CENTRE FOR BRAIN RESEARCH

AN AUTONOMOUS CENTRE OF THE INDIAN INSTITUTE OF SCIENCE

ANNUAL REPORT

2022-23

Contents

From the Director

CBR: Aspirational Outcomes and Impact

The Centre for Brain Research (CBR) is an autonomous centre embedded within the Indian Institute of Science ecosystem, set up to foster inter-disciplinary research and translation in basic and clinical neuroscience, to understand neurodegenerative disorders of the aging brain through advanced genetic, biochemical, neuroimaging, and neurocognitive investigations. The Centre aims to understand how cognitive functions can be preserved during aging and how the burden of neurodegenerative disorders can be reduced through early diagnosis, prevention, postponement, and innovative interventions. Towards these goals, CBR brings together neuroscientists, neuro-physicians (psychiatrists and neurologists), engineers, geneticists, and computational scientists to conduct mission-oriented translational research and innovation.

The Centre started functioning in 2014 and the new building housing the Centre's state-of-the-art infrastructure was formally inaugurated by Honourable Prime Minister Shri Narendra Modi in June 2022. CBR is funded by a charitable organisation, Pratiksha Trust, founded by Mr. Kris Gopalakrishnan and Ms. Sudha Gopalakrishnan. CBR also receives competitive funding from external agencies. More recently, in a historic gesture, the Pratiksha Trust has pledged support to CBR in perpetuity, with an initial outlay of ₹450 Crores for the next 10 years.

CBR's aspiration is to dedicate itself to a deep intellectual pursuit in quest of reducing the burden of neurodegenerative disorders and elevating the quality of life for an important part of society, namely the elderly population and their families. To accomplish its mission of finding scientific methods for early diagnosis, prevention, postponement, evidence-based interventions, and effective management of these diseases, CBR is determined and uniquely well-positioned to tackle challenging problems that have defied understanding for decades. A multidisciplinary approach is key to addressing these problems; CBR has assembled and is also working towards upscaling a competent team of molecular and cellular biologists, neuroscientists, clinician-researchers, computational geneticists, and data scientists. With a multi-disciplinary approach, there are multiple dimensions along which CBR is assiduously striving to achieve excellence.

These dimensions include:

1. To become a global research hub of excellence in the scientific study of normal and pathological aging of the brain to unravel the mysteries of neurogenerative disorders of the elderly population.
2. To assume a leadership role in the scientific conduct of longitudinal studies of rural and urban cohorts; such longitudinal studies involving multi-modal assessments and evidence-based interventions in carefully selected cohorts of human subjects are central to a comprehensive understanding of the aging brain.
3. To be a front runner in the creative use of artificial intelligence and machine learning techniques on neuroimaging and other modes of data to decipher the risk factors and protective factors for neurodegenerative disorders.
4. To emerge as a thinktank and policy advisor to the Government in public health initiatives connected with neurodegenerative diseases and shape the policies for effective management of neurogenerative conditions.
5. To bridge the science-society gap in the area of neurodegenerative diseases by spearheading the nation's efforts to reach out to the different sections of society to dispel any misconceptions about neurodegenerative disorders and educate everyone on the advances in the area.
6. To realize bench-to-bedside translation of discoveries by actively engaging with leading research groups, the global industry, and the startup ecosystem.

With a solid platform for cutting-edge research, innovation, and engagement laid, the time is now ripe for CBR to scale up and strengthen its noble pursuits. In the coming years, CBR will endeavour to achieve excellence in all the above dimensions and beyond. In this endeavour, CBR looks forward to establishing and nurturing synergistic partnerships and to continued support from all its diverse stakeholders.

Prof. Y Narahari, Director

Cover photo: The CBR fraternity on the occasion of the Centre's showcase at the IISc Open Day, 4 March 2023

Momentous Milestones

Inauguration of the CBR Building

The new building of Centre for Brain Research was formally inaugurated on 20th June 2022, by the Honourable Prime Minister of India, Shri Narendra Modi. The grand ceremony took place in the august presence of the Governor of Karnataka (Shri Thaawarchand Gehlot), the then Chief Minister of Karnataka (Shri Basavaraj Bommai), Union Minister, Parliamentary Affairs; Coal; and Mines (Shri Pralhad Joshi), CBR Donors (Mr. Kris Gopalakrishnan and Mrs. Sudha Gopalakrishnan, Founding Trustees – Pratiksha Trust), and other esteemed dignitaries. Prof. Govindan Rangarajan, Director – Indian Institute of Science, briefed the Prime Minister on CBR's vision and flagship research projects.

The inauguration coincided with the laying of the foundation of the upcoming Bagchi-Parthasarathy Multispeciality Hospital on the IISc campus.

The CBR building, generously funded by the Pratiksha Trust, has a built-up area of 1,10,000 sq. ft. with state-of-the-art laboratories (for genetics, informatics, cognitive science, molecular neuroscience, and related research), faculty offices, a lounge for study participants, clinical assessment rooms, board rooms, an auditorium, and provisions to house brain and DNA banks.

Reinforced Enthusiasm for Aging Brain Research and Innovation

On 15th February 2023, Pratiksha Trust (co-founded by Mr Kris Gopalakrishnan and Mrs Sudha Gopalakrishnan) kindly signed an MoU with CBR and IISc to continue its acclaimed patronage for fundamental and translational research on brain aging and aging-related brain disorders. Through this MoU, the Pratiksha Trust generously affirmed its support to CBR in perpetuity, with an initial outlay to the tune of INR 450.27 crore (approximately USD 55 million) over the next 10 years, for research, innovation, and translation. This agreement is viewed as a landmark development in philanthropic support for deep science in India. The significant continuation of support through this MoU will help scale up the research and innovation activities at the Centre to a great extent.

"The human brain is one of the world's biggest mysteries, which is yet to be fully understood. By funding this Centre, with the help of IISc, we are working towards creating and sustaining a globally recognised, state-of-the-art research and innovation hub that will be at the cutting edge of research on the human brain. We are committed to supporting this Centre in its mission to reduce the pain, agony, and burden of an important part of our society: the elderly population. We wish the Centre all success and hope that it becomes the world's leading centre for aging brain research by 2030."
– Mr. Kris Gopalakrishnan

"India's elderly population is expected to grow rapidly to a staggering 32 crore by 2050, leading to a corresponding increase in the burden of dementia and other aging-related neurodegenerative diseases. CBR is uniquely positioned to take on the challenge of tackling this impending healthcare and socioeconomic crisis. I thank Mr. Kris Gopalakrishnan and Mrs. Sudha Gopalakrishnan for their continued commitment to such crucial research and the unprecedented level of support that they have given." – Prof. Govindan Rangarajan

Research and Innovation at CBR

Research and Innovation at CBR

1. Flagship Research Projects

The Centre for Brain Research spearheads large-scale research projects that address some of India's major health challenges and have significant implications, particularly, for the aging population.

Longitudinal Cohort Studies on Aging

Prospective, population-based, longitudinal aging studies are crucial for understanding the risk factors and protective factors for dementia and other neurodegenerative diseases associated with aging. CBR conducts two such unique studies. Srinivaspura Aging, Neuro Senescence and COGnition (CBR-SANSCOG) study and Tata Longitudinal Study of Aging (CBR-TLSA) are parallel, prospective, community-based, cohort studies in India – rural and urban, respectively – for comprehensive evaluation of risk and protective factors associated with cognitive changes due to normal ageing, dementia, and other related disorders. Both cohorts comprise of cognitively healthy individuals aged 45 years and above, of both genders. However, they have distinct population characteristics with respect to socio-economic status, migration, literacy, and lifestyle. Participants in the rural study are recruited from the villages of Srinivaspura Taluk in Kolar District in Karnataka, through an area sampling strategy, whereas the urban cohort is recruited through convenience sampling, from urban Bangalore, India. Harmonization in assessments across the two studies enables head-to-head comparison of the outcome measures.

1.1. Srinivaspura Aging, Neuro Senescence and COGnition (CBR-SANSCOG) Study

Funding: CBR

CBR-SANSCOG study is a first-of-its-kind, large, prospective cohort study that is being conducted in the rural Indian population (projected n=10,000), from the villages of Srinivaspura taluk in Kolar district of Karnataka. This study aims to understand the risk and protective risk factors for dementia and related disorders. It follows an interdisciplinary, multimodal approach including detailed clinical, neurocognitive, biochemical, genetic, and neuroimaging assessments, with long-term follow-up.

Prior to recruitment of participants, we liaise with the local public health officials and work closely with the grassroot level leaders and community health workers, to build better

connections with the community and to create awareness about our study. Recruited participants undergo detailed assessments that are done following a three-visit protocol. The first visit happens at the participant's home, during which socio-demographic data and written consent to participate in the study are obtained. The second visit is at the project site office in Srinivaspura or in a mobile unit, where detailed clinical and neurocognitive assessments are carried out. Biochemical and genetic tests are done through periodic blood collection camps at the villages due to logistic reasons. The third visit involves neuroimaging, where a subset of the cohort undergoes brain MRI at the Indian Institute of Science (IISc) or National Institute of Mental Health and Neurosciences (NIMHANS) in Bangalore.

Recruitment for the study started in January 2018. The pilot phase of the study (n=1,000) was completed in March 2019. The main phase of the study is currently ongoing, and the follow-up assessments commenced in February 2020. The study progress for the period 1st April 2022 to 31st March 2023 is outlined below.

Recruitment

During this period, 2997 new participants from 47 villages were recruited (a total of 7133 recruitments from 111 villages since the start of the study).

Camps

A total of 50 awareness camps were conducted in various villages. In addition, 226 blood collection camps and 149 feedback/consultation camps were conducted during the above-mentioned period (a total of 124 awareness camps, 403 blood collection camps, and 303 feedback/consultation camps since the start of the study).

Assessments – baseline & follow-up

As many as 2549 baseline assessments and 549 follow-up assessments were completed (total of 6093 baseline assessments and 1340 follow-up assessments since start of the study).

Brain MRI

Around 800 brain MRI scans were performed during this period (a total of 1306 scans since start of the study).

Parameter	1st April 2022 – 31st March 2023	Overall
Participants consented	2997	7133
Villages recruited from	47	111
Baseline assessments	2549	6093
Follow-up assessments	549	1340
Brain MRI	800	1306
Interim telephonic + home visit contact	587	1851
Based on interim contact, participants interested in follow-up	391	1655
Blood sample collection camps	226	403
Sample collection completed	3004	7044
Feedback/consultation sessions completed	149	303
Village surveys	0	35
Awareness programs	50	124

1.2. Tata Longitudinal Study of Aging (CBR-TLSA)

Funding: Tata Trusts

CBR-Tata Longitudinal Study of Aging (TLSA) is an ongoing, one-of-its-kind, large-scale, prospective, population-based cohort study on aging conducted in the urban metropolitan city of Bangalore, India. This cohort study (projected number=1,000) is designed to identify risk factors and protective factors for dementia and related disorders by carrying out annual, multi-modal assessments (clinical, cognitive, biochemical, genetic, and neuroimaging) on subjects of both genders aged 45 years and above and follow the trajectories of aging focussing on the various risk and preventive factors influencing aging brain and preceding cognitive impairment or cognitive resilience.

The recruitment strategies involve community awareness and outreach programs by our research personnel to inform the participants about healthy aging, neurodegenerative disorders, and the CBR-TLSA study. The participants who give consent undergo detailed clinical, neurocognitive, biochemical, genetic, and neuroimaging assessments, which are done in 1-2 visits. The first visit occurs in CBR, IISc campus, where participants undergo detailed clinical and cognitive assessments. During the second visit, which occurs in the JN Tata MRI Centre,

IISc campus, they undergo neuroimaging. Blood samples are drawn at their residence for biochemical and genetic assessments. Recruitment for the study started in 2015 and, so far, around around 1300 participants have consented for the study, and all of them have completed their baseline assessments. A higher number of subjects (up to 1500) are planned to be recruited to compensate for follow-up attrition and missing data and to maintain a steady state follow-up of > 1000 elderly individuals.

Phase 1 of TLSA concluded in December 2021 and Phase 2 of the project has been initiated. Phase 2 also entails a multimodal intervention trial which is now being planned to be initiated in a pilot exploratory mode. An expert committee consisting of international and national experts to oversee the same has been constituted; the Committee met in February and March 2023 to discuss various aspects of the trial and offer valuable feedback.

During the period 1st April 2022 to 31st March 2023, we recruited 548 new participants and completed 578 follow-up assessments. A total of 1086 blood investigations (536 baseline + 550 follow-up) and 599 brain MRI (430 baseline + 169 follow-up) were carried out during this period.

Particulars	Overall (June 2015 to March 2023)							This Year (April 2022 to March 2023)						
Participants consented	1299							548						
Clinical and cognitive assessments	BL	F1	F2	F3	F4	F5	F6	BL	F1	F2	F3	F4	F5	F6
	1299	656	318	211	130	35	4	548	287	77	82	97	31	4
Brain MRI	BL	F1	F2	F3	F4	F5	F6	BL	F1	F2	F3	F4	F5	F6
	867	231	143	43	67	8	2	430	61	33	16	49	8	2
Blood investigations	BL	F1	F2	F3	F4	F5	F6	BL	F1	F2	F3	F4	F5	F6
	1172	566	291	200	121	32	4	536	256	78	89	94	29	4

1.3. GenomeIndia

Funding: Department of Biotechnology, Government of India

CBR is the National Co-ordinator for the pan-Indian mission-mode GenomeIndia project which is aimed at identifying the genetic variations in Indians by Whole Genome Sequencing (WGS)

of 10,000 representative individuals in the first phase. The consortium involves 20 national institutes across 15 different states in the country.

Indian population is world's second largest at >1.3 billion and extremely diverse with the presence of 4500+ ethnic groups. The common as well as rare genetic variations at single nucleotide resolution and structural variants level obtained from GenomeIndia will help us to understand the genetic underpinnings of complex polygenic multifactorial diseases, rare inherited disorders, as well as determine individuals' response to drugs, in addition to serving as the reference genetic dataset for our population.

Specific objectives:

I. Create an exhaustive catalogue of genetic variations (common, low frequency, rare, SNPs and structural) in Indians.
II. Create a reference haplotype structure for Indians. This reference panel can be used for imputing missing genetic variation in future Indian population GWA studies.
III. Design genome-wide arrays for research and diagnostics at an affordable cost.
IV. Establish a biobank for DNA and plasma collected for future use in research.

In this project, CBR has collected close to 3000 samples from various regions and communities in the country spanning the northern and southern states. Genome-wide array based genotyping has been executed for 3342 samples and whole genome sequencing for 2823 of these samples have been carried out after quality checks, primarily based on known and cryptic relatedness among the samples in a community specific manner. For 2707 samples, the genomic variant-level gvcf files have been generated and analyzed. Further, joint genotyping has been performed for 2084 samples, resulting in a discovery set of about 70 million variations in Indians. From the ongoing analysis, it was found that about 25% of biallelic single nucleotide variations are unique to Indians upon checking against gnomAD, dbSNP, Indigenomes, and 1000Genomes datasets. More checks on this are currently being carried out, especially against GenomeAsia dataset.

A substantial proportion of these novel variants are also singletons. Earlier, IndiGenomes have reported 32% novelty on genetic variations in their discovery callset. The novel genetic variations identified are mostly in the rare category. Nevertheless, considering merely the number of variants having alternate allele frequency <5% , these are prevalent enough to be of implications in large scale association studies. Also, these can comprise a better population reference dataset that can be used for precise screening in disease genetics. While conducting population subgroup specific analyses, it was observed that, the proportion of rare variants shared between multiple population groups are the least, followed by low frequency ones, and highest overlap being noted for common variants, thus, alluding to the population specificity of

the variants discovered. A genome-wide reference imputation panel has been constructed with the updated dataset, showing improved imputation accuracy and allelic concordance for Indian population genotypes compared to that of TOPMed and Haplotype Reference Consortium panels. Currently, methods are being developed to fine-map neurodegeneration specific loci and other genomic loci known to be implicated in complex disease traits onto the new GenomeIndia generated map of genetic variations. This will help in gaining preliminary perception of comparative disease propensities at the population level. It may be noted that these are ongoing and preliminary results from 2084 samples, and changes in results and interpretations are to expected upon completion of the analysis of sequencing data from all 10000 samples.

1.4. Young and Late-onset Parkinson's Disease (YLOPD) Study

Funding: SKAN Research Trust

The 'Young and Late-onset Parkinson's Disease' (YLOPD) study is a longitudinal study on Parkinson's disease (PD), the second most common neurodegenerative disorder characterized by slowness in movements and impaired posture and balance.

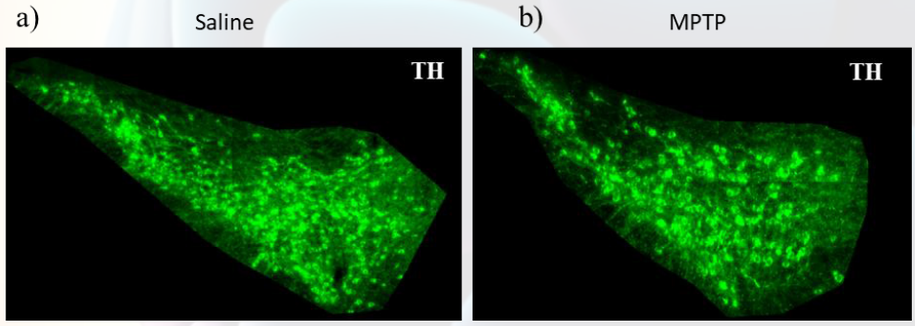
Funded by the SKAN Research Trust, the study began in 2021 as a collaborative undertaking between CBR and the National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru. This study aims to recruit 1000 patients with young and late-onset PD and follow them up periodically to study the natural history of the disease.

Existing literature shows that people who develop young-onset PD (YOPD) have different initial symptoms, non-motor symptoms, environmental risk factors, rate of progression, choice of deep brain stimulation target, and quality of life impairment as compared to late-onset PD (LOPD). Growing evidence highlights the importance of YOPD and LOPD and their impact on a person's quality of life. However, the multifactorial causation, neuroanatomical features, and genetic architecture of YOPD and LOPD are not fully understood; the YLOPD study strives to address this crucial gap.

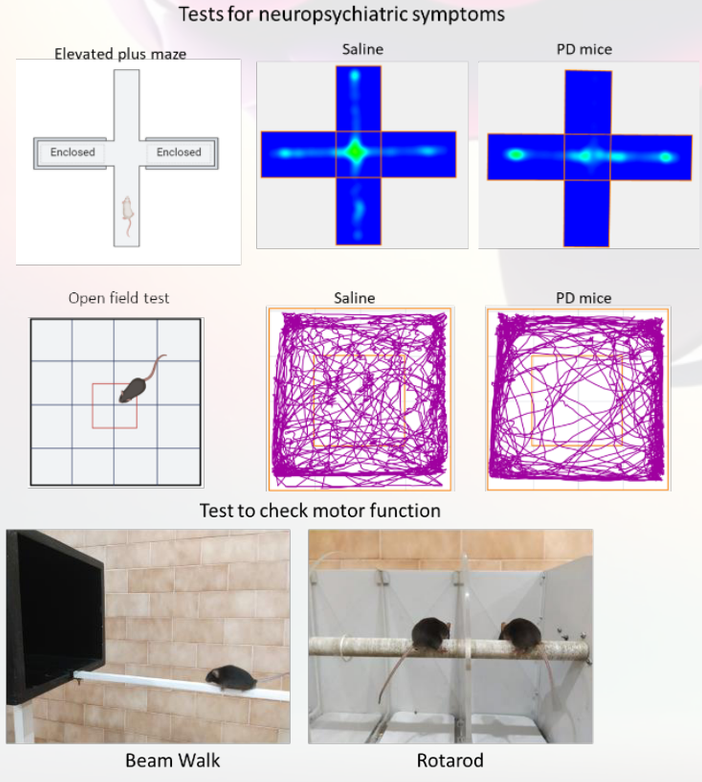
The YLOPD study involves comprehensive multimodal evaluation of clinical, electrophysiological, and cognitive functions, brain and retinal imaging, genome-wide association and whole genome sequencing, blood-based inflammatory and protein biomarkers, and studies on heavy metal and pesticide exposure with emphasis on differential involvement in YOPD and LOPD.

The study is focused on linking the insights from clinical literature to explore translational research in animal models of PD in order to decipher molecular underpinnings of the emergence of non-motor symptoms (NMS) and motor symptoms (MS). In PD it is known that degeneration

of substantia nigra (SNpc) dopaminergic neurons and their projections to striatum causing dopamine depletion is associated with MS. However, a broad spectrum of neuropsychiatric symptoms, including NMS (like anxiety and depression) frequently observed in PD, are probably related to other non-dopaminergic neurons and their projections to target regions in the brain. The etiology, in terms of aggregation of the presynaptic protein α-synuclein in Lewy bodies or in the neurites that may contribute to NMS, is not clear. We are using the MPTP (1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine hydrochloride) neurotoxicity mouse model of PD at sub-chronic dosing and α-synuclein- dependent progressive disease mice model of PD to understand the molecular basis for the emergence of these NMS.



Our mouse model of PD shows a loss of dopaminergic neurons in the substantia niagra, thereby closely mimicking the clinical condition.



Schematics and images from behavioural experiments on mice models of PD

To investigate non-motor symptoms, mice are subjected to a series of behavioural tests such as the elevated plus maze, open field test, and forced swim test. These tests allow us to assess anxiety- and depression-like behaviours. Tests such as the rotarod test, tail swing test, and beam walk test aid in the assessment of motor coordination and balance in the mice. Data from these experiments, together with those from histopathology analyses and complementary studies, would lead to a comprehensive view of the potential mechanisms of disease progression.

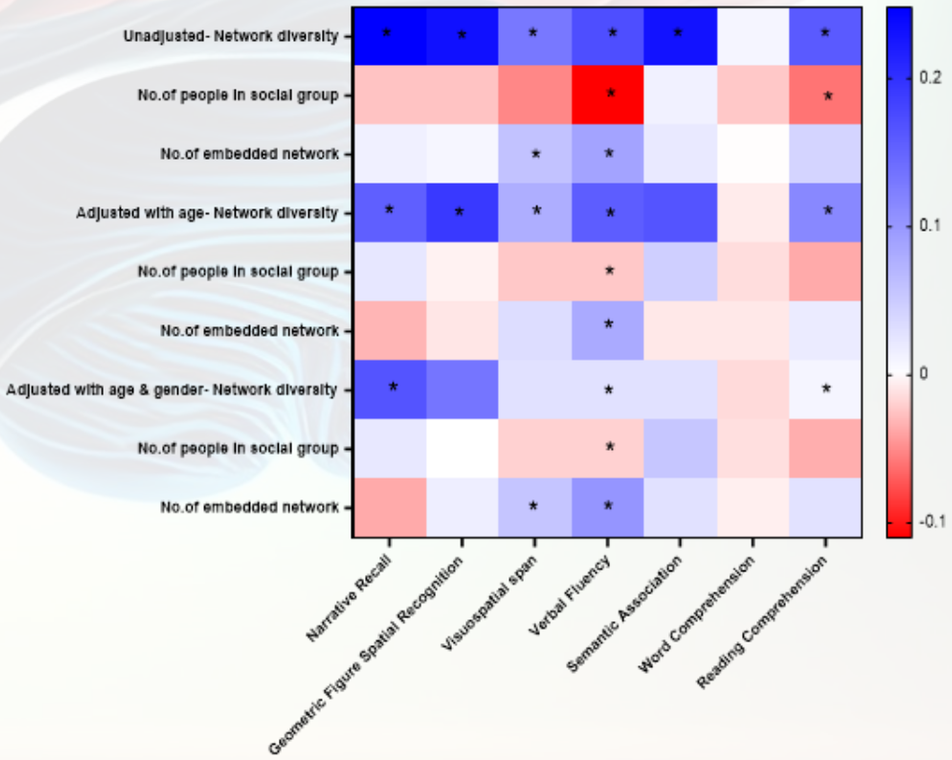
This 'bench-to-bedside' study is expected to shed light on many unanswered questions on PD which can be effectively used to support the implementation of effective interventions and modification of existing treatment protocols.

2. Research and Innovation Snippets

Association between social networking and cognition among aging rural Indians

Research question

Is there an association between social networking and performance on distinct cognitive domains among cognitively healthy middle-aged and older adults from rural India?

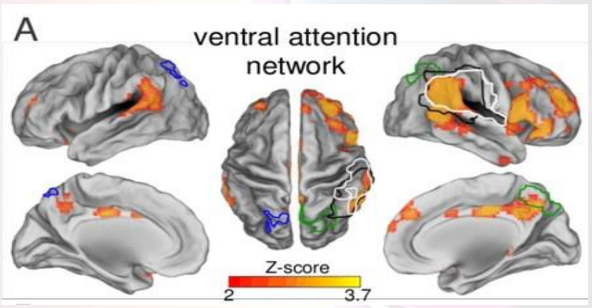


Highlights

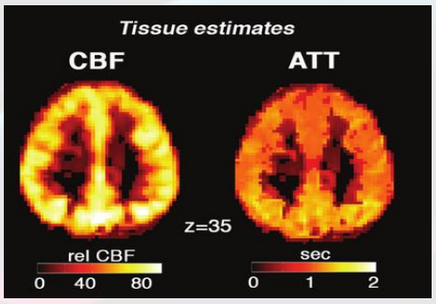
- Cohen's Social Network Index was used to assess social networking and a computerized, neurocognitive test battery (COGNITO) was used to assess performance on multiple cognitive domains.
- Better social networking in all three social dimensions (network diversity, no. of people in social network, no. of embedded networks) was associated with better cognitive functions in multiple, distinct cognitive domains.

Reference: Rai P, Sundarakumar JS & SANSCOG Study Team. Association between social networking and cognition among middle-aged and older adults in rural India. (Abstract submitted to AAIC 2023)

CBR-IISc FAME Study



Resting state network using fMRI data



Perfusion image using 3D PCASL data

- CBR-IISc fMRI and ASL for MCI in Elderly population (CBR-IISc FAME Study), in collaboration between the groups of Prof. Thomas Gregor Issac (CBR) and Dr. Vaanathi Sundaresan (CDS, IISc).
- It is a unique study that uses combined fMRI and ASL MRI techniques to study functional changes at early stage of Alzheimer's disease.
- fMRI gives BOLD signal changes whereas 3D PCASL provides cerebral blood flow changes in these subjects which helps us to identify early marker for diagnosing MCI.

Studies on the genetic architecture of neurodegeneration and cognition

70 million genetic variants identified in the Indian population, and population specificity of discovered variants highlighted, especially by rare variants.

A few thousand variants discovered that have implications for high loss-of-function.

Improved estimation of genotypes and allele frequencies in our CBR study cohorts with information from these reference set of genetic variants.

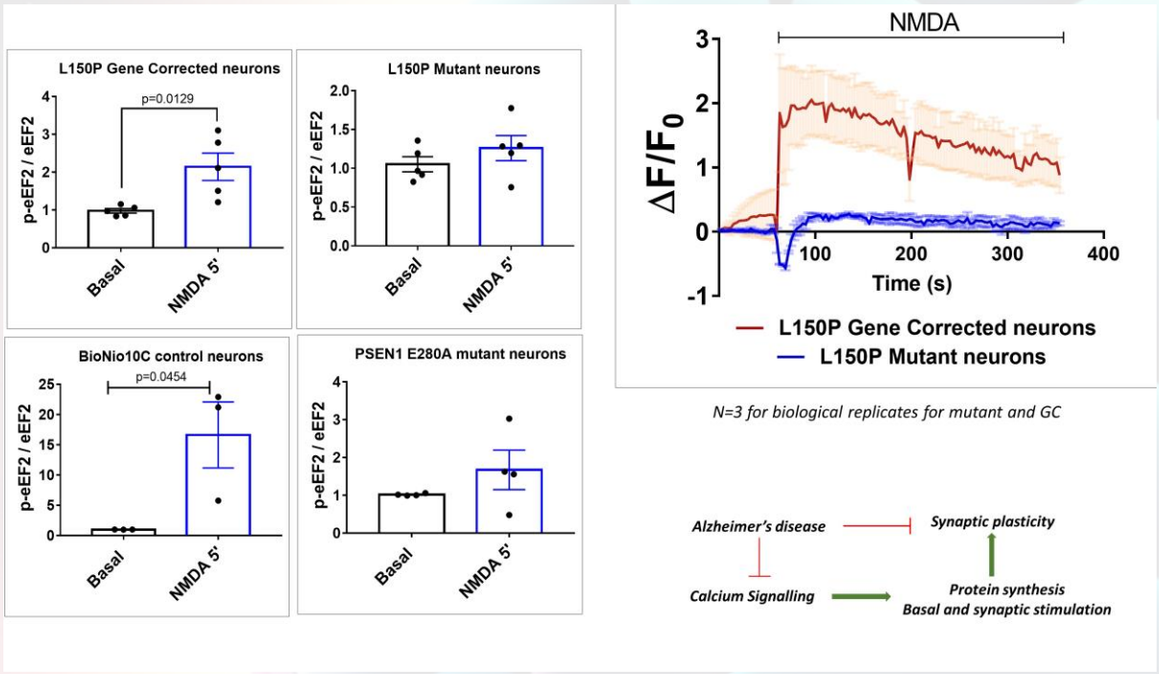
Suggestive genetic association for metabolic traits counted as risk factors for neurodegeneration, as well as for cognitive scores in SANSCOG study dataset.

Preliminary results of causal risk conferred by metabolic risk parameter upon cognitive scores in SANSCOG study dataset.

Reference: Chakraborty S, Kahali B*. Exome-wide analysis reveals role of LRP1 and additional novel loci in cognition. Human Genetics and Genomics Advances. 2023. PMID: 37305557

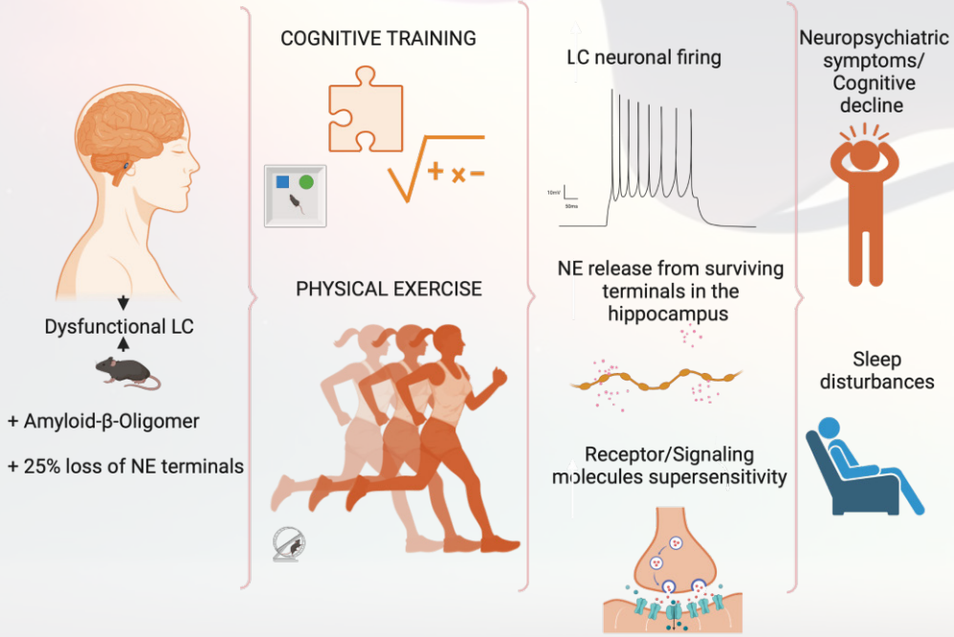
Defective calcium signaling leads to protein synthesis dysregulation in AD neurons

- AD neurons were generated from familial AD iPSCs carrying either L150P or E280A mutations on PSEN1.
- Mutant neurons completely lack a response to neuronal activity (stimulation of NMDAR receptor).
- The neurons from mutant lines also lack proper calcium signaling on activity.
- Prof. Muddashetty's lab is investigating the link between calcium signalling and protein synthesis and if it is possible to rescue protein synthesis defects by manipulating calcium signal.

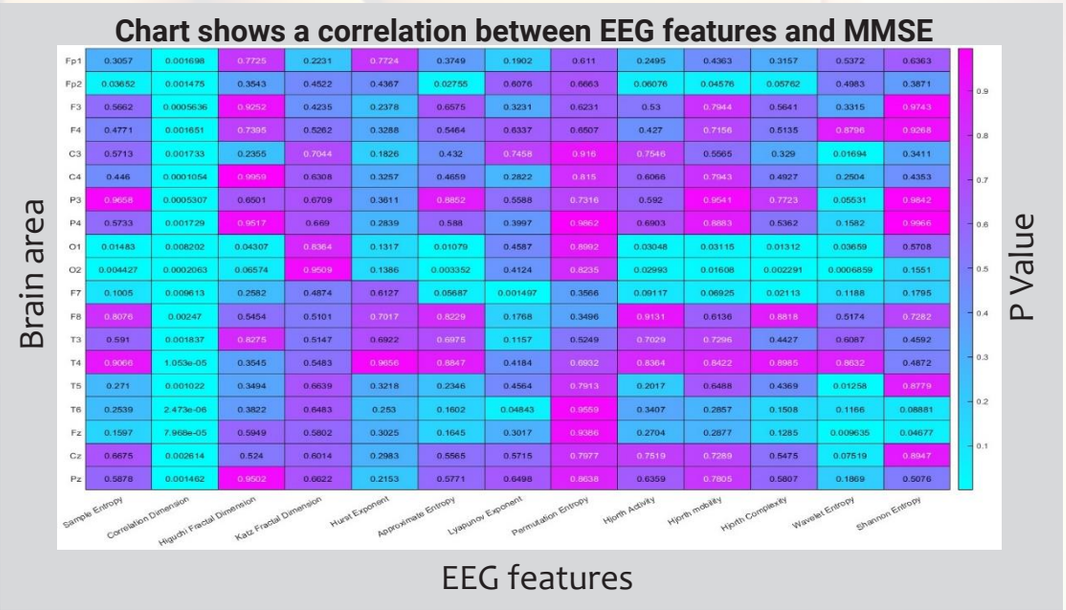


Sex-specific locus coeruleus dysfunction expedites Alzheimer's disease

- LC dysfunction is prevalent during early Alzheimer's disease.
- LC is sexually dimorphic in mice.
- Preliminary data from Dr. Karunakaran's lab indicates that stimulating LC in APP/PS1 mice accelerates disease progression.

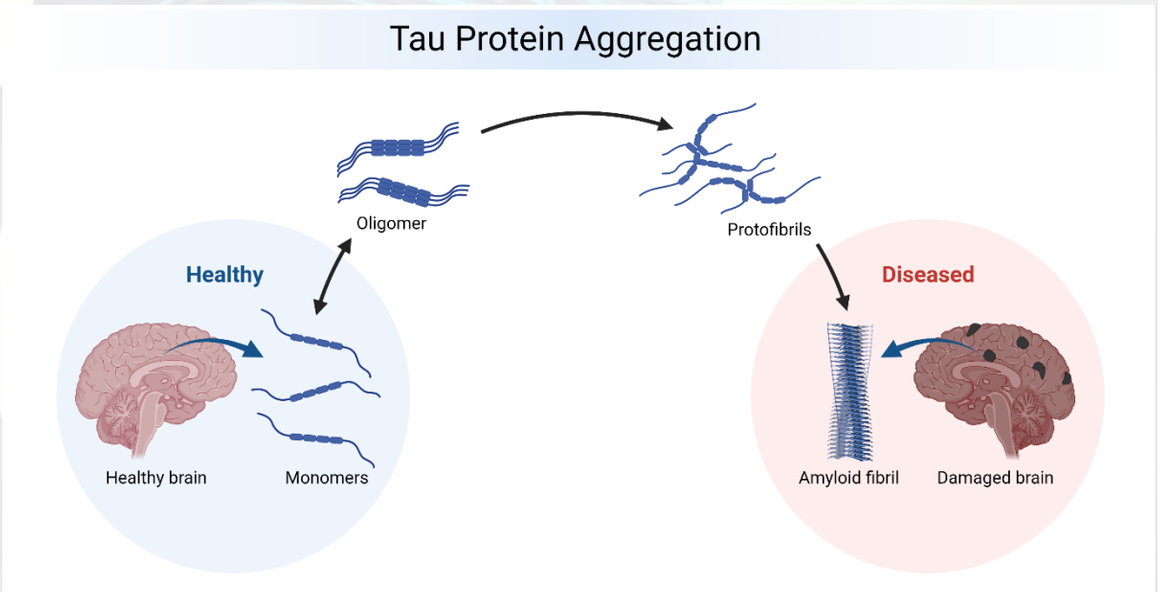


Computing and Controlling Brain Rhythms



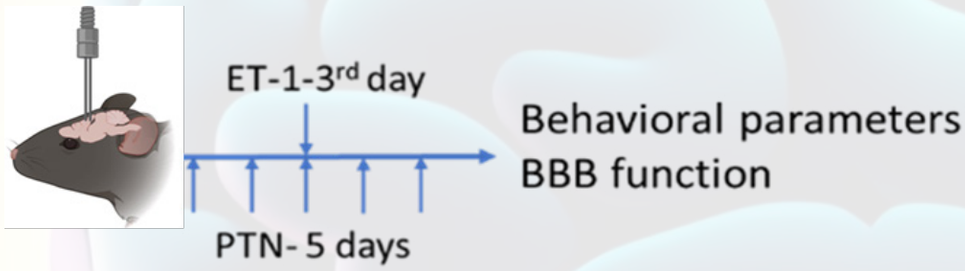
- Dr. Adaikkan's group has found neural EEG complexity-specific and brain area-specific EEG feature associations with MMSE (min mental state examination) scores in human healthy, MCI (mild cognitive impairment), and AD subjects.
- Developed a software/application to analyze neural EEG complexity.
- Developed MATLAB-based software packages and analyzed the relationship between EEG features and cognition.

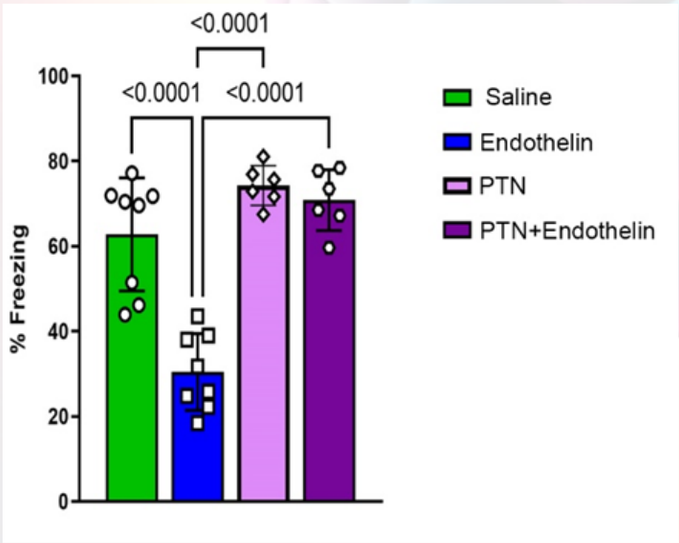
Molecular basis of tau protein propagation

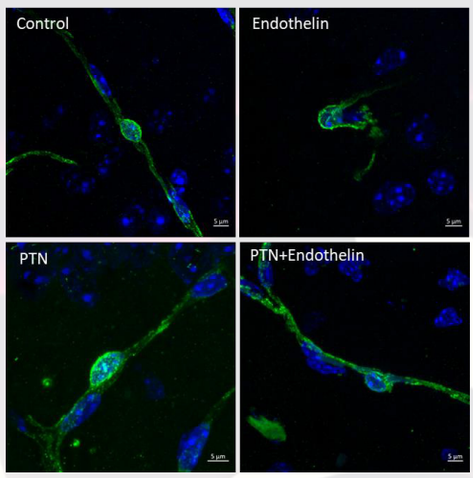


- Tau proteins start to aggregate through unknown mechanisms and eventually spread from one brain region to another, initiating the progression of dementia.
- Dr. Ramamoorthy's group uses a multidisciplinary approach to understand the molecular basis of tau protein propagation across the brain regions.

Pleiotrophin protects blood brain barrier against ET-1 vascular insult



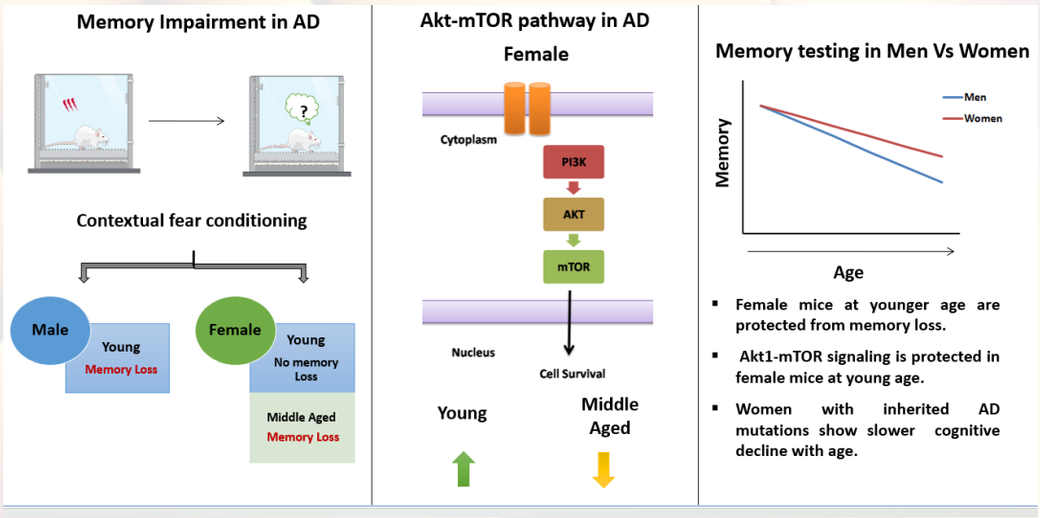




- Infusion of pleiotrophin, a trophic factor involved in maintenance of pericyte the component of blood-brain barrier, was able to preserve the structural integrity of vasculature and thereby reverse memory loss following vascular insult.
- Dr. Diwakar's lab seeks to identify such trophic factors in reversal of transient ischemic attack after single insult to preserve the structural integrity of vasculature as a preventive approach during dementia.

Reference: Diwakar L, Gowaikar R, Chithanathan K, Gnanabharathi B, Tomar DS, and Ravindranath V. "Endothelin-1 mediated vasoconstriction leads to memory impairment and synaptic dysfunction". (2021). Scientific reports. https://doi.org/10.1038/s41598-021-84258-x.

Sex difference in evolution of cognitive decline in Alzheimer's disease



Reference: Kommaddi, R. P., et al., (2023, April 12). Sex difference in evolution of cognitive decline: studies on mouse model and the Dominantly Inherited Alzheimer Network cohort. Translational Psychiatry, 13(1).

3. Faculty Research Projects

Besides contributing to the Centre's flagship projects, faculty members pursue fundamental and applied research in diverse areas of brain aging. Some interesting findings/highlights are outlined in this section.

3.1. Prof. Ravi Muddashetty, Associate Professor

Defective calcium signaling leading to protein synthesis dysregulation in AD neurons

Funding: CBR

The loss of cognition which is a hallmark of Alzheimer's disease (AD) is associated with synaptic defects and progressive loss of synapses. Activity-mediated protein synthesis is an important aspect of synaptic function and essential for memory. It is now quite well established that defects in protein synthesis have a major role in the synaptic dysfunction in AD neurons. Activity-mediated protein synthesis in neurons is primarily driven by the stimulation of two major classes of glutamate receptors namely NMDAR and mGluR. Work from my lab previously established that these receptors generate a distinct translation response that is regulated by specific signaling pathways (Dastidar et al, 2020). We have also shown that calcium signaling is particularly important for NMDAR-mediated protein synthesis response (Ramakrishna S et al 2021). The distinct calcium signal in neurons is generated by the release of calcium into the

cytoplasm from different sources, namely extracellular calcium through NMDAR and voltage-gated calcium channels (VGCC), calcium from intracellular sources namely through Ryanodin and IP3 receptors from the endoplasmic reticulum (ER). We are investigating the different sources of calcium that enter neurons on NMDAR stimulation and their individual and collective impact on protein synthesis. NMDAR stimulation evokes a biphasic protein synthesis response involving an initial translation inhibition followed by translation activation. This response is essential for synaptic plasticity. In the current study, we show that NMDAR stimulation evokes a clear spatiotemporally regulated release of calcium from different sources which in turn is responsible for generating the biphasic protein synthesis response. We show that the calcium influx through NMDAR and voltage-gated calcium channels (VGCC) primarily induces translation inhibition while calcium release from internal sources (particularly from ER) leads to translation activation.

This work is very relevant in the context of CBR as we show that the neurons from the AD patients (iPSC-derived neurons) clearly show dysregulated calcium signaling and resultant defects in activity-mediated protein synthesis which is essential for cognition. We derived glutamatergic neurons from familial AD mutant (L150P-PSEN and PSEN1 E280A) human iPSC lines and their corresponding gene-corrected lines. While the gene-corrected (GC) neurons showed proper calcium signal and translation response for NMDAR stimulation, the mutant neurons completely lacked proper calcium signaling and corresponding protein synthesis response. Based on this work we can clearly link the calcium signal defects protein synthesis dysregulation in AD neurons. Understanding the link between calcium signaling and protein synthesis will not only help in understanding the synaptic pathology in AD but also could open up possibilities for novel therapeutic approaches.

3.2. Prof. Bratati Kahali, Associate Professor

Genetic architecture of cognitive changes associated with aging for gaining insights into dementia: causal role of metabolic risk factors and its shared genetic etiology with cognition in population-based studies

Funding: Department of Biotechnology (DBT), Science and Engineering Research Board (SERB) - Department of Science and Technology (DST), National Supercomputing Mission (NSM), and CBR

Metabolic risk factors like midlife adiposity, type 2 diabetes, hypertension, and dyslipidemia could influence risk of dementia in late life. This work aims to determine genetic predisposition of the Indian population to these complex metabolic and cognitive conditions and estimate their causal interrelationships.

Specific objectives:

I. Identify the common and rare single nucleotide variations as well as structural and copy number variations in the Indian population-based cohorts designed to understand the risk and protective factors of dementia through whole genome sequencing data analysis.
II. Identify loci associated with metabolic traits, that is fasting blood glucose (FG), glycosylated hemoglobin (HbA1c), serum triglycerides (TG), total, high density and low-density lipoprotein cholesterol (TC, HDL, LDL), systolic and diastolic blood pressure (SBP, DBP), waist to hip ratio adjusted for body mass index (WHR, WHRadjBMI), body mass index (BMI), body fat percent (BFP); and neurocognitive outcomes, namely, Hindi Mini Mental State Examination (HMSE) and domain-specific scores of COGNITO (Computerized assessment of adult information processing), white matter hyperintensity (WMHV) and hippocampal volumes (HCV) by conducting genome-wide association studies in the Indian population.
III. Generate polygenic risk scores for cognitive measures and dementia rating in the Indian population comprising the study individuals. This will aid in systematic genome-wide evaluation of the genetic risk and protective factors associated with cognitive change in case of healthy aging as well as for dementia in the Indian population.
IV. Investigate the causal interrelationships between the above-mentioned metabolic risk factors and neurocognitive measures by performing Mendelian Randomization analysis.

This study is currently ongoing, and after quality checks performed on genotypic and phenotypic data for 4400+ Indian individuals, the current analyzable dataset consists of 4448 individuals typed for 452,606 variants. Before proceeding with genomic level association and causal studies, our own Indian reference imputation panel was constructed with WGS-derived genotypes from the CBR-TLSA project merged with known South Asian haplotypes to impute array-based genotypes in the CBR-SANSCOG cohort. Another reference imputation panel with the GenomeIndia dataset was also constructed. Upon comparison of imputation accuracy across variant allele frequencies, it was observed that both of our constructed reference panels perform better (at least 5% increase in accuracy) than both Haplotype Reference Consortium HRC and TopMed panels. We retained only those variants which have an imputation accuracy r-sq > 0.5 to test for association with cognition and metabolic phenotypes.

As part of cognition and metabolic risk parameter phenotypes, currently, HMSE scores, g-factor for COGNITO (Computerized assessment of adult information processing) scores, TG/HDL ratio, waist-to-hip ratio adjusted by BMI (WHRAdjBMI), fasting blood sugar and glycated Haemoglobin (HbA1c) have been considered individually. Appropriate correction for gender, age, and educational levels have been carried out in the mixed model regressions. From preliminary results, three genome-wide association signals associated with TG:HDL were observed in

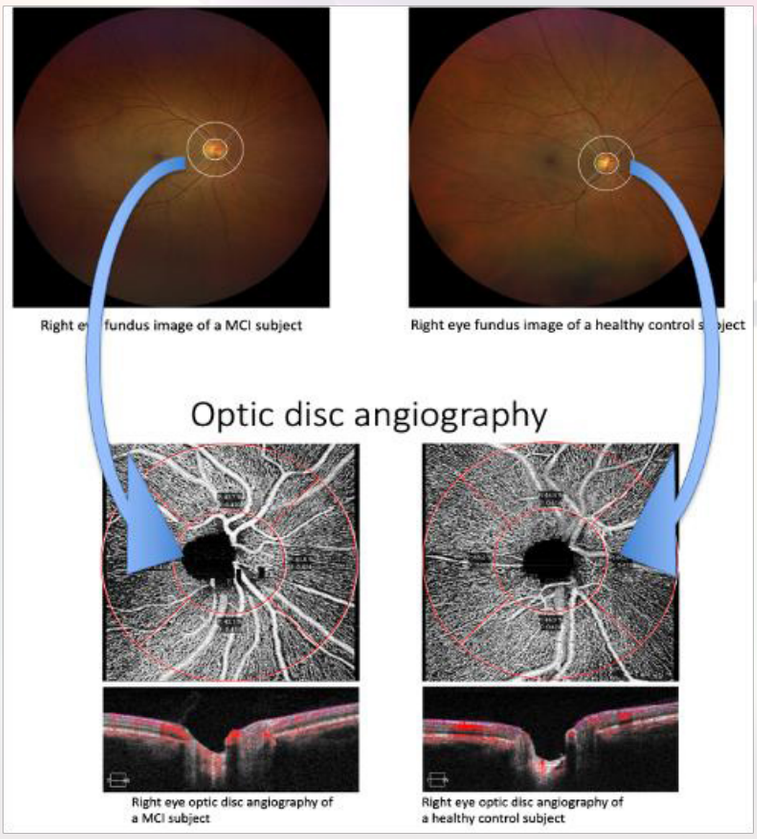
chr11q23.3. For HMSE, one genome-wide association signal was obtained. Factor analysis was performed on phenotypes from four domains of COGNITO (attention, language, memory, visuospatial ability) to obtain the g-factor for COGNITO. One genome-wide significant hit was obtained for this g-factor. For WHRAdjBMI, fasting blood sugar and HbA1c, seven, four, and five suggestively associations were uncovered, respectively. Out of a handful of suggestively significant hits obtained for HMSE scores, one variant is a stop-gain in gene known to be linked to cognitive deficits in schizophrenia. Pilot causality testing of the suggestively associated TG:HDL variants on HMSE was conducted with revealing preliminary promising results. We intend to perform polygenic risk analysis, functional annotation and pathway-based analysis, and cognitive resilience assessments, along with deep functional characterization to understand the contribution of these variants towards cognition and neurodegeneration in the future.

3.3. Prof. Thomas Gregor Issac, Associate Professor

CBR-NETRA (Neurodegeneration - Early detection using Trans-Retinal Angiography) Study

Funding: TATA Trusts and CBR

Our lab has been focussing on deciphering and utilising the learning from the longitudinal cohort studies – CBR-TLSA and CBR-SANSCOG. -The current initiative aims at improving the early understanding to identify and detect predementia syndromes. In this regard, data from Optical

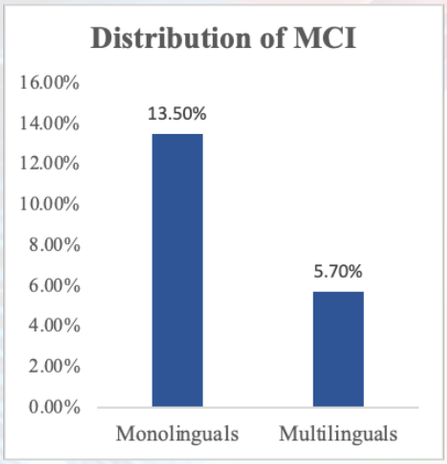


Coherence Tomography (OCT) has been looked into with great interest. This innovative project, titled CBR-NETRA (Neurodegeneration- Early detection using Trans-Retinal Angiography) Study, aims to identify some early markers of predementia in the elderly population. OCT provides an opportunity as a window into the brain. Our studies have identified that retinal perfusion is impaired in mild cognitive impairment.

Our lab also looks into the role of environmental factors like the effect of air pollution, water quality, effect of electromagnetic radiation which could influence cognitive functioning in the elderly population. We utilise ambient air quality monitoring devices to identify air quality and particulate matter characterization and quantification for the same.

Apart from the risk factors, our lab also looks into the role of protective factors like multilingualism and adequate control of vascular risk factors which tend to protect the vulnerable elderly from the onset of dementia or delay its progression. Below are some results from the CBR-SANSCOG study which looks at the link between language and cognition

	Monolinguals	**Multilinguals**	**P-value**
Healthy (CDR = 0)	794 (86.5%)	2648 (94.3%)	<0.001*
MCI (CDR= 0.5)	124 (13.5%)	159 (5.7%)	
Total	918	2807	



Independent variable	**B value**	**Unadjusted OR**	**Adjusted OR**	**P-value**
Language category	0.368	2.38	1.44* 95% CI (1.1 - 1.9)	<0.001

The preliminary results suggest that the odds of developing cognitive impairment is about 1.44 times in monolinguals compared to multilinguals. This emphasises that multilingualism is a protective factor and mediates cognitive resilience.

Another initiative deals with looking at the utility of neurostimulation techniques like rTMS and neuromodulation strategies like TDCS and TACS for Cognitive function enhancement in Elderly population (NICE initiative). This has been approved by the IEC and is being initiated.

3.4. Dr. Smitha Karunakaran, Assistant Professor

Sex-specific locus coeruleus dysfunction expedites disease progression in APP/PS1 mice

Funding: CBR

Sleep disturbances and neuropsychiatric symptoms are more common during the early stages of neurodegenerative disorders like Alzheimer's (AD) and Parkinson's disease (PD). These symptoms involve a brainstem nuclei called the locus coeruleus (LC). Interestingly, the LC serves as the primary site of disease pathogenesis, with the accumulation of α-synuclein (Braak 1-2) and Tau (Braak 0) in PD and AD, respectively. Notably, in PD, the LC is involved even before the disease progresses to affect the substantia nigra, while in AD, it is affected much earlier than the onset of hippocampus pathology.

Our research utilizing an amyloidogenic mouse model, APP/PS1, indicates that the LC exhibits sexual dimorphism. Considering the higher prevalence of AD in women than men above the age of 65, the sexual dimorphic nature of the LC nuclei could play a role in driving the early stages of AD. For instance, the LC-derived neurotransmitter norepinephrine (NE) is implicated in anxiety, agitation, depression, and sleep disturbances, conditions that are known to be more prevalent in women than men. In the mouse model, in the presence of Amyloid-β oligomers, LC terminals projecting to the APP/PS1 hippocampus degenerate in a sex-specific manner while the neuronal numbers remain intact.

Detecting sex-specific noradrenergic terminal degeneration proves challenging using conventional neuroimaging techniques, and valuable insights into disease progression can only be achieved using animal model systems of disease such as APP/PS1. Stimulating the dysfunctional LC induces aberrant plastic changes in male hippocampus astrocytes in a layer-specific manner. Stimulating a dysfunctional LC in male APP/PS1 mice induced aberrant plastic changes in hippocampus astrocytes which culminated in blood-brain barrier breach at 9-months-old age in these mice. At optimal levels, NE contributes to cognitive enhancement and disease resilience. However, stimulating a dysfunctional LC causes an increase in NE release, resulting in post-synaptic sensitization, elevated neuronal firing rates, and subsequent cognitive decline.

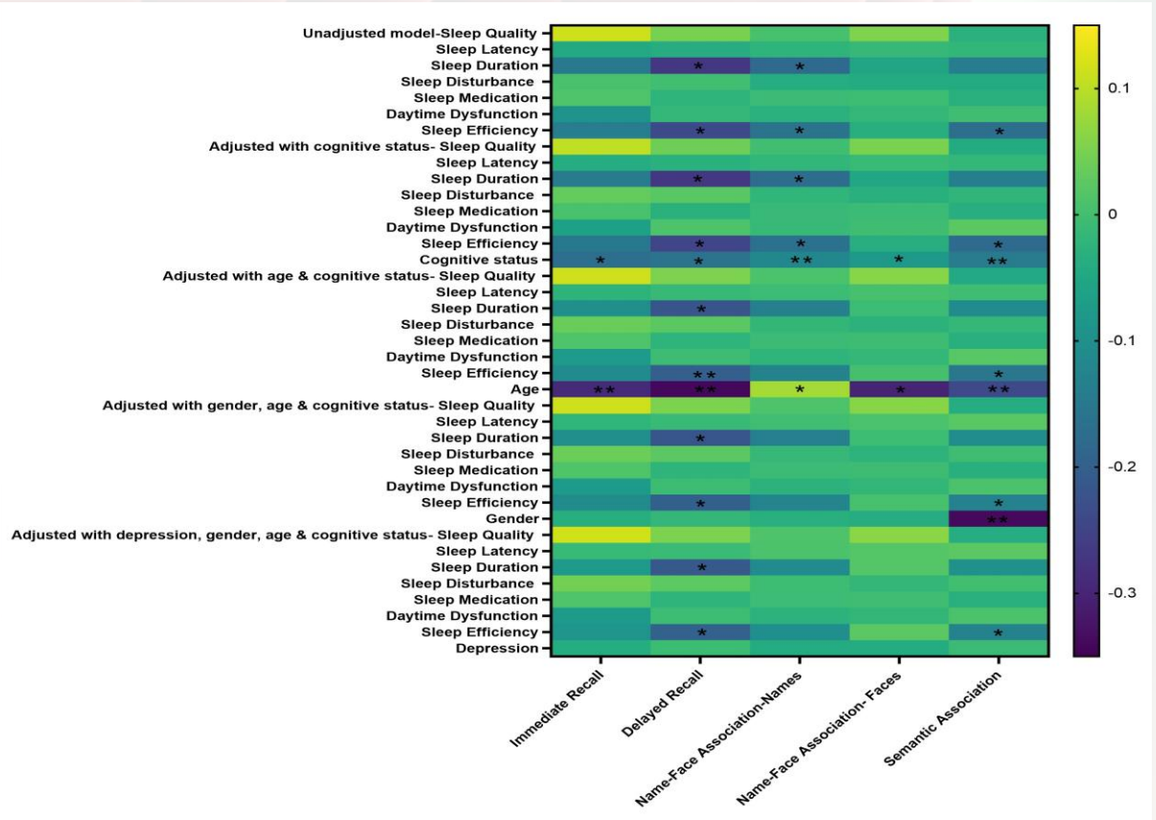
Based on our research findings, LC neuroimaging shows promising potential as an early biomarker for diagnosing individuals who are predisposed to conditions like AD and PD.

3.5. Dr. Jonas S Sundarakumar, Assistant Professor

Association of sleep with memory functions among aging rural Indians

Funding: CBR

The CBR-SANSLab (Software AG Autonomic Nervous System Laboratory), led by Dr. Sundarakumar, will conduct advanced scientific research and explore the potential of cardiac ANS dysfunction as an early biomarker for dementia and related disorders. It will provide for key assessments such as cardiac autonomic reflex tests, heart rate variability analysis (HRV) ECG, heart rate response to deep breathing, heart rate response to standing or tilt, etc., and thereby complement the efforts under CBR's ongoing longitudinal cohort studies of aging.
In addition, Dr. Sundarakumar's lab pursues various interesting research strands stemming from CBR-SANSCOG. One of these is to investigate the association between sleep and subtests of memory among middle and older-aged adults in the rural Indian population.



Based on the analyses, sleep quality, sleep duration, and sleep efficiency were found to be the best predictors of memory performance in the study. The study highlights the importance of addressing sleep quality in preventing memory decline, even in dementia-free individuals.

3.6. Dr. Chinnakkaruppan Adaikkan, Assistant Professor

Computing and Controlling Brain Rhythms

Funding: DBT/Wellcome Trust India Alliance and CBR

The major goals of our lab are to (a) understand the link between brain rhythms and memory and (b) deliver transcranial electrical stimulation (tES) at various brain (awake and NREM & REM sleep) states.

There is a great interest in identifying non-invasive biomarkers for Alzheimer's disease (AD), just like fluid-based biomarkers such as amyloid or tau in the blood plasma. We propose that specific features in brain rhythms thought to stem from how many cell types of the brain in neural circuits communicate could hold information regarding brain functioning and memory. Therefore, we examine the relationship between brain rhythms and memory/dementia using a neural electroencephalogram (EEG) collected non-invasively from the scalp of human subjects. First, we take human EEG and the corresponding subject's cognitive data from public repositories and through our collaborators (total N = 248 including healthy and AD subjects). Second, we perform signal processing using custom-written algorithms in MATLAB, examining 40 meticulously crafted temporal, spectral, and spectro-temporal complexity features in EEG. Third, we conduct regression analysis between these EEG features and memory scores such as mini-mental state exam (MMSE). We find feature-specific and region-specific EEG features correlating with MMSE scores. For instance, the correlation dimension (a measure of chaos and complexity in EEG signal) across the brain significantly correlates with MMSE. In contrast, the occipital visual cortical area (O1 & O2) across many EEG features correlates with MMSE. We are excited about these findings as they demonstrate that EEG features-based biomarker is possible. In the future, we aim to test whether this correlation is present in many cohort studies. Finally, we developed a software application that performs these 40 feature extractions from EEG datasets. Neuroscientists, neurologists, and psychiatrists will likely use our application to study neurological disorders and potentially use it for clinical diagnosis.

Another goal of our lab is to deliver transcranial electrical stimulation (tES) at various brain (awake, and NREM & REM sleep) and neural oscillatory (delta/theta troughs) states. Therefore,

we need an automated software application package that distinguishes awake, NREM & REM epochs of neural oscillations from local field potential (LFP) in real-time to achieve this. First, we used neural recordings in the model mice and simultaneously collected the LFP, electromyogram (EMG), and video recordings. Next, we developed a MATLAB-based software package for characterizing the LFP time series data into various states. To distinguish awake, NREM, and REM epochs, simultaneously collected LFP, EMG, and position/location data of the mice are used in the software package. We find that the measures of Approximate Entropy, Lyapunov Exponent, Permutation Entropy, and Power Ratio (delta/theta) distinguish the REM and NREM from the LFP time series. Thus, our software package successfully detects various states of the mouse brain from the LFP data (with EMG and video records). In the future, we will combine our software package with a tES stimulation device to design a complete system to deliver the tES at desired brain state in conjunction with the neurophysiological data collection.

3.7. Dr. Sivaprakasam Ramamoorthy, Assistant Professor

The molecular basis of dementia progression in Alzheimer's patients

Funding: Alzheimer's Association and CBR

Alzheimer's disease (AD) is the most prevalent neurodegenerative disorder, causing over 70% of dementia worldwide. Each year, approximately 50 million people are diagnosed with AD, and by 2050, more than 150 million people are expected to have the disease. India is projected to have the most dementia patients in the world by 2050. The hallmarks of Alzheimer's disease are the deposition of Aß plaques and neurofibrillary tangles. Neurofibrillary tangles are made of misfolded tau proteins, and they strongly correlate with the onset of dementia. Misfolded tau protein deposition begins in the lateral entorhinal cortex in most cases of Alzheimer's disease. From there, it spreads to synaptically connected regions such as the hippocampus, the temporal cortex, and finally other neocortical regions. It is important to note that the rate of dementia in Alzheimer's patients varies greatly. In other words, the cognitive abilities of some Alzheimer's disease patients rapidly deteriorate, while the cognitive abilities of others can remain relatively unchanged for decades despite having the disease. To accurately predict the course of the disease, customize treatment options, and provide quality care to patients, it will be necessary to disentangle the molecular complexities underlying this variability.

Our lab is broadly interested in understanding the molecular basis of tau pathology and its role in disease progression and heterogeneity in dementia. We are currently working to understand the endosomal-lysosomal dysfunctions in tau pathology and the role of copathology in the progression of dementia in AD patients.

3.8. Dr. Shweta Ramdas, Assistant Professor

Genetic variation in human populations and its role in regulating complex traits

Funding: CBR

Our lab's focus since its beginning in January 2023 is on characterizing genetics of Indian populations, particularly in the context of the genetic variation seen in the mitochondrial genome, and the functions of non-coding genetic variation. In the period Jan-March 2023, we worked on the GenomeIndia project, processing samples and building computational pipelines to get accurate estimates of copy number. We compared different metrics to estimate copy number and found that the choice of metric does not significantly affect these estimates. We have also begun analysis of publicly available gene expression data from smokers and non-smokers, with the goal of identifying differences in gene expression between these two groups, and also identifying if some genetic factors play a role in gene regulation only in smokers (dynamic expression quantitative trait loci, or dynamic eQTLs). The ultimate goal of this research is to identify if the increased risk of smoking on aging can be attributed partially to particular genetic risk factors in the brain that are induced upon smoking. In the next year, we will continue to build on these and related approaches to better understand non-coding genetic variation in the Indian population.

3.9. Dr. Latha Diwakar, Senior Scientific Officer

Molecular underpinnings of vascular dementia

Funding: TATA Trusts and CBR

Small vessels undergo periodic constriction over time, which accumulate negative impact on cognitive function leading to the development of VaD (Vascular Dementia). Although small vessel dysfunction, ischemic attacks, and microbleeds are considered common causes of VaD, very little is known of the underlying pathogenesis. Multi-infarct dementia accounts for the highest cases of dementia. In this study, we wanted to mimic multiple small vessel insults. To this end, the animals were given 3 doses (2ug/2ul) of vasoconstricting peptide ET-1 (Endothelin-1) for a period of 6 weeks at an interval of 21 days before complete reversal of vasoconstriction effect by 30 days. Further, we wanted to demonstrate the protective effect trophic factors like PTN (pleiotrophin) in multiple vascular insults. Many studies have shown that PTN, a trophic growth factor loss is associated pericyte loss and/or neurovascular dysfunction. There are various trophic

factors like PDGFB/PDGFRβ, TGFβ, Notch, VEGF, BDNF which enhance growth in differentiated cells and increase cell proliferation as well as differentiation, one such trophic factor is PTN maintaining pericytes in blood vessels. The normal PTN CSF level is measured as 3.19+0.39nM. We wanted to maintain a high PTN CSF level during vascular constriction induced by ET-1. Thus, we started giving 2µl of PTN, which is at higher concentration through guide cannula in left hemisphere of mice brain injection 2 days prior to ET-1 insult, PTN dosage continued 2 days after ET-1 insult. On the day of vascular insult, ET-1 was injected at an interval of 1 hour after PTN injection. The animals were sacrificed after completion of three time points of ET-1 injection. As ET-1 treatment leads to vasoconstriction, BBB leakage along with pericyte loss, the question of whether pericyte loss is depriving the neurons of pericyte-derived neurotrophic assistance was the question to be answered. We hypothesized that the effect of ET-1 insults can be nullified by maintaining high level of PTN CSF during the insults. We maintained a high PTN CSF level during ET-1 insults by injecting PTN 2 days prior and after to ET-1 as well as on the day of ET-1 injection. We assessed the associative and recall memory of the PTN+ET-1 injected animals, we observed a significant recovery in freezing response in PTN+ET-1 injected almost up to the level of control animals (Figure 1).

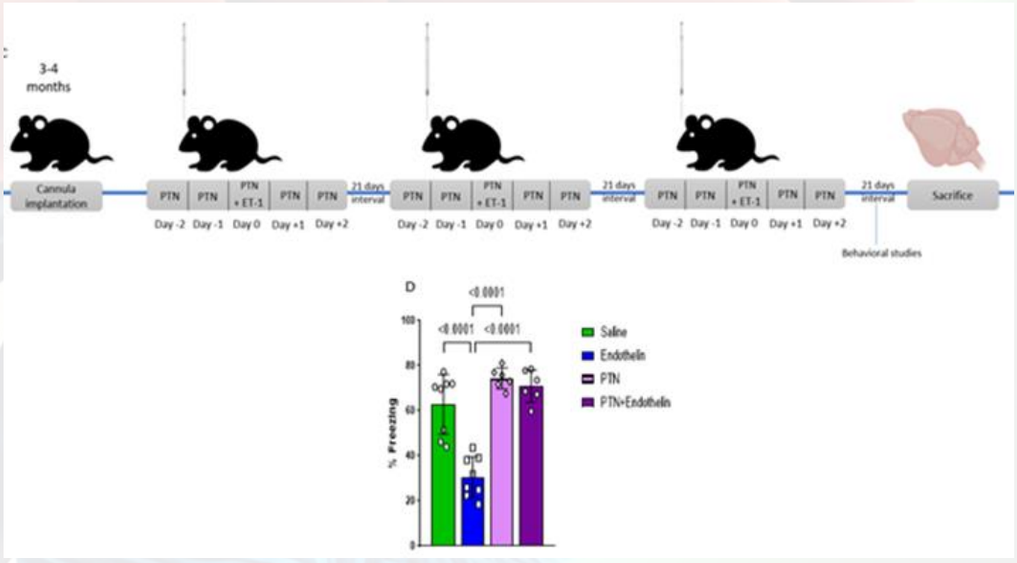


Figure 1: C57 mice injected with single dose of pleiotrophin for 2 days into lateral ventricles. 3rd Day single dose ET-1 was given into the ventricles followed by pleiotrophin for 3 days same timeline was followed for all 3 injections of ET-1. At the end of treatment, contextual fear conditioning test was done, and brain was harvested for histopathology.

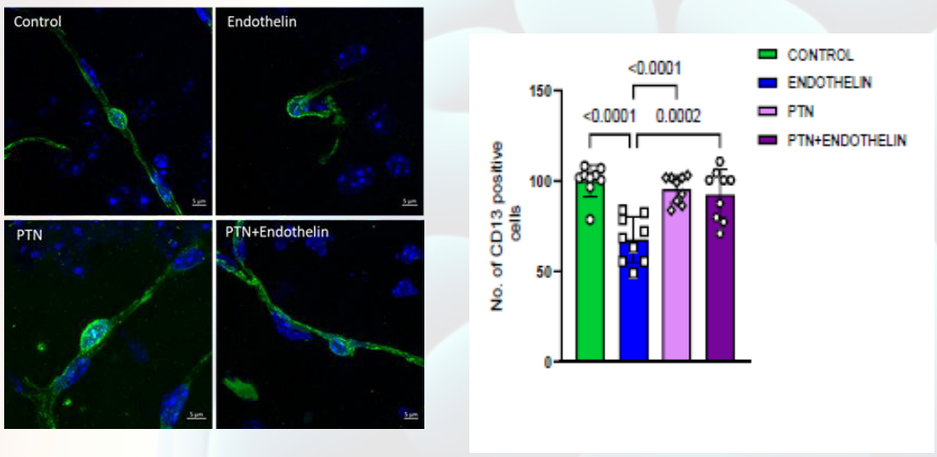


Figure 2: Representative images of immunostaining of pericyte cell marker CD 13 after a single dose and repetitive dose of ET-1 injection with PTN respectively. The graphs also reveal the protective effect of PTN showing significant increment in CD 13 positive cells when multiple doses of ET-1 with PTN were administered to the mice brain with the significant difference between ET-1 and ET-1+PTN treated mice. No significant difference in the number of CD 13 positive cells between ET-1+ PTN and saline-administered mice was observed.

Further, we sought to check for the protective effect of PTN on ET-1 induced vascular dysfunction, in these animals by immunohistochemistry of brain sections. We observed that the endothelial cells disruption caused by multiple ET-1 injection was regained on treatment with ET-1 in presence of high PTN concentration in brain. Similarly, no IgG stain was observed, and blood vessel topography was maintained in case of PTN+ET-1 treated animals for which data is not shown in the report. On maintaining high PTN level during ET-1 injection, loss in CD13 expression was recuperated, and the processes of pericytes were restored to their normal length as well, as seen in the control (Figure 2). The protective effect of PTN was exhibited in the behavioral paradigm with recovery in freezing response suggesting that PTN could prevent the effect of ET-1 mediated vasoconstriction leading to improvement in memory and cognition as well as keeping BBB unscathed improving endothelial cell and pericyte expression.

3.10. Dr. Reddy Peera Kommaddi, Senior Scientific Officer

Investigating the sex-specific differences in Alzheimer's disease pathology

Funding: CBR

Alzheimer's disease (AD) is a multifactorial and progressive neurodegenerative disorder characterized by the abnormal accumulation of amyloid-β plaques in the extracellular space of the isocortical areas and misfolded tau aggregates intracellularly as neurofibrillary tangles,

cerebral atrophy, gliosis, synapse loss, neuroinflammation, and extensive neurodegeneration. Clinical symptoms observed in AD are memory loss and other higher order cognitive impairments. Pathological features of AD could be detected much before (~30 years) the clinical symptoms manifest.

The number of women living with AD is greater than men, which has been attributed to longer lifespan in women. Women (>65 years) are more likely to develop late-onset AD (LOAD). Sex differences in the genetic makeup of resilience and multiple sex-specific molecular mechanisms may underlie resilience to AD pathology. Depending on sociocultural and biological factors, the progression and risk of AD can differ between men and women. Importantly, women are well protected from neurodegenerative diseases than men prior to menopause; however, when the female sex hormone levels drop abruptly during menopause, the clinical outcomes worsen. Although estrogen is a neuroprotective hormone, the molecular mechanisms underlying estrogen's function, social behavioral deficits, and the higher prevalence of AD pathogenesis in women are unknown.

Among the molecular mechanisms, the Akt/mTOR signaling pathway plays a crucial role in neurotransmission and synaptic plasticity. The Akt/mTOR signaling pathway is implicated in the regulation of activity-dependent mRNA translation at the synapses, which is induced by learning and memory formation. However, it has not yet been determined how Akt/mTOR signaling pathways regulate activity-dependent new protein synthesis at synapses. We examined the molecular mechanisms underlying the pathogenesis and progression of AD using a mouse model. We observed a remarkable sex difference in disease progression, with male mice showing early behavioral impairment that worsens over time, whereas female mice did not exhibit impairments until eight months of age. The progression of behavioral deficits in male and female mice is quite different, and it is hypothesized that in male mice, where the deficits begin early, the brain would produce compensatory responses. Until menopause, estrogen is neuroprotective and can counteract the pathogenic effects of β-amyloid accumulation. However, there is a substantial difference in disease progression when estrogen levels decrease. To evaluate the translational potential to performance in humans with AD, we examined the sex-specific difference in the rate of cognitive decline in the Dominantly Inherited Alzheimer Network (DIAN) study, in which participants carry one of the familial mutations in the APP, PSEN1, or PSEN2 genes. We found that the rate of change in performance in cognitive tests (Weschler's logical memory) in mutation carriers showed different trends when the performance was assessed in women versus men as function of age, where men exhibited more rapid cognitive decline than women.

Our findings suggest that premenopausal women are protected from memory deficits, that hormone replacement therapy may be beneficial, and that the cost-benefit ratio must be reevaluated in light of the increasing global burden of AD and the disproportionate impact on women. We conclude that sufficient estrogen levels provide protection in both human and mouse models. Even in the presence of AD mutations, it protects and delays the onset of the disease. Therefore, estrogen provides substantial benefits, and a deeper understanding of the signaling pathways is required to identify creative approaches for reducing the adverse effects of hormone replacement therapy.

Research Publications

Research Publications

The research output of CBR has been published in peer-reviewed, international scientific journals of repute. Citations of the manuscripts that were published during the reporting period are listed below.

Gowda, N. K. C., Nawalpuri, B., Ramakrishna, S., Jhaveri, V., & Muddashetty, R. S. (2022, July 5). NMDAR mediated dynamic changes in m6A inversely correlates with neuronal translation. **Scientific Reports**, 12(1). https://doi.org/10.1038/s41598-022-14798-3

Menesgere, A. L., Sundarakumar, J. S., Shahul Hameed, S. K., & Ravindranath, V. (2022, December 22). Comparison of risk factors for dementia among rural and urban elderly adults-data from two cohort studies in India. **Alzheimer's & Dementia**, 19(6), 2443–2449. https://doi.org/10.1002/alz.12715

Sundarakumar, J. S., Menesgere, A. L., Jain, S., Hameed, S. K., & Ravindranath, V. (2022, December 26). Prevalence of neuropsychiatric conditions and cognitive impairment in two parallel, aging study cohorts from rural and urban India. **Alzheimer's & Dementia**, 19(6), 2469–2478. https://doi.org/10.1002/alz.12741

Menesgere, A. L., Giridhar, V., Bota, R., & Ravindranath, V. (2022, August). Role of Vitamin D on cognitive performance among healthy volunteers of SANSCOG cohort. **Clinical Nutrition Open Science**, 44, 1–8. https://doi.org/10.1016/j.nutos.2022.05.006

Sundarakumar, J. S., Menesgere, A. L., Hameed, S. K. S., & Ravindranath, V. (2022, November). Depression and anxiety during the first and second waves of the COVID-19 pandemic in two large, prospective, aging cohorts in rural and urban India. **Health Science Reports**, 5(6). https://doi.org/10.1002/hsr2.901

Erausquin GA de, Snyder H, Brugha TS, Seshadri S, Carrillo M, Sagar R, Huang Y, Newton C, Tartaglia C, Teunissen C, Håkanson K, Akinyemi R, Prasad K, D'Avossa G, Gonzalez-Aleman G, Hosseini A, Vavougios GD, Sachdev P, Bankart J, Mors NPO, Lipton R, Katz M, Fox PT, Katshu MZ, Iyengar MS, Weinstein G, Sohrabi HR, Jenkins R, Stein DJ, Hugon J, Mavreas V, Blangero J, Cruchaga C, Krishna M, Wadoo O, Becerra R, Zwir I, Longstreth WT, Kroenenberg G, Edison P, Mukaetova-Ladinska E, Staufenberg E, Figueredo-Aguiar M, Yécora A, Vaca F, Zamponi HP, Lo Re VL, Majid A, Sundarakumar J, Gonzalez HM, Geerlings MI, Skoog I, Salmoraighi A, Boneschi FM, Patel VN, Santos JM, Arroyo GR, Moreno AC, Felix P, Gallo CM, Arai H, Yamada M,

Iwatsubo T, Sharma M, Chakraborty N, Ferreccio C, Akena D, Brayne C, Maestre G, Blangero SW, Brusco LI, Siddarth P, Hughes TM, Zuñiga AR, Kambeitz J, Laza AR, Allen N, Panos S, Merrill D, Ibáñez A, Tsuang D, Valishvili N, Shreshta S, Wang S, Padma V, Anstey KJ, Ravindranath V, Blennow K, Mullins P, Łojek E, Pria A, Mosley TH, Gowland P, Girard TD, Bowtell R, Vahidy FS. Chronic Neuropsychiatric Sequelae of SARS-CoV2: Protocol and Methods from the Alzheimer's Association Global Consortium. **Alzheimer's & Dementia: Translational Research & Clinical Interventions**. 2022;8(1):e12348. doi:10.1002/TRC2.12348

D'Souza, M. N., Ramakrishna, S., Radhakrishna, B. K., Jhaveri, V., Ravindran, S., Yeramala, L., Nair, D., Palakodeti, D., & Muddashetty, R. S. (2022, October 1). Function of FMRP Domains in Regulating Distinct Roles of Neuronal Protein Synthesis. **Molecular Neurobiology**, 59(12), 7370–7392. https://doi.org/10.1007/s12035-022-03049-1

Purushotham, S. S., Reddy, N. M. N., D'Souza, M. N., Choudhury, N. R., Ganguly, A., Gopalakrishna, N., Muddashetty, R., & Clement, J. P. (2022, September 5). A perspective on molecular signalling dysfunction, its clinical relevance and therapeutics in autism spectrum disorder. **Experimental Brain Research**. https://doi.org/10.1007/s00221-022-06448-x

Ravindranath, V., Menesgere, A. L., Wallin, M. T., Chapter 58 - Burden of neurological disease, Editor(s): Michael J. Zigmond, Clayton A. Wiley, Marie-Francoise Chesselet, **Neurobiology of Brain Disorders** (Second Edition), Academic Press, 2023, Pages 1047-1064, ISBN 9780323856546.

Adaikkan, C., Wang, J., Abdelaal, K., Middleton, S. J., Bozzelli, P. L., Wickersham, I. R., McHugh, T. J., & Tsai, L. H. (2022, October). Alterations in a cross-hemispheric circuit associates with novelty discrimination deficits in mouse models of neurodegeneration. **Neuron**, 110(19), 3091-3105.e9. https://doi.org/10.1016/j.neuron.2022.07.023

Stezin, A., & Pal, P. K. (2022, September 30). Treatable Ataxias: How to Find the Needle in the Haystack? **Journal of Movement Disorders**, 15(3), 206–226. https://doi.org/10.14802/jmd.22069

Sundarakumar, J. S., Hameed, S. K., Dilip, B., Deepak, S., Kumar, B. V., & Ravindranath, V. (2022, December 9). Approaches to engage an aging, rural cohort in southern India during the COVID-19 crisis and the psychological impact of COVID-19 in this cohort. **Alzheimer's & Dementia**, 19(6), 2460–2468. https://doi.org/10.1002/alz.12726

Ravindranath, V., SANSCOG Study Team (2022, December 28). Srinivaspura Aging, Neuro Senescence and COGnition (SANSCOG) study: Study protocol. **Alzheimer's & Dementia**, 19(6), 2450–2459. https://doi.org/10.1002/alz.12722

Kommaddi, R. P., Verma, A., Muniz-Terrera, G., Tiwari, V., Chithanathan, K., Diwakar, L., Gowaikar, R., Karunakaran, S., Malo, P. K., Graff-Radford, N. R., Day, G. S., Laske, C., Vöglein, J., Nübling, G., Ikeuchi, T., Kasuga, K., & Ravindranath, V. (2023, April 12). Sex difference in evolution of cognitive decline: studies on mouse model and the Dominantly Inherited Alzheimer Network cohort. **Translational Psychiatry**, 13(1). https://doi.org/10.1038/s41398-023-02411-8

Verma, A., Kommaddi, R. P., Gnanabharathi, B., Hirsch, E. C., & Ravindranath, V. (2023, February 23). Genes critical for development and differentiation of dopaminergic neurons are downregulated in Parkinson's disease. **Journal of Neural Transmission**, 130(4), 495–512. https://doi.org/10.1007/s00702-023-02604-x

Kelly, D. E., Ramdas, S., Ma, R., Rawlings-Goss, R. A., Grant, G. R., Ranciaro, A., Hirbo, J. B., Beggs, W., Yeager, M., Chanock, S., Nyambo, T. B., Omar, S. A., Woldemeskel, D., Belay, G., Li, H., Brown, C. D., & Tishkoff, S. A. (2023, February 24). The genetic and evolutionary basis of gene expression variation in East Africans. **Genome Biology**, 24(1). https://doi.org/10.1186/s13059-023-02874-4

Maestre G, Carrillo M, Kalaria R, Acosta D, Adams L, Adoukonou T, Thomas Gregor Issac et al; African Dementia Consortium. "The Nairobi Declaration-Reducing the burden of dementia in low- and middle-income countries (LMICs): Declaration of the 2022 Symposium on Dementia and Brain Aging in LMICs." **Alzheimer's & Dementia** 2023 Mar 11. doi: 10.1002/alz.13025. Epub ahead of print. PMID: 36905253.

Kumar, C., Varghese, M., Duddu, V., Vaitheswaran, S., Srivastava, S., Shaji, K., George, S., Singh, N., Goyal, N., Bakhla, A., Shaji, S., Menon, V., Hussain, T., Grover, S., Mehra, A., Singh, L., Purushotham, A., Desousa, A., Shah, N., . . . Chandra, M. (2023). Indian Psychiatric Society multicentre study: Diagnostic patterns, comorbidity and prescription practices for patients with Dementia. **Indian Journal of Psychiatry**, 65(1), 52. https://doi.org/10.4103/indianjpsychiatry.indianjpsychiatry_736_21

CBR Activities and Initiatives

CBR Activities and Initiatives

CBR has been bustling with activity and exciting initiatives around the year. Snapshots of a few major events are presented here.

Scientific Advisory Committee Meetings

Scientific Advisory Committee meetings were held (online) on 4th April 2022 and (in-person) on 17th December 2022. The Committee reviewed the ongoing research projects and provided feedback and valuable suggestions. New projects proposals were also considered during these meetings. The Committee appreciated the overall progress made in the activities of the Centre.

CBR-IISc Collaborations

With the aim of identifying precise themes for collaboration with various IISc departments, CBR organized an exploratory session on 12th August 2022. This meeting saw participation from at least 10 IISc departments/centres represented by faculty members with expertise and research interests complementary to ongoing studies at CBR. Encouraged by the enthusiasm for collaboration, CBR launched a special funding mechanism by the name CBR-FABRIC (Funding for Aging Brain Research & Innovation Collaboration) program to provide competitive seed grants for focused collaborative projects between CBR and other centres/departments of IISc.

Outreach Events for Volunteers of CBR-SANSCOG and CBR-TLSA

CBR periodically conducts outreach and awareness sessions for the benefit of current and potential participants of the longitudinal cohort studies. For example, on 15th July 2022, CBR hosted an informal gathering (online) of current and prospective participants of the Tata Longitudinal Study of Aging (CBR-TLSA). The TLSA team provided an overview of the progress of the study and updates on recent developments. The session, attended by more than 175 participants from across Bangalore, was very well-received. The current participants unequivocally lauded the team's efforts to coordinate their involvement in the study and manage the assessment sessions smoothly. The TLSA team answered general questions related to the diagnosis, prevention, and management of dementia, and specific questions pertaining to the study's progress and future plans.

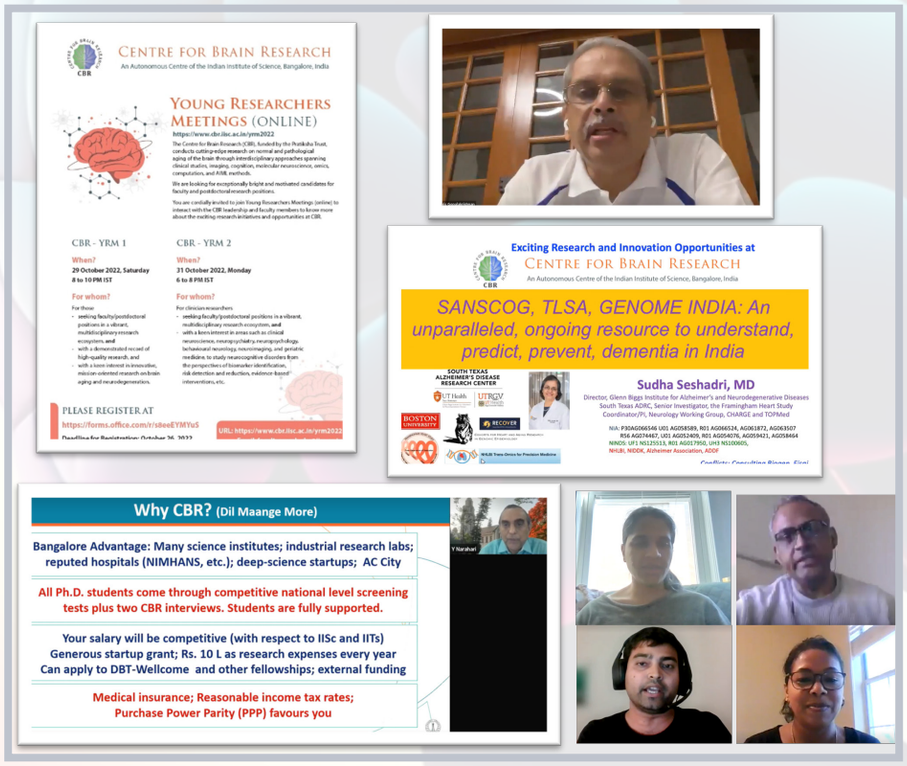
Alzheimer's Awareness Meeting

To commemorate World Alzheimer's Day on 21st September 2022, CBR organized an Alzheimer's awareness meeting (online). Topics covered include an introduction to dementia, epidemiological and research aspects, cognitive impairment and treatment options, the role of complementary medicine, and caregiving. In his inaugural address, the Chief Guest Mr. Kris Gopalakrishnan kindly outlined the vision of CBR and the importance of its longitudinal cohort studies on brain aging. Prof. G. Rangarajan, Director-IISc, offered warm felicitations to CBR on its research and public engagement endeavours.

CBR Currents, a quarterly newsletter

At the Alzheimer's awareness meeting on 21st September 2022, Mr. Kris Gopalakrishnan also launched Wave 1, the inaugural issue of 'CBR Currents', a quarterly newsletter that provides updates on research, innovation, service, and education services at CBR.

Young Researchers Meetings



To attract talented faculty and postdoctoral candidates, CBR organized two well-received Young Researchers Meetings (online) on 29th and 31st October 2022. The latter meeting was targeted specifically at clinicians. The sessions were attended by over 120 aspirants from across the globe. Chief Guests Mr. Kris Gopalakrishnan and Prof. Sudha Seshadri gave lucid summaries of the vision and flagship research projects of CBR. The research and innovation opportunities at CBR were highlighted by the Director and members of the faculty; the meetings included highly interactive sessions to answer the participants' queries.

CBR Session in BCL Workshop

CBR had the pleasure of contributing to Edition IV of the Brain, Computation, and Learning Workshop (BCL 2023). Sponsored by IISc and a generous endowment from the Pratiksha Trust, this highly sought-after interdisciplinary event has been instrumental in facilitating brainstorming and innovative collaborations among computer scientists, neurobiologists,

and research students from across the country. The half-day session on 10th January 2023, orchestrated by CBR faculty members and research staff, touched upon a wide range of topics such as neurocognitive assessment, non-invasive brain stimulation, and the genetic architecture of human cognition. There was also a demonstration of the Hindi Mental State Examination (HMSE), a popular tool used for the assessment of cognitive impairment.

Neuroimaging Training for the CBR Workforce

To support training in the basic principles of neuroimaging, CBR organized (in consultation with Visiting Faculty member Prof. S Senthil Kumaran, Department of NMR, AIIMS New Delhi). an introductory workshop on MRI and functional MRI (from 23rd to 25th January 2023) for Ph.D. students and other young researchers. The workshop was attended by CBR students and research staff and a few participants from IISc, NIMHANS, and St. John's Medical College. Over 3 days, there were theoretical lectures on a wide range of topics - basic principles of MRI, contrast mechanisms, safety guidelines of an MRI facility, MRI-based studies in animal models, structural and functional MRI data acquisition, analyses, and applications, to name a few. The workshop also included hands-on sessions, particularly on data analysis, at the J.N.Tata MRI Centre, IISc campus.

Sharwaree Gokhale Memorial Lecture

A brilliant IAS Officer from the 1974 batch, Ms. Sharwaree Gokhale became the first woman Collector of Mumbai City and retired as Additional Chief Secretary (Environment) after 36 years of distinguished administrative service. In an admirable gesture of payback and service to society, she bequeathed her sprawling apartment in Mumbai to CBR to promote research in neuroscience. She passed away in January 2016; CBR instituted a lecture series in her memory. The fourth lecture in the series was delivered on 15th February 2023 by Dr. Avindra Nath, Clinical Director, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland, USA.

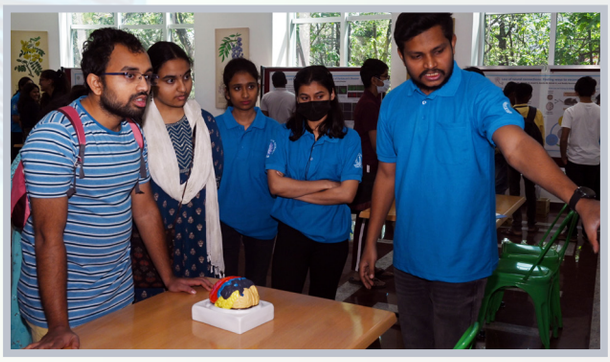
Dr. Nath is a physician–scientist who specialises in neuro-immunology and neurovirology. His research is aimed at studying pathophysiology and developing treatments for neurological infections. The lecture, attended by faculty and students of multiple departments of IISc, focused on Dr. Nath's research on the role of endogenous retroviruses in brain development and neurodegeneration. Mr. Kris Gopalakrishnan, Chair, Governing Council, IISc, and Prof. G. Rangarajan, Director, IISc participated as the guests of honour.

Interaction with the G20 Finance Ministers' Delegation

CBR had the privilege of contributing to the Deep Tech Showcase to the G20 Finance Ministers' delegation that visited IISc on 25th February 2023 as part of the G20 summit. The event was coordinated by the Centre for Nano Science and Engineering, IISc, and was aimed at facilitating the 72-member delegation's engagement with scientists, tech-innovators, and entrepreneurs pursuing affordable and scalable solutions to significant challenges being faced by G20 member countries. Headed by Ms. Nirmala Sitharaman, Union Minister of Finance and Corporate Affairs, and accompanied by Mr. Kris Gopalakrishnan and Prof. G. Rangarajan, the delegation gained an overview of the vision of CBR and the goals of its flagship research projects.

CBR Showcase at the IISc Open Day

For the first time at its new building, CBR organised and hosted a showcase of its research activities and engagement initiatives at the IISc Open Day (4th March 2023). This included informative poster presentations on the flagship projects and faculty-centric projects, demonstrations, quiz contests on neuroscience for school and college students, a display of the



human brain, a kid's corner, mock clinical and cognitive assessment sessions for elderly visitors, and an interactive session with participants of CBR-TLSA. Over 5000 members of the public visited CBR and gained an appreciation for its research and innovation efforts.




CBR Genomics Hackathon

On 24th March 2023, CBR conducted its first Genomics Hackathon as a part of its flagship project GenomeIndia. Aimed at spreading awareness of the tools and methods used in human genomics, this was a competition where 6 teams of students from institutes across the country were invited to computationally solve a problem in genomics in 11 hours. The teams implemented statistical/ML methods on a human genomic dataset to answer questions about disease risk and underlying genetic structure in human populations in this dataset. Dr. Yogesh Simmhan (IISc) and Dr. Sridhar Sivasubbu (IGIB, New Delhi) kindly contributed as judges and guests of honour.

CSR Funding from Software AG

As part of its Corporate Social Responsibility (CSR) initiative, Software AG India (a multinational enterprise software company headquartered in Germany) has extended generous support to CBR to bolster the latter's mission to minimise the burden of dementia in the elderly population. The endowment from Software AG India will enable the establishment of a state-of-the-art laboratory to investigate the role of the cardiac autonomic nervous system (ANS) functions in brain aging and dementia risk. The CBR-SANSLab (Software AG Autonomic Nervous System Laboratory) will conduct advanced scientific research and explore the potential of cardiac ANS dysfunction as an early biomarker for dementia and related disorders. It will provide for key assessments such as cardiac autonomic reflex tests, heart rate variability analysis (HRV) ECG, heart rate response to deep breathing, heart rate response to standing or tilt, etc., and thereby complement the efforts under CBR's ongoing longitudinal cohort studies of aging.

It is being increasingly felt that public communication of science is important to enhance the impact of research, to generate awareness of contemporary science issues and health challenges, to motivate the next generation of scientists, and to help the public take independent and informed decisions in matters that require scientific knowledge. In this view, two Science-Society partnership initiatives have been envisioned under the aegis of the Software AG Community Outreach Program for Elderly (SCOPE).

(1) Project VIKAS (Visual Infographics, Knowledge, Awareness and workSheets) – Understanding dementia
(2) Project YAAD (Youth and Alzheimer's Dementia) – Empowering the 'future caregivers'

Research work at the CBR-SANSLab and outreach efforts through the SCOPE program will serve to address CBR's multipronged mandate of better understanding the aging brain, preserving cognitive functions in aging, and mitigating the risk and burden of aging-related, neurodegenerative disorders.

CBRAIN (CBR Research and Innovation) Internships

CBR launched CBRAIN Internships, a paid summer internship program, to facilitate rigorous training and preparation of young minds (master's and bachelor's students) for world-class, multidisciplinary research on normal and/or pathological brain aging. The first call attracted an overwhelming 6300 applications from hundreds of institutions (research institutes, central/state/ private universities, engineering/arts and sciences/ medical colleges, public health institutes, and companies) across the country. Following rigorous screening and interviews by faculty members, 20 internships were awarded.

Distinguished Visitors to CBR

Dr. Sethuraman Panchanathan, Director of the National Science Foundation (NSF), USA, and winner of IISc's prestigious Distinguished Alumnus award visited CBR on 10th August 2022. This visit, kindly facilitated by Dr. Kris Gopalakrishnan, provided an opportunity for CBR to give Dr. Panchanathan an overview of the flagship projects' outcomes thus far and the expected impact. Lauding the initiatives, Dr Panchanathan expressed confidence that CBR has the requisite expertise and infrastructure to emerge as an international leader in neurodegeneration research.

CBR had the privilege of briefly hosting **Prof. Margaret Martonosi**, the US National Science Foundation's (NSF) Assistant Director for Computer and Information Science and Engineering (CISE). During her CBR visit on 6th January 2023, she acknowledged the pertinence of CBR's efforts in the context of senior citizen well-being and was deeply appreciative of how CBR is envisioned to be an inspiration for philanthropic funding in biomedical research in India. Prof. Martonosi's visit, like that of NSF Director Prof. Panchanathan's visit, has served to propel CBR's resolve to tackle the neurodegenerative disease burden facing the country.

Dr. Srikanth Ryali, Senior Research Scientist of Psychiatry and Behavioral Sciences at the Stanford University School of Medicine, spoke about his research on developing and applying advanced analytic methods for fMRI data. He also engaged in brainstorming and interactive sessions with the faculty and Ph.D. students. (15-16 December 2022)

Prof. Subhasis Chaudhuri, Director, Indian Institute of Technology Bombay, Mumbai was provided with an overview of CBR's research activities and expressed enthusiasm to explore potential areas of collaboration. (30 December 2022)

Prof. Manoj Saranathan is an MRI physicist at the University of Massachusetts Chan Medical School with longstanding experience (industrial and academic) in MR physics, pulse sequence development, and image processing. He has a special interest in ultra high-resolution imaging of the brain, particularly in the context of disorders such as AD, essential tremor, and multiple sclerosis. He offered useful pointers for the neuroimaging aspects of CBR's current research projects.
(04 January 2023)

Prof. Iracema Leroi, an Associate Professor in geriatric psychiatry at Trinity College, Dublin, and **Prof. Mathew Varghese**, Head of the Geriatric Psychiatry Services and the Geriatric Clinic at NIMHANS visited CBR and interacted with the faculty members. They offered valuable suggestions to enhance the impact of the ongoing longitudinal cohort studies. There was also brainstorming on how CBR could potentially partner with the Global Brain Health Institute (GBHI, a joint venture between Trinity College and the University of California, San Francisco) for capacity-building in aging brain research, innovation, and leadership. (17 January 2023)

Dr. Sourav Ghosh, Associate Professor of Neurology and Pharmacology at the Yale University School of Medicine, visited CBR and discussed potential collaborations. He also gave a talk on his group's animal-based studies aimed at deciphering the effect of the loss or gain of Axl (a member of the TAM subfamily of receptor tyrosine kinases) function on learning and memory deficits and long-term potentiation (LTP). (27 January 2023)

Prof. DK Arvind holds the Chair in Distributed Wireless Computation at the School of Informatics, University of Edinburgh. His expertise spans the design, analysis, and integration of miniature networked embedded systems which combine sensing, processing and wireless networking capabilities targeted at applications in healthcare and environmental monitoring. He delivered a lecture at CBR and interacted extensively with the faculty and students. (31 January 2023)

Prof. Ingrid Hotz, Dr. Ram Kumar IISc Distinguished Visiting Chair Professor, is a Professor in Scientific Visualisation in the Department of Science and Technology, Linköping University, Sweden. She gave a talk titled 'Visualization research from data analysis to science communication- A Neuroscience Perspective'. The talk focused on the use of visualisation for data analysis and exploration and presented an outlook on how similar methods can be used in science communication and from a neuroscience perspective. (01 February 2023)

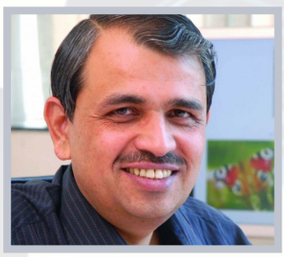
The list of esteemed guests who visited CBR also includes the following eminent personalities.

Mr. Natarajan Chandrasekaran,
Chairman, Tata Sons

Mr. S. Ramadorai,
Former CEO, Tata Consultancy Services

Mr. Anand Mahindra,
Chairman, Mahindra Group

Prof. Vinod Menon,
Cognitive and Systems Neuroscience Laboratory, Stanford University



Prof. L.S. Shashidhara,
Director, National Centre for Biological Sciences

Finance

Finance

Details of Receipts and Payments for the year 2022-23 are as follows.

(In Lakhs)

Sl. No.	Particulars	Receipts	Payments
1	Donations from Pratiksha Trust towards Activities Account	2145.00	2740.00*
2	Other Receipts	84.05	0.00
3	Donations from Pratiksha Trust towards Construction of New Building	0.00	381.96*
4	Funds from External Agencies	1919.64	1905.11
Total		4148.69	5027.08

* Payment is more than the receipt. This was met from the balance carried forward from the previous year.

(In Lakhs)

Funds Received from External Agencies during 2022-23					
			Funds Received during 2022-23		
Project	**Funding Agency/ PI**	**Total Amount Sanctioned**	**For Existing Projects**	**For New Projects**	**Total Funds Received**
GenomeIndia Project	Department of Biotechnology/ Prof Bratati Kahali	5652.00	1538.61	0.00	1538.61
INSACOG Project Phase I & Phase II	Department of Biotechnology/ Prof Bratati Kahali	226.23	4.62	0.00	4.62
Tata Education Trust	Tata Education Trust/Prof Thomas Gregor Issac	3713.20	250.00	0.00	250.00
Ramalingaswami Fellowship	Department of Biotechnology/ Prof Bratati Kahali	32.50	4.91	0.00	4.91
Student Fellowship (Inspire, DBT, CSIR)	Department of Science & Technology/ Department of Biotechnology & Council of Scientific & Industrial Research	8.46	0.00	8.46	8.46
India Alliance DBT Wellcome Trust Grant	Department of Biotechnology/ Dr Chinnakkaruppan Adaikkan	358.89	0.00	43.03	43.03
SANSLab-SCOPE Project	Software AG Community/ Dr Jonas Sundarakumar	140.00	0.00	70.00	70.00
Total		10,131.28	1,798.14	121.50	1,919.64

Governance Structure, Faculty, and Staff at CBR

Governance Structure, Faculty, and Staff at CBR

CBR Society

Centre for Brain Research (CBR) is a registered society under the Karnataka Societies Act 1960. The Society has very eminent persons from different fields as its members. The members of the Society, as of March 31, 2023, are the following.

Prof. G Rangarajan, Director, IISc (Ex officio) [Chair]
Chair, Governing Council, IISc, (Ex officio)
Chief Secretary to Government of Karnataka (Ex Officio)
Additional Chief Secretary to Government of Karnataka (Ex Officio)
Principal Secretary (Finance) Government of Karnataka (Ex Officio)
Secretary, Dept. of IT & BT, Government of Karnataka (Ex Officio)
Shri. Kris Gopalakrishnan, Co-Founder, Infosys
Mrs. Sudha Gopalakrishnan
Shri. Dinesh Krishnaswamy
Shri. S D Shibulal
Prof. Y Narahari, Director, CBR
Prof. Navakanta Bhat, Dean, Division of Interdisciplinary Sciences, IISc
Prof. Vijayalakshmi Ravindranath
Prof. D N Rao, Dept of Biochemistry
Prof. Usha Vijayraghavan, Dean, Division of Biological Sciences, IISc
Prof. H P Khincha, Dept. of Electrical Engg. (Retd), IISc
Dr. Ramesh Babu
Dr. Girija Ramesh Babu
Prof. Anurag Kumar, Dept. of Electrical Communication Engg., IISc
Prof. N Balakrishnan, Supercomputer Education and Research Centre, IISc
Dr. P Satish Chandra
Prof. P Kondaiah, Dept. of MRDG, IISc
Prof. S Mayor,NCBS, Bangalore
Mrs. Sudha Murty
Dr. U B Muthane

Prof. G Padmanabhan, Emeritus Professor, Dept. of Biochemistry, IISc
Mr. S V Ranganath
Prof. M R S Rao, JNCASR, Bangalore
Dr. M S Valiathan
Justice M N Venkatachaliah
Mr. Ashok Soota

Governing Board

The affairs of the CBR are administrated, directed, and controlled by the Governing Board. The Governing Board of the Society shall consist of the following members.

1. Chair, who shall be ex-officio, Director, IISc
2. Four Members of the Society as may be nominated by Pratiksha Trust.
3. Five Members of the Society as may be nominated by the Council of IISc
4. Member Secretary shall be the Director of Centre for Brain Research

The composition of the Governing Board, as of March 31, 2023, is as follows:
Prof. G Rangarajan, Director, IISc (Ex officio) [Chair]
Shri. Kris Gopalakrishnan, Co-Founder, Infosys
Shri. Dinesh Krishnaswamy
Shri. S D Shibulal
Mrs. Sudha Gopalakrishnan
Prof. Navakanta Bhat, Dean, Interdisciplinary Sciences Division, IISc
Prof. Usha Vijayraghavan, Dean, Biological Sciences Division, IISc
Prof. H P Khincha, Dept. of Electrical Engg, (Retd) IISc
Prof. D N Rao, Dept of Biochemistry, IISc
Prof. Y Narahari, Director, CBR [Member Secretary since June 2022]

Prof. Vijayalakshmi Ravindranath, Founding Director, CBR [Member Secretary till May 2022]

International Scientific Advisory Board

An International Advisory Board consisting of international as well as national experts shall be constituted by the Governing Board. The Board meets biannually. International Advisory Board consists of the following members:

Prof. Steven E Hyman, Broad Institute of Harvard and MIT [Chair]
Prof. John Morris, Washington University
Prof. Maria Corrillo, Chief Science Officer, Alzheimer's Association
Prof. Stanley Fahn, Columbia University
Prof. Y Narahari, Director, CBR
Prof. Sudha Seshadri, UT Health Science Center at San Antonio
Prof. Carla Shatz, Stanford University
Prof. Mary Ganguly, Pittsburgh
Prof. Srinath Reddy, PHFI, New Delhi
Prof. B N Gangadhar, NIMHANS, Bangalore
Prof. Bart D Strooper, Director, UK Dementia Research Institute
Prof. Stacie Weninger, President of FBRI, USA
Prof. Vasant Honavar, Penn State University

Scientific Advisory Committee

The Scientific Advisory Committee (SAC) of the Centre for Brain Research monitors and provides guidelines on the scientific activities of the Centre. The members are:

Prof. Srinath Reddy (PHFI, New Delhi) [Chair]
Prof. Ramesh Hariharan (CEO, Strand Genomics, Bangalore)
Prof. Ravindra M Pandey (AIIMS, New Delhi)
Prof. Anurag Agrawal (IGIB, New Delhi)
Prof. K Thangaraj (CDFD, Hyderabad)
Prof. Vidita Vaidya (TIFR, Mumbai)
Prof. Pratima Murthy (NIMHANS, Bangalore)
Prof. S Ganesh (IIT Kanpur, Kanpur)
Prof. Y Narahari (Director, CBR)

Finance Committee

CBR has a Finance Committee which meets every three months to review the financial positions of the Centre and make recommendations to the Governing Board from time to time. The members of the Finance Committee, as of March 31, 2023, are:

Prof. G Rangarajan [Chair]
Prof. Y Narahari, Director, CBR
Mr. K C Ganesh
Prof. P S Anilkumar
Prof. Navakanta Bhat
Mr. T S Vishwanath [Secretary]

Ethics Committee

An Ethics Committee has been constituted by the Governing Board, as mandated by the National Ethical Guidelines for Biomedical and Health Research involving human participants, Indian Council of Medical Research (ICMR) Govt. of India.

Dr. Chandramouli, B.A, Apollo Hospital, Bangalore [Chair]
Prof. D N Rao, Dept. of Biochemistry, IISc
Prof. K N Balaji, Dept. of MCBL, IISc
Dr. Kiran Khanapure, Vikram Hospital, Bangalore
Dr. Girish Baburao Kulkarni, NIMHANS Bangalore
Adv. Arvind Moorchung, Sr Consultant
Prof. Anitha Kurup, NIAS Bangalore
Mr. Alaganandan Balaraman
Prof. Thomas Gregor Issac, CBR
Dr. Jonas S Sundarakumar, CBR [Member Secretary]

Institutional Biosafety Committee

Prof. K N Balaji, IISc [Chair]
Prof. Anita Mahadevan, NIMHANS, Bangalore [DBT Nominee]
Dr. Albert Stezin Sunny, CBR [Biosafety Officer]
Dr. Ravi Manjithaya, JNCASR, Bangalore [External Expert]

Prof. Ravi Muddashetty, CBR
Prof. Bratati Kahali, CBR
Dr. Latha Diwakar, CBR
Dr. Khader Valli Rupanagudi, CBR
Dr. Smitha Karunakaran, CBR [Member Secretary]

Internal Committee against Sexual Harassment

Prof. Bratati Kahali, CBR [Chair]
Dr. Latha Diwakar, CBR
Dr. Khader Valli Rupanagudi, CBR
Ms. Pragati Shukla, Advocate
Mr. P Manivannan, CBR

Faculty and Staff at CBR

Academic Staff

Prof. Bratati Kahali, Associate Professor
Prof. Ravi Muddashetty, Associate Professor
Prof. Thomas Gregor Issac, Associate Professor
Dr. Smitha Karunakaran, Assistant Professor
Dr. Jonas S Sundarakumar, Assistant Professor
Dr. Chinnakkaruppan Adaikkan, Assistant Professor
Dr. Sivaprakasam Ramamoorthy, Assistant Professor
Dr. Shweta Ramdas, Assistant Professor
Dr. Latha Diwakar, Senior Scientific Officer
Dr. Kommaddi Reddy Peera, Senior Scientific Officer

Adjunct Faculty

Prof. Govindan Rangarajan, Dept. of Mathematics, IISc
Prof. Y Narahari, Dept. of Computer Science and Automation, IISc
Prof. HP Khincha, Professor (Retd.), Dept. of Electrical Engineering, IISc

Prof. Arun Kumar, Dept. of Molecular Reproduction Development and Genetics, IISc
Prof. Sridharan Devarajan, Centre for Neuroscience, IISc

Visiting Faculty

Prof. Sivakumar P T, Dept. of Psychiatry, NIMHANS, Bangalore
Prof. Ganesan Venkatasubramanian, Dept. of Psychiatry, NIMHANS, Bangalore
Prof. Girish N Rao, Dept. of Epidemiology, NIMHANS, Bangalore
Prof. Naren P Rao, Dept. of Psychiatry, NIMHANS, Bangalore
Prof. Gaiti Hasan, National Centre for Biological Sciences, TIFR, Bangalore
Dr. Sanjaya Viswamitra, Dept. of Radiology, Sri Sathya Sai Institute of Higher Medical Sciences, Bangalore
Prof. Senthil Kumaran, AIIMS, New Delhi

Scientific Staff

Dr. Khader Valli Rupanagudi, Scientific Officer Grade I
Dr. Albert Stezin Sunny, Scientific Officer Grade I
Dr. Deepashri Agrawal, Scientific Officer Grade I
Dr. Shobha Anilkumar, Scientific Officer Grade II
Dr. Shafeeq K Shahul Hameed, Scientific Officer Grade II
Dr. Prathima Arvind, Scientific Officer Grade II
Dr. Madhankumar Anandhakrishnan, Grants Manager

Research Staff

Dr. Abhishek M L, Research Psychiatrist
Dr. Divya N M, Medical Officer
Dr. Ajith Partha, Medical Officer
Dr. Amitha C M, Medical Officer
Dr. Shobith, P, Medical Officer
Dr. Gnanavathi Reddy Jangam Chandra, Medical Officer
Dr. Sadhana Singh, Research Scientist
Dr. Palash Kumar Malo, Research Associate
Dr. Justin Joseph, Research Associate
Dr. Sarayu Ramakrishna, Research Associate
Dr. Vidhu Agarwal, Post Doctoral Fellow

Dr. Pooja Rai, Project Scientist I
Mr. Shashank Shekhar Padhi, Project Associate I
Ms. Shreya Adhya, Project Associate I
Ms. Aishwarya B H, Project Associate I
Ms. Anjana Menon, Project Associate I
Mr. G Goutham Kumar, Project Associate I
Mr. Aditya Yinaganti, Project Associate II
Ms. Rajitha Narayanasamy, Junior Research Intern
Ms. Meghana R, Junior Research Intern
Mr. Hariprasath Ragupathy, Junior Research Intern
Ms. Meenakshi Menon, Junior Research Intern
Ms. Amrita Mondal, Junior Research Intern
Mr. Chowtapalle Anuraag Chetty, Junior Research Fellow
Ms. Ankita Talukdar, Project Assistant
Ms. Ayana E K, Project Assistant
Ms. Nayanika Kalita, Project Assistant
Dr. D M Parimala, Veterinarian
Mr. Raveendra Vukkala, Field Assistant

Ph.D. Students

Ms. Krithika S
Ms. Haseena P A
Ms. Bindushree K R
Ms. Srishti Kushwaha
Ms. Shreya Chakraborty
Ms. Mayank
Ms. Nimisha B
Ms. Nisa Manzoor Shah
Ms. Rupsa Roy Choudhury
Mr. Anant Gupta
Ms. Dipanwita Santra
Ms. Harsha Bhardwaj
Ms. Jani Sidhi Pushkarbhai
Mr. Mohammed Waseequr Rahman
Ms. Preeti
Ms. Priya Chatterjee
Ms. Sandhya G
Ms. Shruti Pandey
Ms. Syed Wasifa Qadri
Mr. Aniket Das
Ms. Dwaiti Roy
Ms. Manasvi Chopra

Technical Staff

Mr. Jothibasu V, Information System Manager
Mr. Mohammed Hanif Kaba Mujawar, Senior Technical Assistant
Mr. Karthik S, Technical Assistant
Mr. Sangeethkumar Saminathan, Technical Assistant
Ms. Divya S, Technical Assistant
Mr. Anand Kumar E, Technical Assistant
Mr. Vinayak Hosawad, Technical Assistant
Mr. Victor Arul Raj, Technical Assistant
Mr. Anees N K, Technician
Mr. Divakar A, Lab Technician
Mr. Prashant Deora, Lab Technician
Ms. Kavya P, Lab Technician
Mr. Goutham V, Lab Assistant
Mr. Mohana C, Lab Assistant

Mr. Rajesh G, Lab Assistant
Ms. Pavithra D P, Lab Assistant
Ms. Rupanagudi Sunitha, Lab Assistant
Ms. Rehab Hussain, Lab Assistant

Field Staff

Ms. Maina T S, Office Supervisor
Mr. Rajakumar K M, Psychologist
Ms. Savitha B P, Psychologist
Mr. Naresh G, Psychologist
Mr. Rajesh, Field Supervisor
Mr. Harikrishna G, Field Data Collector
Mr. Yashwanthkumar K, Field Data Collector
Mr. Shashikumar, Field Data Collector
Mr. Shivaraj S, Field Data Collector
Mr. Gangaraja V, Field Data Collector
Mr. Madhuresha, Field Data Collector
Mr. Nagesha C, Field Data Collector
Mr. Shankarappa N, Field Data Collector
Mr. Venkataramana K V, Field Data Collector
Ms. Chaithra B K, Field Data Collector
Ms. Sunitha H S, Nurse
Ms. Shylashree Deepak, Nurse
Ms. Swathishree A N, Nurse
Ms. Nethravathi, Nurse
Ms. Pavithra K V, Nurse
Ms. Gayathri P S, Nurse
Ms. Chaithra N, Nurse
Ms. Sushma C V, Nurse
Ms. Vedhavathi H S, Nurse
Ms. Poornima K T, Nurse
Ms. Sujatha S N, Nurse

Administrative Staff

Mr. R Mohan Das, Special Officer [till 30 September 2022]
Mr. T S Vishwanath, Manager (Admin)
Mr. Manivannan P, Finance Officer
Ms. Aruna Poojary, Senior Executive Assistant
Ms. Sudha Srikanth, Senior Executive Assistant
Ms. Sudha Rani P, Senior Executive Assistant
Mr. Ravikumar K L, Executive Assistant
Mr. Rahul Dev, Administrative Assistant
Ms. Triveni, Front Office Executive
Mr. Sudarshan Rao N, Advisor- Civil works
Mr. M R Chandrashekar, Security Advisor

A historic landmark: Pratiksha Trust - IISc - CBR MoU Signing Ceremony, 15 February 2023

CENTRE FOR BRAIN RESEARCH
CBR

CONTACT US

CBR Office
Centre for Brain Research
Indian Institute of Science Campus
CV Raman Avenue
Bangalore 560012. India.

+91 80 2293 3588
Fax: +91 80 2360 7766

office.cbr@iisc.ac.in

cbr.iisc.ac.in