RS)	
	CURRENT YEAR	PREVIOUS YEAR
1. Postage, Telephone and Communication Charges	847,354.00	924,970.00
2. Printing and Stationary	707,897.00	695,283.00
3. Travelling and Conveyance Expenses	6,380,659.00	4,915,017.00
4. Auditors Remuneration	155,549.00	117,794.00
5. Hospitality/Local Meeting Expenses	2,048,063.43	658,490.00
6. Legal & Professional Charges	263,926.00	446,275.00
7. Lease Rent	1,000,000.00	1,000,000.00
8. Bank Charges	6,257.31	11,531.13
9. Advertisement and Publicity	683,123.00	1,611,538.00
10. Misc. Expenses	287,517.00	382,353.00
11. Books & Periodicals	91,680.00	63,694.00
12. Transportation charges	422,872.00	578,714.00
13. Conveyance Reimbursement	113,811.00	97,491.00
14. Honorarium (Others)	327,955.00	352,254.00
TOTAL	**13,336,663.74**	**11,855,404.13**

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SCHEDULE FORMING PART OF INCOME AND EXPENDITURE FOR THE YEAR ENDED 31.03.2012

SCHEDULE 13 - REPAIR & MAINTENANCE	AMOUNT IN (RS)	
	CURRENT YEAR	PREVIOUS YEAR
1. Electricity and power	14,772,160.00	12,572,741.00
2. Insurance Others	2,368,136.00	1,780,795.00
3. Repairs & maintenance (Office)	8,582,885.00	8,424,474.00
4. Manpower (House Keeping)	1,747,152.00	1,535,376.00
5. Vehicle Running and Maintenance	125,331.00	176,559.00
6. Manpower (Security)	4,869,212.00	4,127,335.00
7. Horticulture	1,204,731.00	1,092,004.00
8. Repairs & Maintenance (Buildings)	1,508,136.00	2,072,610.00
9. Repairs & Maintenance (Lab Equipment)	1,943,560.56	2,908,210.00
10. Repairs & Maintenance (Office Equipment)	162,282.00	28,594.00
11. Insurance Charges vehicle	28,793.00	26,740.00
12. Repairs & maintenance office equip. (AMC)	440,454.00	109,798.00
13. Petrol Diesel CNG etc.	1,730,657.00	198,497.00
TOTAL	**39,483,489.56**	**35,053,733.00**

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SCHEDULE FORMING PART OF INCOME AND EXPENDITURE FOR THE YEAR ENDED 31.03.2012

SCHEDULE 14 - TRAINING AND NETWORKING EXPENSES	AMOUNT IN (RS)	
	CURRENT YEAR	PREVIOUS YEAR
1. Subscription to Journals	1,963,364.35	1,457,101.00
2. Training Expenses	10,762,137.00	11,734,666.00
3. Contingencies (CSIR/UGC/DBT/ICMR Students)	52,977.00	288,229.00
4. Conference & workshop Expenses	3,255,245.11	709,446.00
5. Student Medical Exp.	53,466.00	84,638.00
TOTAL	**16,087,189.46**	**14,274,080.00**

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SCHEDULE FORMING PART OF INCOME AND EXPENDITURE FOR THE YEAR ENDED 31.03.2012

SCHEDULE 15 - LABORATORY AND ANIMAL HOUSE CONSUMABLS	AMOUNT IN (RS)	
	CURRENT YEAR	PREVIOUS YEAR
1. Lab consumables and chemicals	32,911,280.15	29,646,593.51
2. Medicines and Consumables Animal	1,764,509.00	1,291,864.00
3. Animal House Maintenance	0.00	89,279.00
TOTAL	**34,675,789.15**	**31,027,736.51**

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SCHEDULE-16

National Brain Research Centre

NBRC

National Brain Research Centre, Manesar, Gurgaon

SIGNIFICANT ACCOUNTING POLICIES & NOTES ON ACCOUNTS FORMING PART OF THE BALANCE SHEET AS AT 31ST MARCH, 2012 AND INCOME & EXPENDITURE ACCOUNT FOR THE YEAR ENDED 31ST MARCH, 2012

SIGNIFICANT ACCOUNTING POLICIES & NOTES ON ACCOUNTS

1. Accounting Convention:

1.1 The financial statements are prepared on the basis of historical cost convention, unless otherwise stated and on the accrual basis of accounting.

1.2 The Centre is gradually 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 & Payment 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 less depreciation.

3.2 Physical verification of assets has not been conducted during the year and the records of the fixed assets have not been maintained in the standard format.

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 of Department of Atomic Energy.

3.4 NBRC has entered into a Memorandum of Understanding (MOU) with Directorate of Construction, Services and Estate Management (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&SE from time to time to be utilized by DC&SE for construction. Total amount deposited with DC&SE is Rs.44, 46, 52,000.00 till 31st March 2012. Pending completion of construction, the payments made to DCSEM 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 DCSEM; Now Memorandum of Understanding (MOU) with Directorate of Construction, Services and Estate Management (DC&SEM) is discontinued. NBRC has now engaged Civil & Construction Wing (CCW) AIR, Prasar Bharti, as Project Management Consultant (PMC) for completing balance work.

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 & Project grants.

4. Depreciation:

4.1 Depreciation on fixed assets is charged to Income & Expenditure Account for the current year amounting to Rs. 92, 12,397.00 on the basis of Written down Method as per Schedule XIV of Companies Act. Rates of Depreciation applied as per the rate prescribed under Straight Line Method of Schedule XIV of Companies Act. However no depreciation/ amortization have been charged on Patents & Copy Rights till date.

4.2 Depreciation provided for current year on the fixed assets of Project for Rs. 84, 85,452.00 and which has been directly debited to the fixed assets funds account. These assets were created through the Non-Recurring and project based grant from the funding agencies.

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.

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 Accounts in PNB Manesar related to the Grants. The submission of the returns of these accounts has been made up to Financial Year 31.03.2009 under the FCR Act.

8. Lease:

The Centre 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.

9. Retirement Benefits:

9.1 The Centre 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 Centre has not made any provision for gratuity and leave encashment during financial year 2011-2012 as against the requirement of AS-15 issued by ICAI. However the amount of gratuity and leave encashment to the extent of Rs. 79, 67,087.00 and Rs. 41, 52,326.80 already exists on 31.03.2012, 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. Others

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

11.2 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.

11.3 Schedules 1 to 16 along with Annexure I to LX are annexed to and form an integral part of the Balance Sheet as at 31st March 2012 and the Income and Expenditure Account for the year ended on that date.

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

SANTOSH KUMAR CHOUDHARY
(Deputy Finance Officer)

PROF. SUBRATA SINHA
(Director)

ATUL KUMAR WADHWA
FOR A.K WADHWA & ASSOCIATES
(CHARTERED ACCOUNTANTS)
PROPRITER
M.NO.088237

PLACE: GURGAON
DATED: 28.06.2012

A. K. WADHWA & ASSOCIATES
CHARTERED ACCOUNTANTS
175-B, NEW COLONY,
GURGAON (HARYANA) -122001
PH: 0124-4077950, 2320959

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

CONSOLIDATED STATEMENTS OF PROJECT GRANTS AND EXPENDITURE FOR THE YEAR ENDED 31.03.2012

S. NO. /Annex No	NAME OF PROJECT	OPENING BALANCE AS ON 01.04.11	ADDITION DURING 2011-12	INTEREST EARNED FROM THE PROJECT FUND	CAPITAL EXPENDI-TURE DURING 2011-12	REVENUE EXPEN-DITURE DURING 2011-12			CLOSING BALANCE AS ON 31.03.12
						MANPOWER	OTHERS	TOTAL EXPENDITURE	
1	DIST.INFORMATION CENTRE	-204726.00	0.00	0.00	0.00	0.00	0.00	0.00	-204,726.00
2	PROG.OF COOP -INDIA CYRIA	3558649.00	0.00	0.00	0.00	0.00	0.00	0.00	3,558,649.00
3	WELCOME TRUST-DR.NEERAJ	-7617249.92	0.00	0.00	0.00	0.00	0.00	0.00	-7,617,249.92
4	WELCOME TRUST-DR.REMA	-5597696.00	0.00	0.00	0.00	0.00	0.00	0.00	-5,597,696.00
5	MOLE ROLE OF TRANSC. FACTORS	-644021.00	0.00	0.00	0.00	0.00	0.00	0.00	-644,021.00
6	MULTIFACTORIAL RISK FACTOR	-29346.00	0.00	0.00	0.00	0.00	0.00	0.00	-29,346.00
7	FUNC. MAGNETIC RESONANCE IMAGING	-355435.00	0.00	0.00	0.00	0.00	0.00	0.00	-355,435.00
8	MATERIAL MALNUTRITION DR.SHYAMALA	-579048.00	0.00	0.00	0.00	0.00	0.00	0.00	-579,048.00
9	MSC.NEUROSCEINCE	5073.00	0.00	0.00	0.00	0.00	0.00	0.00	5,073.00
10	STOCHASTIC RESONANCE-DR.ROY	-471.00	0.00	0.00	0.00	0.00	0.00	0.00	-471.00
11	CSIR-DR.BASU	-379752.81	0.00	0.00	0.00	0.00	-379,752.81	-379,752.81	0.00
12	DEMENTIA MEETING	2624507.00	0.00	0.00	0.00	0.00	0.00	0.00	2,624,507.00
13	COMP.ANALYSIS OF SPEECH IMP.	-547567.00	0.00	0.00	0.00	0.00	0.00	0.00	-547,567.00
14	SPINAL CORD PLASTICITY ILTP	-31869.00	0.00	0.00	0.00	0.00	0.00	0.00	-31,869.00
15	REP.OF DEG.RETINAL NEURONS	-1173815.00	1,490,000.00	0.00	0.00	83,108.00	233,077.00	316,185.00	0.00
16	STUDY OF MOLE.MECHANISM	-68830.00	0.00	0.00	0.00	0.00	0.00	0.00	-68,830.00
17	AUTOMOUS NAVIGATION	302040.00	-302,040.00	0.00	0.00	0.00	0.00	0.00	0.00
18	BBNSC - DR.REMA	1809628.00	0.00	0.00	0.00	0.00	0.00	0.00	1,809,628.00
19	BBNSC - DR.DHINGRA	166156.00	0.00	0.00	0.00	0.00	166,012.00	166,012.00	144.00
20	BBNSC - DR.SHYAMALA	-392947.00	0.00	0.00	0.00	0.00	0.00	0.00	-392,947.00
21	BBNSC DR.NEERAJ	775977.00	0.00	0.00	0.00	0.00	479,040.00	479,040.00	296,937.00
22	BBNSC DR ELLORA	-403419.00	0.00	0.00	0.00	0.00	0.00	0.00	-403,419.00
23	BBNSC DR.PANKAJ	114047.00	0.00	0.00	0.00	0.00	114,000.00	114,000.00	47.00
24	BBNSC DR.SOUMYA	207246.00	0.00	0.00	0.00	36,000.00	170,000.00	206,000.00	1,246.00
25	CELLULAR & MOLE.BASIS - DR PANKAJ	-34974.00	0.00	0.00	0.00	0.00	0.00	0.00	-34,974.00
26	EST.OF TRANSLATIONAL RES.UNIT	5765410.00	0.00	0.00	1,457,968.00	0.00	0.00	1,457,968.00	4,307,442.00
27	JAPANESE ENCEPH.VIRUS-DR.BASU	-47545.00	0.00	0.00	0.00	-47,996.00	0.00	-47,996.00	451.00
28	FUNCTIONAL ROLE OF E6-AP-DR.JANA	3358.00	0.00	0.00	0.00	0.00	0.00	0.00	3,358.00
29	CHARAC.OF MOLECULAR INTERAC.-PRAVAT	0.00	203,971.00	0.00	0.00	0.00	77,723.00	77,723.00	126,248.00
30	COGNITIVE NEURO SCIENCE W/S-ADITIYA MURTHY	-437464.00	0.00	0.00	0.00	0.00	0.00	0.00	-437,464.00
31	IMPLICATION OF ALZHEIMERS DISEASE-SHIV KR.SHARMA	343230.00	257,000.00	0.00	275,000.00	135,935.00	80,152.94	491,087.94	109,142.06
32	INNOVATIVE BIOTECHNOLOGIST-ELLORA SEN	379426.32	0.00	0.00	0.00	0.00	88,452.32	88,452.32	290,974.00
33	EBM INCLUDING ALZHEIMER DISEASE-Dr. VIJAYLAXMI	-230717.00	0.00	0.00	0.00	0.00	0.00	0.00	-230,717.00
34	DRDO -Dr.ELLORA SEN	133932.00	0.00	0.00	0.00	0.00	0.00	0.00	133,932.00
35	RAMALINGA SWAMY-Dr. RANJIT Kr. GIRI	285779.00	1,400,000.00	0.00	101,285.00	1,026,000.00	205,179.00	1,332,464.00	353,315.00
37	MULTILINGUALISM-DR. NANDINI	1091888.00	437,200.00	0.00	974,237.00	144,000.00	256,374.00	1,374,611.00	154,477.00
38	DBT GRANT-DR. KALLOL DUTTA	139176.00	366,800.00	0.00	0.00	333,600.00	53,725.00	387,325.00	118,651.00
39	INDO-JAPAN TRAVEL-Dr. JANA	106532.00	0.00	0.00	0.00	0.00	0.00	0.00	106,532.00
40	INDO-JAPAN TRAVEL OF PROF. KOYOHIRO(DR.JANA)	25000.00	0.00	0.00	0.00	0.00	25,000.00	25,000.00	0.00
41	INDO-US & NIH RO1-DR. PANKAJ	1049512.19	554,309.00	0.00	0.00	553,775.00	574,690.61	1,128,465.61	475,355.58
42	IRON DEFICIENCY MEMORY DIS FUNCTION-DR. SAYALI	444660.00	700,000.00	0.00	0.00	600,000.00	175,542.00	775,542.00	369,118.00
43	DBT PRION GRANT-DR. RANJIT K GIRI	5064.00	100,000.00	0.00	0.00	0.00	105,064.00	105,064.00	0.00
44	ROLE OF MOL.EVENT IN ALZHEIMER DISEASE-DR. MANDAL	1174199.00	653,000.00	0.00	425,538.00	440,378.00	210,724.00	1,076,640.00	750,559.00
45	CSIR-DR. NIHAR RANJAN JANA	33000.00	36,818.00	0.00	0.00	172,422.00	32,735.00	205,157.00	-135,339.00
46	DBT GRANT-DR. ARKADEB DUTTA	122491.00	353,600.00	0.00	0.00	279,600.00	50,421.00	330,021.00	146,070.00
47	PERCEPTION ENGINEERING PROJECT OF DIT-DR. NEERAJ JAIN	950000.00	0.00	0.00	128,458.00	160,000.00	325,111.47	613,569.47	336,430.53
48	PERCEPTION ENGINEERING PROJECT OF DIT-DR. PRAVAT	1000000.00	0.00	0.00	120,000.00	664,289.00	161,928.00	946,217.00	53,783.00

49	PERCEPTION ENGINEERING PROJECT OF DIT-DR. N C SINGH	960000.00	0.00	0.00	0.00	253,070.00	118,443.00	371,513.00	588,487.00
50	PERCEPTION ENGINEERING PROJECT OF DIT-DR. P.K ROY	665000.00	0.00	0.00	225,606.00	0.00	47,249.00	272,855.00	392,145.00
51	DRDO PROJECT-DR. ANIRBAN BASU	289600.00	700,400.00	0.00	0.00	78,709.00	725,680.39	804,389.39	185,810.61
52	DBT FUNDED E6-AP(2) PROJECT OF DR. NIHAR RANJAN JANA	-12661.00	300,000.00	0.00	65,900.00	73,935.00	165,241.00	305,076.00	-17,737.00
53	FUNCTIONAL IMAGING STUDY OF DYSLEXIA-DR. N.C SINGH	1223219.00	0.00	0.00	401,351.23	697,839.00	187,198.00	1,286,388.23	-63,169.23
54	EPILEPSY PROJECT OF NBRC	280326161.00	0.00	26,073,745.78	0.00	0.00	1,150,646.00	1,150,646.00	307,249,260.78
55	MOTIVATED BEHAVIOUR IN MALE ZEBRA FINCHES-DR. SOUMYA	977756.00	400,000.00	0.00	0.00	192,000.00	660,824.65	852,824.65	524,931.35
56	MULTI DISPLINARY SYSTEM OF PARKINSON DISEASE-DR. NC SINGH	1187428.00	0.00	0.00	0.00	0.00	-1,572.00	-1,572.00	1,189,000.00
57	UNDERSTANDING THE SIGNALING CIRCUITIES-DR. ELLORA SEN	1948476.00	1,495,000.00	0.00	1,100,000.00	136,103.00	1,315,371.83	2,551,474.83	892,001.17
58	TWO PHOTON MICROSCOPE FACILITY FOR ADVANCE RESEARCH	96648530.00	0.00	6,559,769.00	313,845.03	0.00	122,481.00	436,326.03	102,771,972.97
59	UNDERSTANDING THE PSYCHOLOGICAL FUNCTION OF MALIN	996268.00	0.00	0.00	487,541.96	102,575.00	727,052.91	1,317,169.87	-320,901.87
60	NEURAL NETWORK MECHANISM-DR. YOGANARASHIMHA	8681000.00	0.00	0.00	0.00	0.00	0.00	0.00	8,681,000.00
61	IBRO SCHOOL WORKSHOP- PROF. P. K. ROY	-2255158.00	0.00	0.00	0.00	0.00	-1,582,319.00	-1,582,319.00	-672,839.00
62	DST SERC SCHOOL WORKSHOP-DR. SOUMYA IYENGAR	446722.00	-390,346.00	0.00	0.00	0.00	0.00	0.00	56,376.00
63	BITS PILANI DR. PRAVAT K. MANDAL	0.00	250,000.00	0.00	0.00	0.00	0.00	0.00	250,000.00
64	CIRCADIAN SYSTEM LINKAGE (DST) DR. SOUMYA IYENGAR	0.00	1,109,600.00	0.00	0.00	0.00	125,652.00	125,652.00	983,948.00
65	COLLABORATION FOR TRANS. & CLIN. RES. (GLUE) PROF. P K ROY	0.00	3,684,000.00	0.00	0.00	637,000.00	29,175.00	666,175.00	3,017,825.00
66	CSIR -II STUDY THE ROLE OF NEURAL IMMUNE RESPNCE DR. BASU	0.00	763,750.00	0.00	0.00	0.00	1,061,606.24	1,061,606.24	-297,856.24
67	DST AUSTISM SPECTRUM DISORDER DR. NANDINI C. SINGH	0.00	1,200,400.00	0.00	0.00	0.00	0.00	0.00	1,200,400.00
68	DST COGNITIVE SCIENCE RESEARCH INITIATIVE (CSI) DR. CHAITRA RAO	0.00	300,000.00	0.00	0.00	0.00	0.00	0.00	300,000.00
69	DIT McGILL LINKAGE (NKN) PROF. PRASUM KUMAR ROY	0.00	2,611,000.00	0.00	0.00	0.00	0.00	0.00	2,611,000.00
70	ICMR HIV ASSOCIATED NEUROCOGNITIVE DISORDER (HAND) DR. PANKAJ	0.00	544,268.00	0.00	0.00	0.00	135,101.00	135,101.00	409,167.00
71	ROLE OF HUMAN UMBILICAL CORD BLOOD STEM (AIIMS) DR. PANKAJ	0.00	300,000.00	0.00	0.00	0.00	136,534.59	136,534.59	163,465.41
72	DBT NATIONAL BIOSCIENCE AWARD 2010 (DR. ANIRBAN BASU)	0.00	300,000.00	0.00	0.00	0.00	232,409.00	232,409.00	67,591.00
73	DBT 5TH MEETING OF EGN-CDB (DR. SHIV KUMAR SHARMA)	0.00	200,000.00	0.00	0.00	0.00	132,125.00	132,125.00	67,875.00
74	DST ITPAR WORKSHOP ON COGNITIVE NEUROSCIENCE (DR. NANDINI C.)	0.00	300,000.00	0.00	0.00	0.00	0.00	0.00	300,000.00
	Total (A)	**395,921,628.78**	**20,318,730.00**	**34,633,514.78**	**6,076,730.22**	**6,752,342.00**	**8,694,098.14**	**21,523,170.36**	**429,350,703.20**
36	DELCON E-LIBRARY CONSORTIUM (B)*	13,344,303.00	164988146.00	0.00	0.00	0.00	177572323.44	177,572,323.44	760125.56
	Grand Total (A+B)	**409,265,931.78**	**185,306,876.00**	**34,633,514.78**	**6,076,730.22**	**6,752,342.00**	**186,266,421.58**	**199,095,493.80**	**430,110,828.76**

**DelCon E-Library consortium is a part of Earmark Endowmwnt fund so it has not been included in the consolidated of project fund.*

SANTOSH K CHOUDHARY
DY. FINANCE OFFICER

PROF. SUBRATA SINHA
DIRECTOR

FOR A.K WADHWA & ASSOCIATES
CHARTERED ACCOUNTANTS

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