ANNUAL REPORT
2021-2022

CENTRE FOR BRAIN RESEARCH

AN AUTONOMOUS CENTRE OF THE INDIAN INSTITUTE OF SCIENCE

Contents

CBR at a Glance

The Centre for Brain Research (CBR) is an autonomous, not-for-profit, research hub located in the Indian Institute of Science campus. It was established in 2014 through an exemplary endowment from the Pratiksha Trust founded by Dr. Kris Gopalakrishnan and Mrs. Sudha Gopalakrishnan. The Trust has also generously funded the construction of the recently completed CBR building. The building was inaugurated and dedicated to the Nation by Prime Minister Shri Narendra Modi on June 20, 2022.

CBR receives strategic advice from an International Advisory Board and a National Scientific Advisory Committee comprising eminent leaders in the field. Professor Vijayalakshmi Ravindranath is the Founding Director of the Centre.

The research and innovation activities of CBR are dedicated to preserving cognitive functions during aging and to discovering scientific methods for early diagnosis, prevention, postponement, and cure of neurodegenerative diseases of the elderly population.

The CBR Mandate

CBR's mandate is to conduct cutting-edge translational research on normal and pathological aging of the brain aimed at identifying risk factors and protective factors for neurodegeneration. The goal of CBR is to reduce the burden of dementia through early diagnosis, prevention, and innovative, scientifically proven interventions.

The CBR Mission

CBR strives to achieve its mandate through interdisciplinary research spanning genetics, molecular neuroscience, clinical studies, imaging, cognition, and computational methods including data science and machine learning techniques. It promotes high-end capacity-building to foster interdisciplinary neuroscience research in India. It enables collaboration platforms to establish and nurture a pan-India community of practice in research on the aging brain and neurodegenerative diseases.

Established through philanthropy, CBR has started receiving extramural grants for specific, mission-oriented research projects from multiple agencies such as the Department of Biotechnology, Science and Engineering Research Board, Tata Trusts, SKAN Research Trust, Bill & Melinda Gates Foundation, and Fidelity Foundation. Besides supporting basic research in diverse areas of neurodegeneration and human genomics, CBR is spearheading prestigious projects having significant implications for the aging population.

I. Research at CBR

1. Flagship Research Projects

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

1. 1. Longitudinal Cohort Studies on Aging

Prospective, population-based, longitudinal aging studies form an important approach in the understanding of the risk factors and protective factors for dementia and other neurodegenerative diseases associated with aging. This approach will help in developing strategies to prevent, delay onset, or mitigate the course of dementia, the burden of which is growing in epidemic proportions across the world, particularly in India. Given the unique geographical, socio-cultural, linguistic, ethnic, and genetic diversity of Indians, it is important to understand the underpinnings for aging-related disorders such as dementia in the Indian population. However, there is a dearth of large-scale, long-term, prospective studies on aging in India.

CBR conducts two such unique studies. Srinivaspura Aging, Neuro Senescence and COGnition (SANSCOG) study and Tata Longitudinal Study on Aging (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 SANSCOG study are recruited from the villages of Srinivaspura Taluk in Kolar District in Karnataka, through an area sampling strategy, whereas those in TLSA are recruited through convenience sampling, from urban Bangalore, India. Harmonization in assessments across the two studies enables head-to-head comparison of the outcome measures.

A. Srinivaspura Aging, Neuro Senescence and COGnition (SANSCOG) Study

Funding: CBR

SANSCOG study (projected number = 10,000 individuals) is a first-of-its-kind, large, cohort study in the rural Indian population that follows an interdisciplinary, multimodal approach including detailed clinical, neurocognitive, biochemical, genetic, and neuroimaging assessments. 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 in the villages due to logistic reasons. Genetic testing involves genome-wide association studies (GWAS) for all SANSCOG participants and Whole Genome Sequencing (WGS) for a subset of the cohort. The third visit involves neuroimaging, where a subset of the cohort undergoes brain MRI at the Indian Institute of Science (IISc) or the National Institute of Mental Health and Neurosciences (NIMHANS) in

Bangalore. During the third visit, SANSCOG participants also undergo other specialized tests such as Optical Coherence Tomography (OCT), Carotid Doppler, Pulmonary function testing (Spirometry), as well as Gait and Balance assessments.

Figure 1: Snapshots from the SANSCOG team's community engagement initiatives for awareness generation and cohort retention

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 follow-up assessments commenced in February 2020. The progress of the study for the period 1 April 2021 to 31 March 2022 is outlined below:

Second wave lockdown and suspension of the study: The study had to be suspended due to the second wave of the COVID-19 pandemic and the associated lockdowns in Kolar district. Owing to this, we were unable to carry out recruitment or regular clinical and cognitive assessments from 21 April to 21 June 2021.

Engaging our participants during the second wave lockdown: Throughout the second wave lockdown period, we kept in touch with our participants telephonically to enquire about their well-being and to provide any medical guidance, when necessary. A total of 2368 telephonic calls were made by the field team and we reached out to 2095 participants. The assessment team also carried out telephonic assessments for depression and anxiety during this period. A total of 820 participants consented, out of which 611 participants completed their depression and anxiety assessments telephonically.

Restarting the study after the second wave: Following the relaxation of lockdowns by the government, our field team conducted a survey to assess the willingness of participants to come for assessments if we restarted the study. A total of 232 participants, who were enrolled in the study and yet to come over for assessments, participated in the telephonic survey. A majority (63%) of participants reported willingness to come over for assessments; further to this positive response from the participants, we restarted the study with COVID-19 safety precautions in place.

Ramping up recruitments: After restarting the study, we quickly ramped up recruitment and assessments – conducting baseline assessments in the project office and follow-up assessments in the mobile unit in parallel. Following completion of 2 PHCs (Dalasanur and Nambihalli), we started recruitment from villages attached to the third PHC, namely Ronur PHC. House-to-house surveys were conducted by our field team with the support of the ASHA workers of the respective villages. Further, awareness camps were conducted in each village to recruit participants. We were able to ramp up our daily assessments to 12-13 per day, with 8-9 assessments being done in the Srinivaspura project office and 4 assessments in the mobile unit. Follow-up assessments also picked up pace and were being conducted parallelly.

Third wave lockdown and suspension of the study: The study had to be suspended again due to the third wave of the COVID-19 pandemic. Owing to this, we were unable to carry out recruitment or regular clinical and cognitive assessments from 9 January to 8 February 2022.

Engaging our participants during the third wave lockdown: Throughout the third wave lockdown period, we kept in touch with our participants telephonically to enquire about their well-being and provide any medical guidance, when necessary. A total of 2874 telephonic calls were made by the field team and we reached out to 2124 participants. The assessment team also carried out telephonic assessments for depression and anxiety during this period. A total of 1763 participants consented, out of which 643 participants completed their depression and anxiety assessments telephonically. We found that 29.4% of our participants had depression on the Geriatric Depression Scale (GDS) and 6.8% had anxiety symptoms on Generalized Anxiety Disorder (GAD) assessment.

Restarting the study and progress after the third wave: We restarted the study on 9 February 2022 with appropriate COVID-19 safety precautions in place. There was an increased rate of cancellations during the initial few weeks, but this has been gradually decreasing. We are now conducting special tests, such as OCT and Spirometry; a technician is being trained for performing Carotid Doppler. We have also been able to increase the number of MRIs / OCTs to 18 per week (3 x 6 days), following the recruitment of an additional MRI technician.

Table 1 depicts the summary of all study activities during the last year as well as overall study progress.

Table 1: Progress of SANSCOG Study

Particulars	1 April 2021 – 31 March 2022	Overall (1 Jan 2018 – 31 March 2022)
Participants consented	1515	4136
Villages recruited from	30	64
Baseline assessments	1334	3548
Follow up assessments	665	791
Brain MRI	390	506
Interim telephonic + home visit contact	66	1264
Based on interim contact, participants interested in follow-up	66	1264
Blood sample collection camps	99	177
Sample collection completed	1788	4040
Feedback/consultation sessions completed	90	154
Village surveys	3	35
Awareness programs	27	74
Community engagement activities	0	4

B. Tata Longitudinal Study of Aging (TLSA)

Funding: Tata Trusts

Tata Longitudinal Study of Aging (TLSA) is an ongoing, large-scale, prospective, population-based cohort study 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 periodic, 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.

Prior to recruitment, awareness programs are conducted in the city, to inform the participants about the disease and the study. The participants who give consent undergo detailed clinical, neurocognitive, biochemical, genetic, and neuroimaging (MRI and MRS) assessments, which are done in 1-2 visits. The first visit occurs in the Centre for Neuroscience, Indian Institute of Science where participants undergo detailed clinical and cognitive assessments. During the second visit, which also occurs in the Indian Institute of Science, they undergo neuroimaging. Blood sample is drawn at their residence for biochemical and genetic assessments. Recruitment for the study started in 2015 and so far, around 750 participants have consented for the study, and all of them have completed their baseline assessments.

Phase 1 of TLSA concluded in December 2021 and Phase 2 of the project has been approved for funding by Tata Education Trust for a period of 5 years from January 2022.

During the period 1 April 2021 to 31 March 2022, we have recruited 271 new participants and completed 212 follow-up assessments. A total of 467 blood investigations (256 baseline + 211 follow-up) and 220 brain MRI (156 baseline + 64 follow-up) were carried out during this period.

Due to the COVID-19 pandemic, assessments had to be stopped from 5 January to 15 February 2022. During this time, participants were contacted over phone or email to check on their well-being. More than 550 participants were contacted. When necessary, the doctors in the clinical team also offered telephonic health-related advice to the participants who sought help for their medical problems. We resumed clinical assessments from 16 February 2022.

The study progress for the period 1 April 2021 to 31 March 2022 is summarised below.

Table 2: Progress of TLSA study

Particulars	Overall						April 2021 to March 2022					
Participants consented	751						271					
Clinical and cognitive assessments	BL	F1	F2	F3	F4	F5	BL	F1	F2	F3	F4	F5
	751	369	241	129	33	4	271	45	73	65	25	4
Brain MRI	BL	F1	F2	F3	F4	F5	BL	F1	F2	F3	F4	F5
	437	169	110	27	18	0	156	1	47	3	13	0
Blood investigations	BL	F1	F2	F3	F4	F5	BL	F1	F2	F3	F4	F5
	636	310	213	111	27	3	256	47	82	59	20	3

Figure 2: Glimpses into the TLSA team's efforts to engage with the urban aging population in order to generate awareness on dementia and encourage participation in the study

Investigation 1: Relationship between ApoE and Cognition

We analyzed the performance on global cognition, processing speed, working memory, auditory attention, verbal short-term memory, and visuospatial skills, to ascertain between APOE ε4 carriers and non-carriers among healthy participants of TLSA.

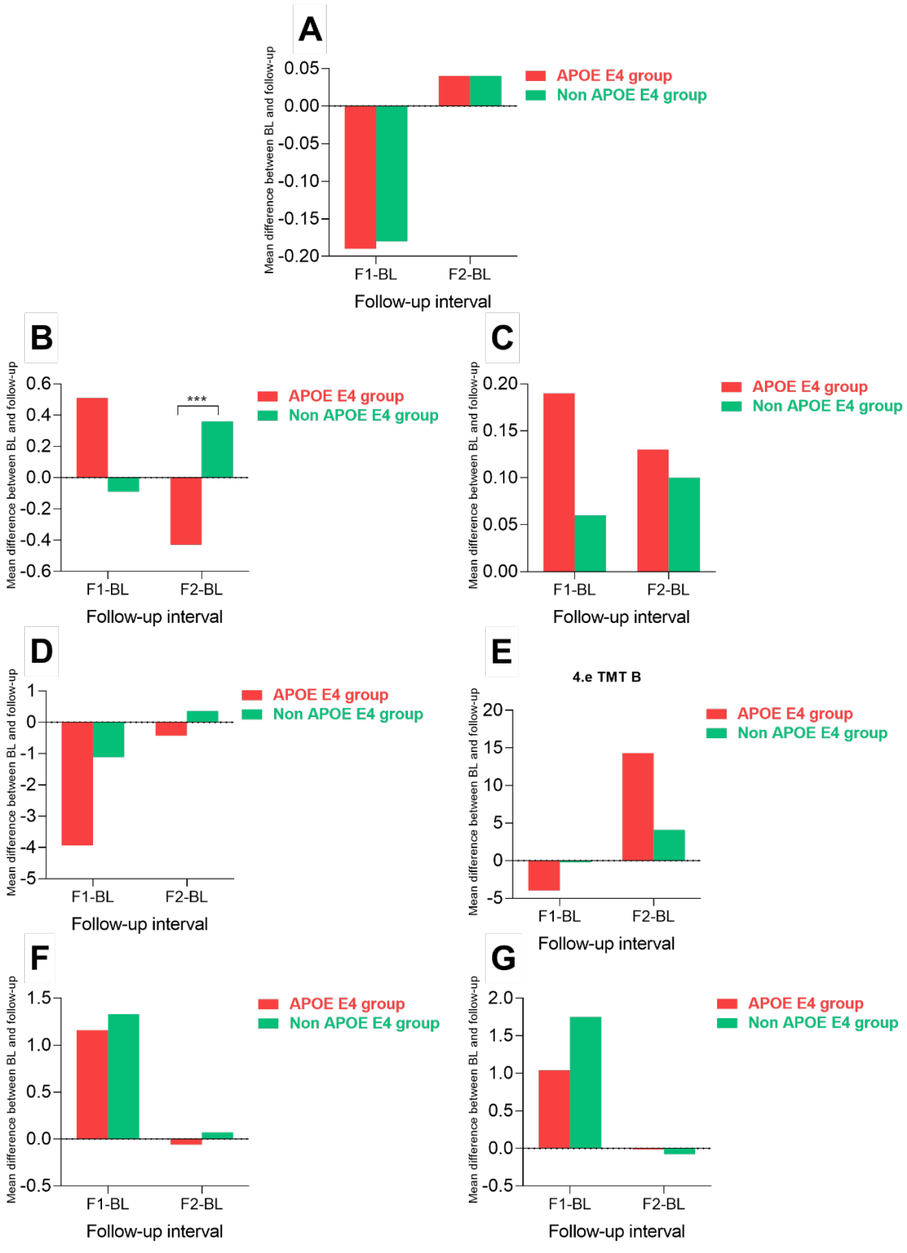


Figure 3: Cognitive performance of study sample (TLSA)

Figure 3 shows cognitive performance of study sample at follow-up evaluation. It shows results of Generalized Linear Model comparing the estimated marginal mean differences in cognitive performance (plotted on the y axis) from baseline and first, second follow-up visit of study sample for ACE total scores (A), Digit-span forward scores (B), Digit-span backward scores (C), time taken for Trail Making Test A measured in seconds (D), time taken for Trail Making Test B measured in seconds (E), total scores for Modified Taylor Complex Figures in immediate recall phase (F) and total scores on Modified Taylor Complex Figures delayed recall phase (G) between APOE ε 4 group (Nf1=65, Nf2=42) and non-APOE ε 4 group (Nf1=198, Nf2= 117); $p < 0.001$.

APOE ε4 carriers showed a faster cognitive decline in auditory attention and verbal short-term memory as measured by digit forward test (B = -0.79; p = 0.001) compared to non-carriers at two years of follow up. The presence of APOE ε4 allele did not affect the rate of cognitive decline on other cognitive domains.

The presence of specific cognitive deficits in APOE ε4 carriers could potentially be a composite biomarker for early cognitive decline in people carrying this allele.

Investigation 2: Association of cardiovascular risk factors with cognitive impairment

We also estimated the odds of developing cognitive impairment with known cardiovascular risk factors such as hypertension, diabetes mellitus, obesity, physical inactivity and high-risk CAIDE scores (>/= 9). Findings are represented in Figure 4.

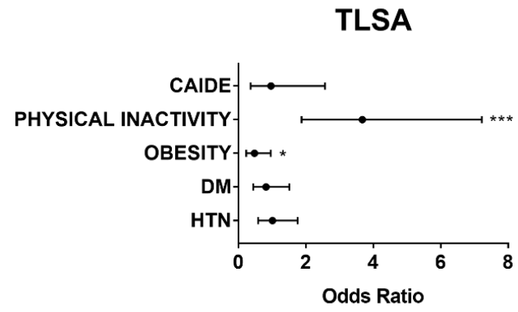
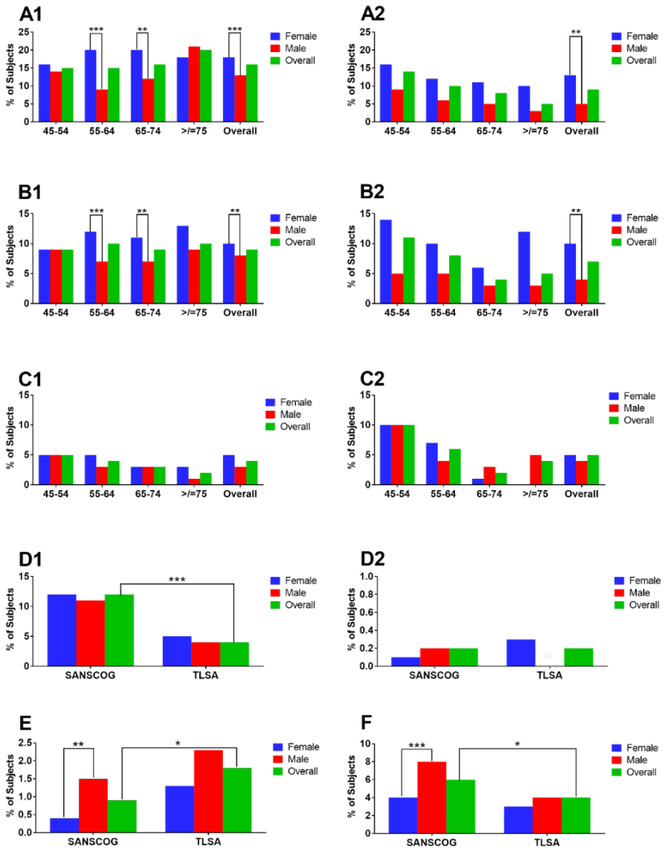


Figure 4: Association of cardiovascular risk factors with dementia

Investigation 3: Neuropsychiatric risk factors for dementia in rural and urban Indians

Neuropsychiatric conditions, such as depression, early-life stressful events, stroke, and head injury can be potential risk factors for dementia. When prevalence rates of these conditions were compared between rural (n=3262) and urban (n=693) aging individuals in southern India, we found that depression prevalence was significantly higher in rural than urban participants, with female preponderance in both groups. Early life stressor (childhood parental death) and head injury were significantly more in rural than urban, whereas stroke was more in urban. Depression (both self-reported and clinician-rated) and stroke significantly increased the odds of having dementia (Clinical Dementia Rating ≥ 0.5) in rural Indians.



* p ≤ 0.05 ** p ≤ 0.01 *** p ≤ 0.001

A1. Age and gender-wise depression (on self-reported Geriatric Depression Scale) among rural (SANSCOG) subjects.
A2. Age and gender-wise depression (on self-reported Geriatric Depression Scale) among urban (TLSA) subjects.
B1. Age and gender-wise depression (on clinician-rated Hamilton's Depression Rating Scale) among rural (SANSCOG) subjects.
B2. Age and gender-wise depression (on clinician-rated Hamilton's Depression Rating Scale) among urban (TLSA) subjects.
C1. Age and gender-wise past history of depression (self-reported) among rural (SANSCOG) subjects.
C2. Age and gender-wise past history of depression (self-reported) among urban (TLSA) subjects.
D1. Gender-wise history of early life stressor – childhood parental death between rural (SANSCOG) and urban (TLSA) subjects.
D2. Gender-wise history of early life stressor – childhood parental divorce between rural (SANSCOG) and urban (TLSA) subjects.
E. Gender-wise history of stroke between rural (SANSCOG) and urban (TLSA) subjects.
F. Gender-wise history of head injury between rural (SANSCOG) and urban (TLSA) subjects.

Figure 5: Comparison of prevalence of neuropsychiatric risk conditions in rural (SANSCOG) and urban (TLSA) subjects

1. 2. 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 (Figure 6).

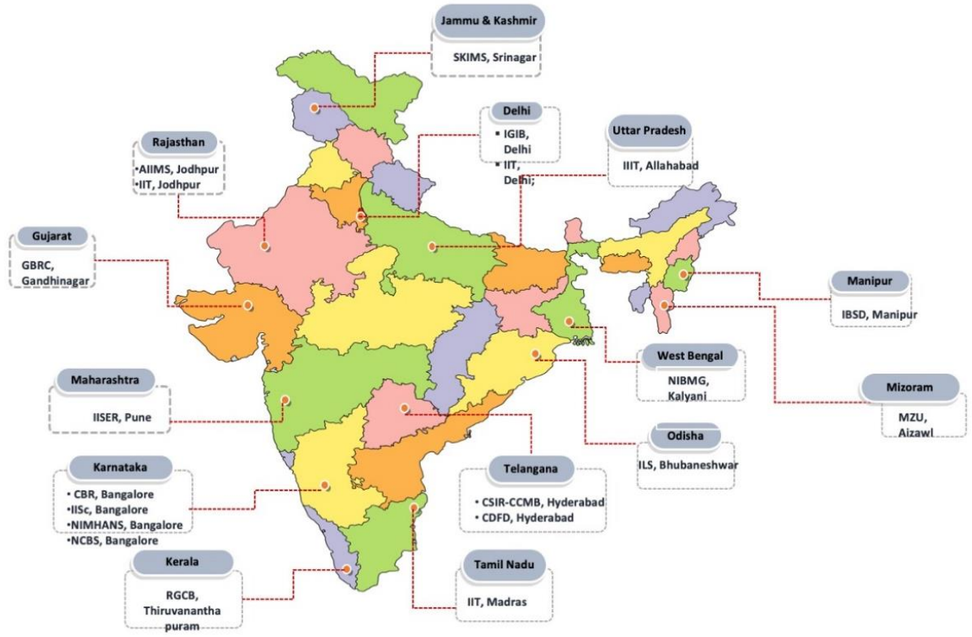


Figure 6: Details of the 20 partner institutions in the GenomeIndia Project (map courtesy: DBT)

Since genetic variations in individuals are (a) population-specific, (b) could predispose them to certain diseases, (c) cause inherited disorders, and (d) determine their response to drugs, it is pertinent that such variants be mapped in the Indian population. With more than a billion individuals spread across >4500 ethnic groups following unique socio-cultural practices through past several hundreds of years, the genetic diversity of the current day Indian population shaped by these factors is a powerhouse for understanding genetic basis of disorders and tracking migration and evolutionary patterns. Thus, the Indian population harbors distinct variations and often, many disease-causing mutations are amplified within some of these groups. Therefore, Indian population-based or disease-based human genetics research is the need of the hour to better understand the disease susceptibilities in our population based on an individual's genetic makeup.

GenomeIndia project aims to construct an exhaustive catalogue of genetic variations for our diverse population, by identifying the common, low frequency, rare, single nucleotide polymorphisms or SNPs, and genetic variations present in our population through whole genome sequencing of representative population groups across the country. The variations data will be made available through a web portal. This reference catalogue of genetic variations will help in identifying the causal variations for monogenic disorders in our population. Currently, India also does not have a country-specific genome wide genotyping array, and the results from GenomeIndia will facilitate designing such array(s) that will make large-scale comprehensive genetic studies affordable in our country.

Specific aims of the project

(1) Create an exhaustive catalog of genetic variations (common, low frequency, rare, single nucleotide polymorphisms or SNPs and structural variations) in Indians.

(2) Create a reference haplotype structure for Indians. This reference panel can be used for imputing missing genetic variation in future GWA studies.

(3) Design genome-wide arrays for research and diagnostics at an affordable cost.

(4) Establish a biobank of DNA and plasma collected for future use in research.

The project was sanctioned by Department of Biotechnology, Government of India in January 2020. The total funding is INR 237.74 crores. As part of this project, CBR has helped conduct several workshops in the partner institutions between January and March 2020 for population identification, community outreach, and best practices for sample collection. Most importantly, one of the workshops was taught by instructors from Broad Institute of MIT and Harvard who are part of the GATK and Terra developing team, the program suite used worldwide for this purpose.

At CBR, 2173 individuals have been contacted for probable participation in the study. 1997 individuals from varied population groups have consented and been recruited into the study. Sample collection and phenotyping have been done for these 1997 individuals. In total, 11987 individuals have been recruited into the project by all the sample collecting institutes. CBR has installed the data collection app for the participating sample collecting institutes that would aid in having background information of study subjects as well as storing and transferring anthropometric, biochemical data for all subjects enrolled in the project from across 13 sample collecting institutes in the country.

Genome-wide genotyping (GWAS) on Precision Medicine Research Array (PMRA Affymetrix) upon the high-throughput GeneTitan scanner has been performed for the 2719 samples at CBR. Whole genome sequencing upon a next generation sequencing platform (Illumina Novaseq 6000 for WGS) has been done for 2205 samples at CBR, out of 5232 WGS carried out by all four sequencing institutes. CBR also has approved biobanking facility where DNA samples will be stored in a cryo-preserved protected manner as per global standards.

CBR houses a scalable storage system of 4 Petabytes for data storage and high-performance computing infrastructure of >300 Teraflops capacity, that supports data analysis and storage of the massive amounts of multimodal data generated by human studies spearheaded by CBR.

The WGS and analysis have been thoroughly benchmarked with four standard Corriell cell lines obtained from the NIST Genome in a Bottle consortium, resulting in high concordance of variants obtained.

CBR has analyzed data from the WGS. Call rate is in the range of 96 to 99%, and mean genotype quality for most samples is >70. The average transition-transversion ratio is 1.8 across autosomes and sex chromosomes. About 45 million genetic variations were identified from 1011 individuals; ~41 million of them are single nucleotide polymorphisms (SNPs), and ~4 million are short insertions and deletions (InDels). Among the SNPs and InDels that are present in both Indians as well as other populations, about 1.5 million variations differ in prevalence among Indians and others by at least 15% frequency of the alternate allele. About 10 million SNPs are unique to the Indian population, and 0.5 are novel InDels. Majority of the novel variations uncovered in Indian population are of low frequency (1-5% frequency) or rare (<1%).

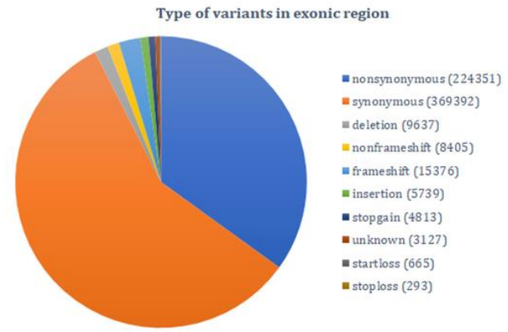


Figure 7: The distribution of exonic variations as inferred from 1011 Indian samples

About 52% and 37% of all the variations are intergenic and intronic respectively. Out of the exonic variants, ~35% are non-synonymous, and ~57% are synonymous changes. About 3% of the insertions and deletions are present in exonic region, which points to enormous (till now untapped) consequences in terms of protein coding variations affecting phenotypic changes on our population.

1. 3. The Indian SARS-CoV-2 Genomic Sequencing Consortium (INSACOG)

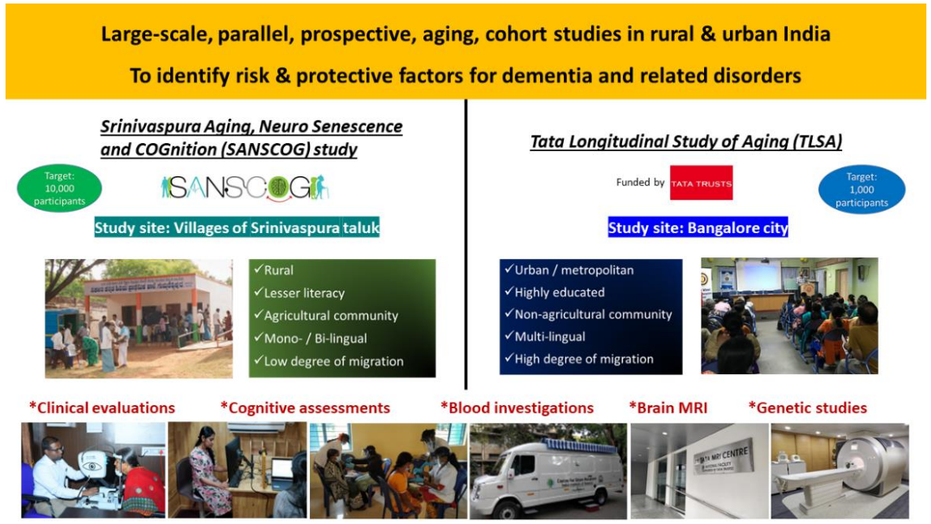
CBR serves as a Regional Genome Sequencing Laboratory in the Indian SARS-CoV-2 Genomic Sequencing Consortium (INSACOG). INSACOG is a consortium of 38 laboratories across the country, jointly initiated by the Union Ministry of Health and Department of Biotechnology (DBT) with Council for Scientific & Industrial Research (CSIR) and Indian Council of Medical Research (ICMR). The goal of the consortium is to monitor the genomic variations in the SARS-CoV-2 by a sentinel sequencing effort which is facilitated by the National Centre for Disease Control (NCDC), Delhi involving the Central Surveillance Unit (CSU) under Integrated Disease Surveillance Programme (IDSP). The data generated by the genome sequencing laboratories is being processed and analysed as per the field data trends to investigate any linkages between the genomic variants and epidemiological trends. This helps to understand super spreader events and outbreaks and strengthen public health interventions across the country and thereby contribute to breaking the chains of transmission. Linking this data with the IDSP data and patients' symptoms allows a better comprehension of the viral infection dynamics, morbidity, and mortality trends.

So far, we have received more than 6700 viral samples from the Institute for Stem Cell Science and Regenerative Medicine (InStem) – National Centre for Biological Sciences (NCBS) and Bangalore Medical College Hospital and Research Centre. Whole-genome sequencing of SARS-CoV-2 and subsequent genomic analyses were carried out. The resultant data has been deposited to appropriate portals. The variants of the virus detected were mostly BA.2, BA.1 and sublineages, and Delta, in the order of numbers detected.

The preparations for sequencing under phase II of the project are underway.

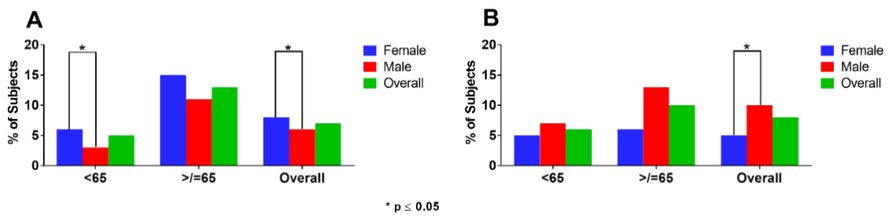
2. Research and Innovation Snippets

SANSCOG & TLSA – longitudinal cohort studies to identify risk factors for dementia in India



Comparison of dementia prevalence between rural and urban Indians.

Dementia is rising in epidemic proportions in India. However, due to India's vast diversity, there could be geographical variations including significant rural-urban differences (as some previous Indian studies have shown). In our study, we found that though there was no significant difference in overall prevalence of dementia (Clinical Dementia Rating ≥ 0.5). Women had higher prevalence than men in rural individuals, whereas this was reverse in urban individuals. These preliminary findings give us direction to explore the causes of these unique gender differences in dementia.



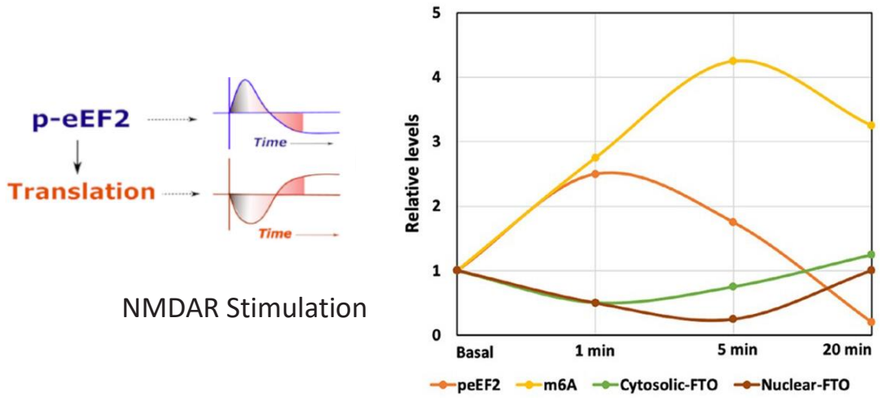
Comparison of age-wise and gender-wise prevalence of dementia in (A) rural Indians from SANSCOG study cohort and (B) urban Indians from TLSA cohort

References:

1. SANSCOG Study Team. Srinivaspura Aging, Neuro Senescence and COGnition (SANSCOG) study: Study Protocol. *Alzheimer's & Dementia,* 2022 (In Press).
2. Jonas Sundarakumar, Shafeeq K Shahul Hameed, Abhishek ML, Shubham Jain, SANSCOG & TLSA Study Teams, Vijayalakshmi Ravindranath. Prevalence of neuropsychiatric conditions and cognitive impairment in two parallel, aging study cohorts from rural and urban India. *Alzheimer's & Dementia*, 2022 (In Press).

Epitranscriptome-mediated regulation of synaptic protein synthesis

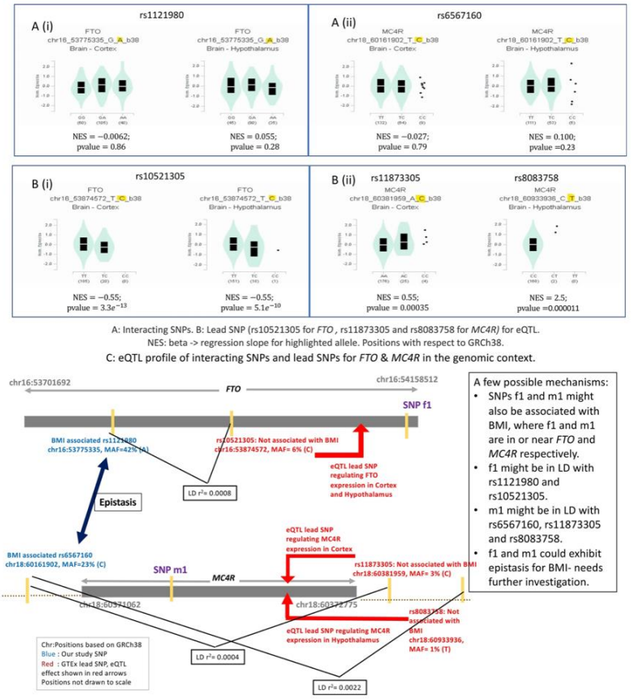
Making new proteins 'as and when required' is an important component of memory formation and storage. Understanding the actual mechanism of this process will go a long way in elucidating the factors that contribute to the loss of memory and cognition in dementia. Our recent work highlights the role of a major RNA modification (m6A) in regulating protein synthesis in response to a neuronal activity (NMDAR stimulation) that is critical for memory formation. Our work shows that the m6A modification alters dynamically to facilitate specific protein synthesis in response to NMDAR stimulation which is aided by the altered activity of the enzyme (FTO) which regulates this modification. We demonstrate the concerted action of multiple factors such as eEF2 phosphorylation, FTO activity, and level of m6A to bring about the biphasic protein synthesis response (initial inhibition followed by late activation) to NMDAR stimulation. This is likely to play an important role in memory formation.



Reference: NMDAR-mediated dynamic changes in m A inversely correlates with neuronal translation. Naveen Kumar Gowda, Bharti Nawalpuri, Sarayu Ramakrishna, Vishwaja Jhaveri, **Ravi Muddashetty**. *Scientific Reports* (2022) doi.org/10.1038/s41598-022-14798-3

The genetic basis of inherited traits and complex disorders

- Dr Kahali's lab has developed efficient human whole genome sequencing analytical pipeline in Docker container that utilizes significantly less memory in 40% less time. (https://github.com/BratatiKahaliLab/Containerized_WGS_Data_Pipeline)
- The lab has developed a reference genotype imputation panel for the Indian population and demonstrated better imputation accuracy for rare and low frequency biallelic genetic variants.
- The lab has identified significant epistatic interactions influencing human complex traits, such as obesity, that highlight the neuronal influence in the genetic architecture of the trait and metabolic abnormalities characterized by obesity with tissue-specific expression of associated genes in liver, pancreas, and adipose for various allelic combinations.



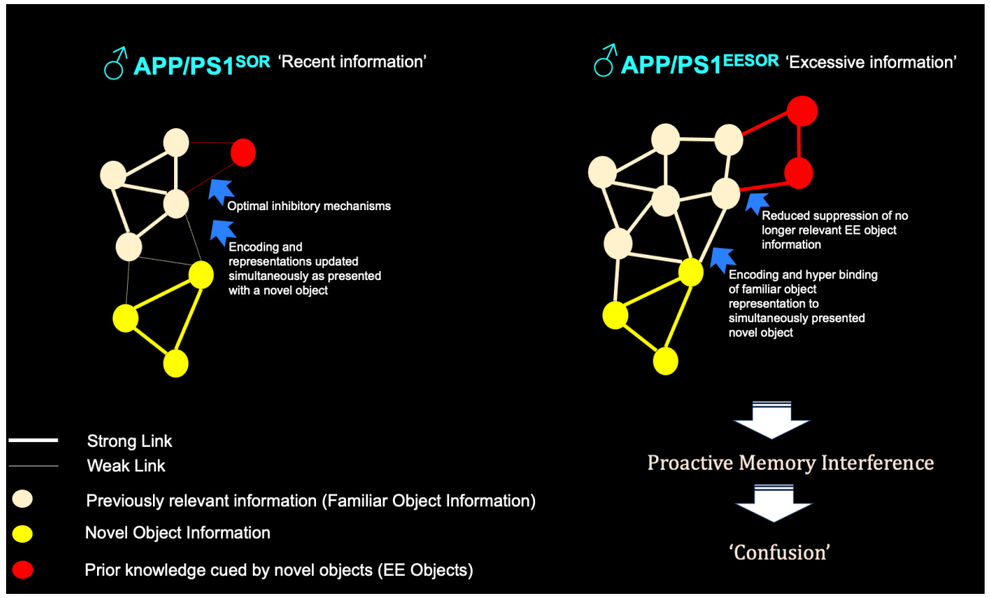
A: Interacting SNPs. B: Lead SNP (rs10521305 for *FTO* , rs11873305 and rs8083758 for *MC4R)* for eQTL.
NES: beta -> regression slope for highlighted allele. Positions with respect to GRCh38.
C: eQTL profile of interacting SNPs and lead SNPs for *FTO* & *MC4R* in the genomic context.

eQTL profile of FTO (i) and MC4R (ii) SNPs in relevant tissues. (**A**) eQTL profile of FTO (rs1121980) and MC4R (rs6567160) in brain cortex and hypothalamus. (**B**) eQTL profile of lead SNP of FTO (rs10521305) and lead SNPs of MC4R (rs11873305 and rs8083758 expressed in brain cortex and hypothalamus respectively). (**C**) eQTL profile of interacting SNPs and lead SNPs for FTO and MC4R in the genomic context. Possible mechanisms of action of epistatic SNPs in regulating expression of relevant genes.

Reference: Sheldon D'Silva, Shreya Chakraborty, **Bratati Kahali**. Concurrent outcomes from multiple approaches of epistasis analysis for human body mass index associated loci provide insights into obesity biology. *Scientific Reports* 12, 7306 (2022).

Overload of irrelevant information interferes with new learning in a mouse model of Alzheimer's disease

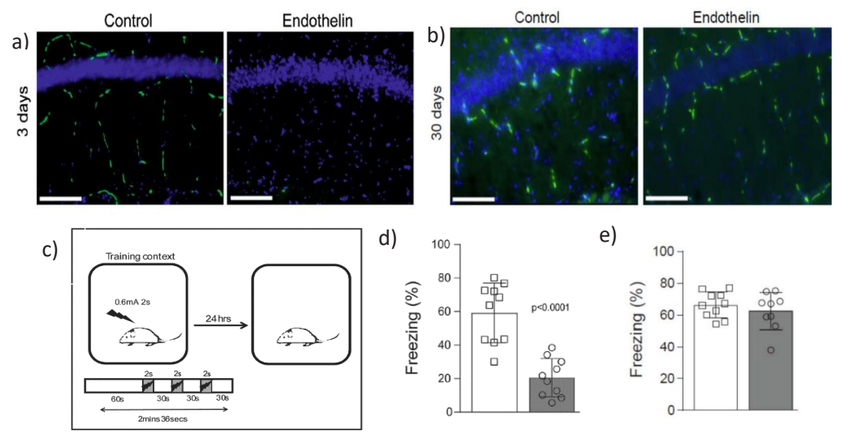
Earlier studies have demonstrated that memory dysfunction during early Alzheimer's disease (AD) is associated with an increased susceptibility to memory interference leading to confusion in landmarks, medication, objects etc. Results from behavioural experiments in Dr Karunakaran's lab indicate that both 2-month-old male and female APPswe/PS1dE9 mice, a mouse model of AD, display intact object recognition memory. However, post weaning environmental enrichment (EE) leads to a decrease in discrimination of novel object from the familiar object by male but not female APP/PS1 mice. Crucially, it has been found that the memory impairment in APP/PS1 mice was not due to a lack of attention or disinterest in exploring objects, rather paradoxically, male mice who underwent EE demonstrated a decreased tendency to discriminate the familiar object from the novel object unlike their female counterpart.



Reference: Shanice Jessica Hermon, **Smitha Karunakaran**. (2022). Duality in recognition memory deficits in APPswe/PS1dE9 mice. *Behavioural Brain Research*, 2022 (Under review)

Memory impairment after transient vasoconstriction in mice

Dementia is a major public health concern in aging population. Growing evidence suggests that blood vessel-related problems (known as vascular dysfunction) play a role in developing cognitive impairment in elderly. There is limited understanding of mechanisms behind vascular dysfunction in small vessels due to the unavailability of appropriate mouse models. For the first time, we have developed a mouse model (by intraventricular bilateral injection of ET-1 in C57BL/6 mice) that will be helpful to understand vascular abnormalities in small vessels.

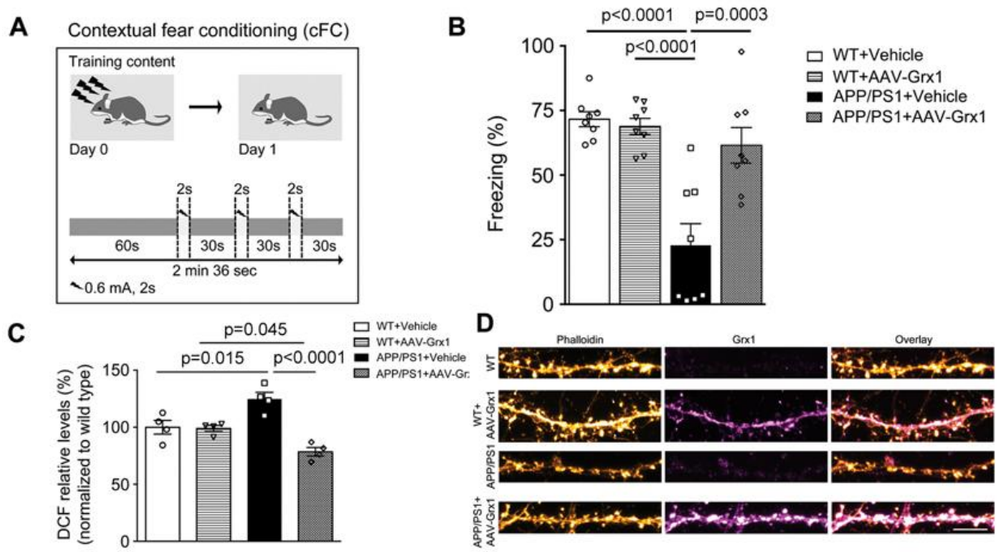


The vasoconstriction in small vessels nearby the lateral ventricles caused low expression of CD 31, a marker for endothelial cell in vessels indicating vasoconstriction after 3 days of injection (Fig. a) leading to memory impairment observed as a decrease in freezing response in contextual fear conditioning test (Fig. d). However, recovery in freezing behaviour seen after 30 days of ET-1 injection (Fig. e) by resumed expression of CD31 in vessels indicated the importance of vascular event in synaptic function. So, this mouse model mimics the human pathology transient ischemia.

Reference: **Latha Diwakar**, Ruturaj Gowaikar, Keerthana Chithanathan, Barathan Gnanabharathi, Deepika Singh Tomar, Vijayalakshmi Ravindranath. Endothelin-1 mediated vasoconstriction leads to memory impairment and synaptic dysfunction. *Scientific Reports* (2021).

Glutaredoxin-1 stabilizes Aβ mediated F-actin loss and recall memory deficits in Alzheimer's disease mouse model

Synaptic dysfunction, considered to occur early in AD is often seen as loss of dendritic spines, which are the sites of excitatory signalling in the brain. Fibrillar actin (F-actin) is highly enriched in dendritic spines and determines the shape of spine and undergoes restructuring during synaptic plasticity. We observed reduced levels of F-actin resulting in spine loss and memory deficits in AD mouse model. To understand the molecular mechanisms behind such reduction in F-actin in AD, we analysed the oxidative modifications of actin that affects its polymerization. We observed an increase in glutathionylation as a result of decreased levels of glutaredoxin1 (Grx1), an oxidoreductase enzyme that reduces glutathionylated proteins. This was associated with spine loss and memory deficits. Upon over expressing Grx1, we observed recovery in recall memory deficits, stabilization of F-actin levels and nanoarchitecture in dendritic spines. Our findings suggest that increasing Grx1 levels is a potential target for novel disease-modifying therapies for AD.



(A) Schematic representation of cFC experiment. (B) Bar graph representing freezing response in vehicle or AAV6-Grx1 injected WT or APP/PS1 mice. (C) Bar graph showing relative DCF levels in hippocampal lysates. (E) F-actin stabilization in AAV6-Grx1 expressing APP/PS1 primary cortical neurons.

Reference: **Reddy Peera Kommaddi**, Deepika Singh Tomar, Smitha Karunakaran, Deepti Bapat, Siddharth Nanguneri, Ajit Ray, Bernard L Schneider, Deepak Nair, Vijayalakshmi Ravindranath. Glutaredoxin1 Diminishes Amyloid Beta-Mediated Oxidation of F-Actin and Reverses Cognitive Deficits in an Alzheimer's Disease Mouse Model. *Antioxidants & Redox Signaling.* 2019 Dec 20;31(18):1321-1338.

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3. Faculty Research Projects

Besides contributing to the Centre's flagship projects, the CBR faculty members pursue fundamental and applied research in diverse, key areas of brain aging. The goals of these projects and the major findings/highlights of the year are outlined in this section.

3. 1. Prof. Ravi Muddashetty, Associate Professor

Protein synthesis dysregulation in neurodegenerative diseases

Funding: CBR

The goal of the lab is to understand the molecular pathways contributing to the synaptic pathology in Alzheimer's disease (AD). In this context, we are primarily focusing on the defects in protein synthesis contributing to the synaptic dysfunction. We approach this topic from two distinct angles: (i) study the effect of APOE4 (a major risk factor for AD) on basal and activity mediated protein synthesis in neurons (ii) study the translation dysregulation in AD neurons from human patient-derived iPSCs with mutations in PSEN1.

Our recent work on APOE4 (Ramakrishna S *et al*., 2021) has led us to identify its impact on neuronal protein synthesis by disrupting calcium signaling. Continuing this work, we show that mGluR and NMDAR stimulation lead to a very different spatio-temporal release of calcium in neurons which in turn is likely to induce their signature translation response (Figure 8). We are now investigating how APOE4 causes an imbalance in calcium release and subsequent translation response to both NMDAR and mGluR stimulation which is essential for memory and cognition.

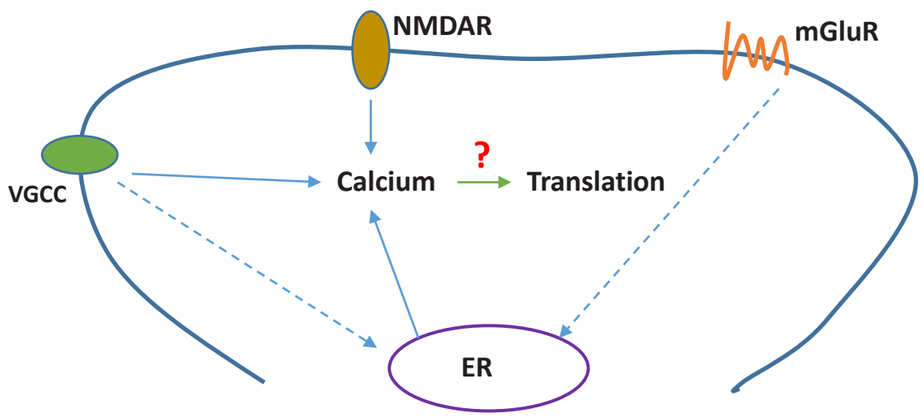


Figure 8: Schematic representing the complex interplay between mGluR and NMDAR mediated calcium signal and synaptic protein synthesis in neurons

Our recent work on epitranscriptome (Gowda NK *et al*., 2022) highlights the role of a major RNA modification (m6A) in regulating protein synthesis in response to a neuronal activity (NMDAR stimulation) that is critical for memory formation. Our work shows that the m6A modification alters dynamically to facilitate specific protein synthesis in response to NMDAR stimulation which is aided by the altered activity of the enzyme which regulates this modification (FTO). We demonstrate the concerted action of multiple factors such as eEF2 phosphorylation, FTO activity, and level m6A to bring about the biphasic protein synthesis response (initial inhibition followed by late activation) to NMDAR stimulation.

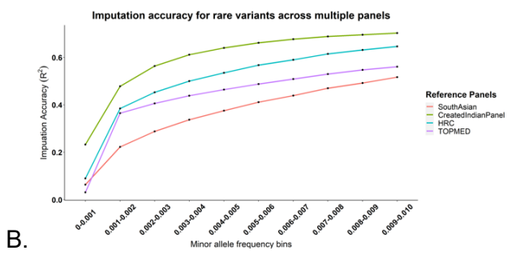
3. 2. Dr. Bratati Kahali, Assistant Professor

Understanding the genetic basis of inherited traits and complex disorders through advanced analyses at genome-wide level

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

The genotype data of 2600 Indian individuals from Affymetrix PMRA genome-wide arrays have been analyzed in our lab for quality checks pertaining to sample level and variant level QC. For the genome-wide association analysis to progress in Indian samples, currently we are developing a pipeline for accurate and efficient genotype imputation for Indian samples. We have created a merged imputation panel to be used as reference for Indian genotype datasets, by merging haplotypes from 1000 genomes project with those from 1011 Indian WGS data. For low frequency and rare genetic variants, this merged imputation reference panel currently performs better than current industry standards in terms of accuracy (Figure 9).

A.



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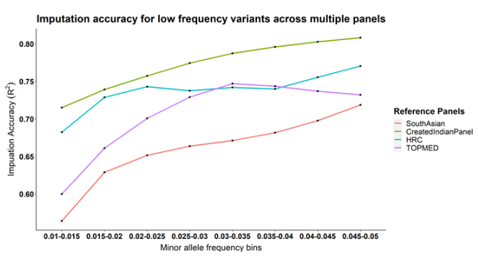

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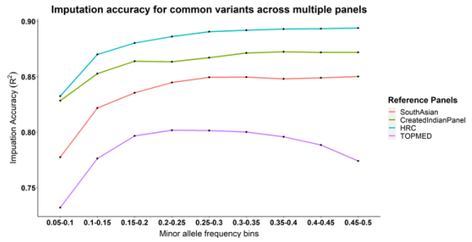


Figure 9: Comparing our developed genetic variant imputation panel against widely used industry standards for rare and low frequency variants in the population

Apart from genome-wide association studies, gene-gene interactions can also contribute to our understanding of genetic basis of complex traits. However, this entails huge computational complexity and burden. Towards this aim, we have assessed different regression based, machine learning based, information theory based, multidimensionality reduction based, and Bayesian theory- based approaches for deciphering gene-gene interactions underlying the biology of complex traits. We have detected two pairwise epistatic interactions, between rs2177596 (*RHBDD1*) and rs17759796 (*MAPK1*), rs1121980 (*FTO*) and rs6567160 (*MC4R*) associated with human body mass index (BMI) (Figure 10).

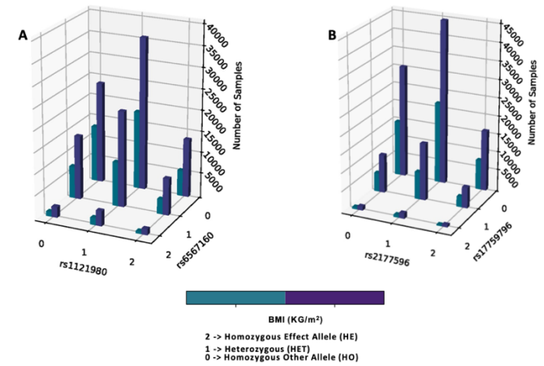


Figure 10: Gene-gene interactions associated with human BMI

Gene interaction maps and tissue expression profiles constructed for these interacting loci highlights co-expression, co-localisation, physical interaction, genetic interaction, and shared pathways characterized by obesity. Detecting epistasis could thus be a promising approach to understand the effect of simultaneously interacting multiple genetic loci in disease etiology, beyond single locus effects.

3. 3. Dr. Smitha Karunakaran, Assistant Professor

Role of locus coeruleus projections in maintaining cognitive function in normal and pathological ageing such as dementia

Funding: CBR

During early stages of human Alzheimer's Disease (AD), patients display subtle impairments in visual recognition which relies on familiarity judgement (PMID: 20930281, PMID: 23271330) which leads to confusion in landmarks, medication, objects etc. Studies in our

laboratory are focused on understanding the functional role of hippocampus projecting locus coeruleus (LC) noradrenergic system, and their influence on the hippocampal memory circuitry in a familial AD mouse model, APP/PS1. ß-adrenergic signalling is known to be activated by environmental novelty or environmental enrichment (EE; PMID: 30093491, PMID: 23473322, PMID: 27904493, PMID: 26804338). Post weaning EE is known to enhance hippocampal synaptic plasticity to prevent the impairment of hippocampal long term memory potentiation by Amyloid-ß oligomers. However, these studies perforce include EE effects on male APP/PS1 mice using spatial and working memory tasks (PMID: 30093491; PMID: 23473322; PMID: 20086049; PMID: 29274291).

In mice, recognition memory is assessed using the spontaneous object recognition task (SOR), which relies on the observation that mice preferentially explore a novel object over a familiar one; and the object-location (O-L) task where recognition memory for spatial location of objects is tested. Our results indicate that both 2-month-old male and female mice display similar O-L task deficits, however their object recognition memory is intact. Crucially, we found that the memory impairment upon O-L task across male and female mice APP/PS1 mice were quite distinct. Female APP/PS1 mice displayed an increased tendency to explore both the objects failing to discriminate the object in the new location, whereas male APP/PS1 mice displayed a lack of interest in exploring objects. Interestingly, total exploration time was significantly higher both in male and female APP/PS1 during the training phase the previous day indicating that learning has occurred however in a maladaptive way. Post weaning EE led to improved preference for the displaced object in the O-L task in both male and female APP/PS1 mice. However, post weaning EE led to a decrease in discrimination of novel object from the familiar object in the SOR task by male but not female APP/PS1 mice. EE exposure significantly enhanced preference for novel object in Wild Type (WT) as reported earlier. Male APP/PS1 mice did not display lack of attention or disinterest in exploring the object, but they failed to discriminate the novel object from the familiar one upon post weaning EE.

Taken together, our results suggest that post weaning EE ameliorates O-L memory in both male and female APP/PS1 mice, however, it leads to SOR deficits in male but not female APP/PS1 mice. Overload of irrelevant information might have interfered with object memory retrieval in perirhinal cortex during SOR recall, but might provide advantage to hippocampus that benefits from extraneous knowledge during O-L recall. We further observed that the patterns of Extracellular signal-regulated kinase (ERK1/2, a MAPK family member) activation 7 days post behavioural training were distinctly different in male mice.

In future we aim to understand mechanism of memory consolidation upon SOR and O-L tasks at different stages of memory formation both in the hippocampus using c-Fos, GluN1 and pERK as a marker. We will further delineate the deficits in the dentate gyrus-CA3 inhibitory circuit (somatostatin and parvalbumin positive interneurons) that underlie the evolution of hippocampal-cortical ensembles during memory consolidation.

3. 4. Dr. Latha Diwakar, Senior Scientific Officer

Molecular underpinnings of vascular dementia

Funding: TATA Trusts and CBR

Vascular Dementia may begin as mild cognitive changes due to blockade of blood vessels that worsen gradually because of multiple minor strokes, leading to cumulative damage. Patients with multiple micro infarcts as well as repeated occurrence of micro infarcts have high risk of developing dementia. Therapies to delay progression of cognitive impairments

are required to minimize deficits associated with dementia. In human subjects of such studies, the presence of ischemic brain injury, commonly detected in pathology as macro- and micro- infarcts and small vessel disease were highly prevalent in older persons as independent risk factors for dementia. Early intervention to delay progression of cognitive impairments are required to improve the deficits associated with dementia. MRI imaging shows these cerebrovascular lesions as White Matter Hyperintensities (WMH) adding significant burden to dementia over the age. Our longitudinal studies at CBR show significant burden of vascular factors contributing to WMH in our study subjects. Therefore, we are interested in studying molecular mechanisms involved in development of these WMH leading to cognitive deficits. We have developed an animal model of small vessel constriction using ET-1, which results in memory loss due synaptic dysfunction following blood-brain barrier (BBB) breakage. This model now helps us understand novel insights of vascular pathology during dementia.

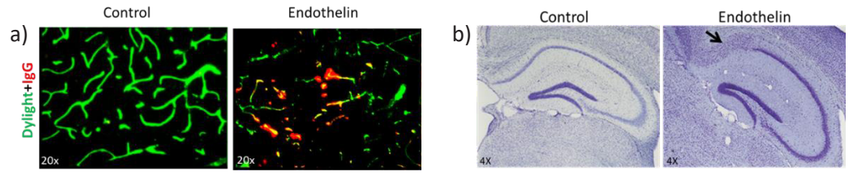


Figure 11: a) Dylight (green) positive blood vessels and anti-IgG (red) staining for blood derived IgG during BBB leakage. b) Cresyl violet staining showing loss of neurons in the hippocampus of the mice injected with ET-1.

There are animal models to study large vessel stroke such as carotid artery occlusion; however, we do not have animal models to study small vessel insult. In view of such a scenario, the established animal model helps to study transient as well as multiple small vessel insults impacting BBB leading to learning and memory deficits. The model has demonstrated the similarities in early molecular events between vascular dementia as well as early Alzheimer's disease (AD). Such vascular insults in presence of mutations which are risk factors for AD would increase the disease pathology. It is often hypothesized that in the presence of increased β-amyloid, vascular insults could act synergistically to trigger the neurodegenerative process including synaptic dysfunction leading to cognitive impairment. Apart from reduced cerebral blood flow and changes in BBB leading to cognitive impairment independent of Aβ, the vascular deposition of Aβ could potentially accelerate the neurodegeneration as in cases of cerebral amyloid angiopathy seen in AD patients. This model now helps us gain novel insights of vascular pathology during dementia.

3. 5. Dr. Reddy Peera Kommaddi, Senior Scientific Officer

Studying sex specific differences in Alzheimer's disease pathology

Funding: CBR

Alzheimer's disease (AD) is an age-related disorder. Sex-related differences have been observed in the progression of dementia. This difference plays a critical role in the prevalence, prognosis, and severity of pathological changes in AD. Women living with dementia including AD are more than men. Postmenopausal women exhibit rapid and sharp cognitive decline and other AD outcomes as compared to men. Neuroprotective effect of estrogen is well established. But, neuroprotective effects of estrogen are lost when women

enter the postmenopausal age. Therefore, it is important to focus not only on the interaction between male and female but also on the factors that contribute to the male and female disparity. Synaptic and cognitive dysfunctions occur several decades prior to the clinically detectable symptoms manifest. However, the underlying pathogenic mechanisms are not clear. Therefore, our aim is to elucidate the clinical implications of sex differences in AD, the underlying cognitive functions, and early molecular mechanisms in human subjects and AD mouse models.

In order to demonstrate the consequence of the presence of amyloidogenic mutations, such as APP, PSEN1, and PSEN2 on cognitive functions between men and women, we have obtained the longitudinal and cross-sectional psychometric or cognitive functional data from Dominantly Inherited Alzheimer Network (DIAN) cohort. Decline in cognitive performance as a function of chronological age was assessed in men and women from DIAN participants. Upon performing the linear mixed effects model on the longitudinal data, we observed that among the mutation carriers, men showed a significantly greater decline in performance on both immediate and delayed tests of Wechsler's logical memory as compared to women irrespective of age.

We tried to test this phenomena using familial AD mouse model (APP/PS1) and investigated the molecular mechanisms underlying the learning and memory deficits. We assessed the recall memory deficits and found that female APP/PS1 mice did not show recall deficits until 8 months of age unlike male APP/PS1 mice where memory recall deficits were observed as early as 2 months of age. Activity-dependent protein synthesis is essential for synaptic plasticity; we observed that activity-dependent protein synthesis at the synapse was affected in female APP/PS1 mice after 8 months of age. Further, we tried to examine the protective role of estrogen. We ovariectomized (OVX) female mice and observed that the OVX female APP/PS1 mice showed recall deficits and new protein synthesis was abolished at early age. Thus, our results indicate that the appearance of memory recall deficits occurred in female AD mice only when they aged. However, the underlying molecular mechanisms explaining the recall deficits in APP/PS1 female mice after 8 months of age are not clear. Akt-mTOR signaling cascade has emerged as an essential regulator for synaptic plasticity. Therefore, we investigated the status of phosphorylation of Akt and mTOR and their downstream targets. We found that dysregulation of Akt1-mTOR signaling at the synapse is delayed in female APP/PS1 mice compared to male APP/PS1 mice in which this dysregulation occurred early.

II. Collaborations

To further its mission, the Centre for Brain Research (CBR) entered into collaboration with several like-minded organisations, particularly in the realm of neurodegeneration research. These exciting partnerships are expected to synergise with and provide impetus to CBR's ongoing research efforts.

SKAN Research Trust

In June 2021, CBR entered into a Partnership and Grant Agreement with SKAN Research Trust. SKAN, a public charitable trust set up by the Soota and Karedan families, aims to promote research and development in medical science, with a focus on the treatment of geriatric and neurological diseases. The partnership will focus on research on Parkinson's disease, bipolar disorders, strokes, and common linkages between different neurological disorders. As SKAN's strategic partner for neurological research, CBR is building a consortium of partners to handle the first project on Parkinson's disease. A grant of INR 20 crores has been committed by SKAN.

Alzheimer's Disease Data Initiative (ADDI)

The ADDI, a US-based charitable medical research organization, is dedicated to transforming Alzheimer's disease (AD) research, accelerating progress towards new treatments and cures for AD and related dementias. CBR partnered with the ADDI to make data on longitudinal studies of aging available for researchers worldwide to promote collaboration. The project proposal submitted to the ADDI was approved and an award of USD 78,400 per year has been sanctioned for an initial period of 5 years.

"*The COVID-19 crisis has demonstrated the need for global collaboration. I am optimistic that this partnership with ADDI will not only drive more dementia research across the globe but will promote global collaboration to end Alzheimer's disease and related dementias*." – Dr Kris Gopalakrishnan, Founder Trustee, Pratiksha Trust.

Fidelity Bermuda Foundation

CBR secured funding from Fidelity Bermuda Foundation for a research project titled 'The BANGLE project: Bangalore Edinburgh Collaboration for Brain Health and Dementia Prevention' under the direction of Professor Graciela Muniz Terrera, Chair of Ageing, Health and Methods in the Edinburgh Dementia Prevention research group, University of Edinburgh, UK. An award of USD 357,953 has been sanctioned for the project.

III. Presentations

CBR researchers presented their research hypotheses, findings, and views through lectures, posters, and flash talks at various prestigious national and international meetings.

1. Kahali B. Whole genome sequencing in human cohort studies informs the genetic architecture of complex phenotypes. 'Brain Computation and Disease' symposium under the Pratiksha initiative at the Indian Institute of Science, 2 July 2021 (Invited talk)

2. Diwakar L, Hussain R, Maurya SK, Ravindranath V. Structural changes at synapse due to Blood Brain Barrier leakage by recurrent vascular insult leads to memory deficits. Society for Neuroscience conference, 2021 (Abstract)

3. Diwakar L, Hussain R, Ravindranath V. Blood brain barrier dysfunction caused by repeated Endothelin-1 injection leads to irreversible memory impairment. Alzheimer's Association International Conference, 2021 (Poster presentation)

4. Kommaddi RP, Diwakar L, Gowaikar R, Chithanathan K, Karunakaran K, and Ravindranath V. Sex-specific differences in cognitive functions and synaptic dysfunction in Alzheimer's disease mouse model. Alzheimer's Association International Conference, 26-30 July 2021 (Poster presentation)

5. Muddashetty R. Memory - how the brain 'remembers' it. International Brain Research Organization (IBRO) meeting, 12 November 2021 (Lecture)

6. Muddashetty R. 'Lost in translation'- the role of Protein synthesis in Alzheimer's disease. Indian Institute of Science Education and Research Kolkata, 8 December 2021 (Lecture)

7. Ramakrishna S, Muddashetty R. APOE4 affects basal and NMDAR mediated protein synthesis in neurons by perturbing calcium homeostasis. Brain Conference on RNA Mechanisms and Brain Disorders organized by the Federation of European Neuroscience Societies, Rungstedgaard, Denmark, 20-23 October 2021 (Poster presentation)

8. D'Souza M, Muddashetty R. Functional role of FMRP domains in regulating distinct mechanisms of neuronal protein synthesis. India | EMBO Lecture course (virtual) titled 'RNA Binding Proteins: From RNA binding to condensation and aggregation' organized by the National Centre for Cell Science, Pune, 7-11 February 2022 (Poster presentation and flash talk)

9. Kommaddi RP, Haseena P A, Verma A, Chandran M, Jaleel A, Ravindranath V. Synaptosomal actin interactome analysis in an Alzheimer's disease mouse model. Alzheimer's Association International Conference, 26-30 July 2021 (Abstract)

10. Kommaddi RP, Gowaikar R, Singh K, Haseena PA, Ravindranath V. Synaptic new protein synthesis and Akt1/mTOR signaling pathway is dysregulated in hippocampus of Alzheimer's disease mouse model. Society for Neuroscience Annual Meeting (virtual), Chicago, USA, 8-16 November 2021 (Abstract)

11. Haseena PA, Kommaddi RP, Verma A, Chandran M, Jaleel A, Ravindranath V. Actin interactome analysis of differentially expressed proteins in synaptosomes of Alzheimer's disease mouse model. Society for Neuroscience Annual Meeting (virtual), Chicago, USA, 8-16 November 2021 (Abstract)

12. Karunakaran S. Impairments in navigational search strategy switching during early stages of disease pathogenesis in a mouse model of Alzheimer's disease. Annual Conference of Cognitive Science (ACCS8) hosted online by Amrita Vishwa Vidyapeetham, 20-22 January 2022 (Poster presentation)

13. Kushwaha S, Karunakaran S. β - adrenergic agonist prevents fear memory trace decay in a mouse model of Alzheimer's disease. 49th Meeting of the European Brain and Behaviour Society (EBBS), 4-7 September 2021 (Poster presentation)

14. Hermon SJ, Karunakaran S. Duality in recognition memory deficits in APPswe/PS1dE9 mice. The Alzheimer's Association International Conference, 26-30 July 2021 (Poster presentation)

15. Kushwaha S, Karunakaran S. Noradrenergic dysregulation leads to impaired fear memory persistence in APPSwe/PS1dE9 mouse model of Alzheimer's disease. 2nd Annual Virtual Dopamine (ViDA) Conference, 22-24 June 2021 (Poster presentation)

16. Menesgere AL, Sundarakumar JS, Hameed SKS, Ravindranath V, TLSA Investigators. Comparison of Modifiable Risk Factors for Dementia among Rural and Urban Elderly Adults: Data from two cohorts in India. Alzheimer's Association International Conference (hybrid mode), Colorado, USA, 2021 (Poster presentation)

17. Sundarakumar JS, Menesgere AL, Ravindranath V. Prevalence of neuropsychiatric conditions in two parallel, aging study cohorts from rural and urban India. Alzheimer's Association International Conference (virtual), 26-30 July 2021 (Poster presentation)

18. Tiwari V. Symposium on Novel NMR Methods for the Investigation of Molecular Structure and Interactions. NMR Research Centre, Indian Institute of Science, Bangalore, 28-29 June 2021 (Invited talk)

19. Ravindranath V. 'Global perspective on public policy challenges'. World Dementia Council Summit, London, 28 March 2022 (Panel discussion)

IV. Publications

The research output of CBR has been published/is under consideration for publication in peer-reviewed, international scientific journals of repute.

1. D'Silva S, Chakraborty S, Kahali B. *Concurrent outcomes from multiple approaches of epistasis analysis for human body mass index associated loci provide insights into obesity biology.* **Scientific Reports**, 12, 7306 (2022). https://doi.org/10.1038/s41598-022-11270-0
2. Panda A, Subramanian K, Kahali B. Implementation of human whole genome sequencing data analysis: A containerized framework for sustained and enhanced throughput. **Informatics in Medicine Unlocked**, Volume 25, 2021, 100684, ISSN 2352-9148, https://doi.org/10.1016/j.imu.2021.100684.
3. Palmer ND, Kahali B, Kuppa A, Chen Y, Du X, Feitosa MF, Bielak LF, O'Connell JR, Musani SK, Guo X, Smith AV, Ryan KA, Eirksdottir G, Allison MA, Bowden DW, Budoff MJ, Carr JJ, Chen YI, Taylor KD, Correa A, Crudup BF, Halligan B, Yang J, Kardia SLR, Launer LJ, Fu YP, Mosley TH, Norris JM, Terry JG, O'Donnell CJ, Rotter JI, Wagenknecht LE, Gudnason V, Province MA, Peyser PA, Speliotes EK. *Allele-specific variation at APOE increases nonalcoholic fatty liver disease and obesity but decreases risk of Alzheimer's disease and myocardial infarction.* **Human Molecular Genetics**, 2021 Jul 9;30(15):1443-1456. doi: 10.1093/hmg/ddab096. PMID: 33856023; PMCID: PMC8283205.
4. Sain Basu D, Bhavsar R, Gulami I, Chavda S, Lingamallu SM, Muddashetty R, Veeranna C, Chattarji S, Thimmulappa R, Bhattacharya A, Guha A. *FMRP protects the lung from xenobiotic stress by facilitating the integrated stress response.* **Journal of Cell Science**, 2022 May 1;135(9):jcs258652. doi: 10.1242/jcs.258652. Epub 2022 May 10. PMID: 35319067.
5. Verma V, Kumar MJV, Sharma K, Rajaram S, Muddashetty R, Manjithaya R, Behnisch T, Clement JP. *Pharmacological intervention in young adolescents rescues synaptic physiology and behavioural deficits in Syngap1+/- mice.* **Experimental Brain Research**, 2022 Jan;240(1):289-309. doi: 10.1007/s00221-021-06254-x. Epub 2021 Nov 5. PMID: 34739555.
6. Chandrasekaran A, Dittlau KS, Corsi GI, Haukedal H, Doncheva NT, Ramakrishna S, Ambardar S, Salcedo C, Schmidt SI, Zhang Y, Cirera S, Pihl M, Schmid B, Nielsen TT, Nielsen JE, Kolko M, Kobolák J, Dinnyés A, Hyttel P, Palakodeti D, Gorodkin J, Muddashetty RS, Meyer M, Aldana BI, Freude KK. *Astrocytic reactivity triggered by defective autophagy and metabolic failure causes neurotoxicity in frontotemporal dementia type 3.* **Stem Cell Reports**, 2021 Nov 9;16(11):2736-2751. doi: 10.1016/j.stemcr.2021.09.013. Epub 2021 Oct 21. PMID: 34678206; PMCID: PMC8581052.
7. Ramakrishna S, Jhaveri V, Konings SC, Nawalpuri B, Chakraborty S, Holst B, Schmid B, Gouras GK, Freude KK, Muddashetty RS. *APOE4 Affects Basal and NMDAR-Mediated Protein Synthesis in Neurons by Perturbing Calcium Homeostasis.* **Journal of Neuroscience**, 2021 Oct 20;41(42):8686-8709. doi: 10.1523/JNEUROSCI.0435-21.2021. Epub 2021 Sep 2. PMID: 34475200; PMCID: PMC8528497.
8. Nawalpuri B, Sharma A, Chattarji S, Muddashetty RS. *Distinct temporal expression of the GW182 paralog TNRC6A in neurons regulates dendritic arborization.* **Journal of Cell Science**, 2021 Aug 15;134(16):jcs258465. doi: 10.1242/jcs.258465. Epub 2021 Aug 24. PMID: 34328181.
9. Ravindranath V, Sundarakumar JS. *Changing demography and the challenge of dementia in India.* **Nature Reviews Neurology**, 2021;17(12):747-758. doi:10.1038/s41582-021-00565-x.
10. Sundarakumar JS, Stezin A, Menesgere AL, Ravindranath V. *Rural-urban and gender differences in metabolic syndrome in the aging population from southern India: Two parallel, prospective cohort studies.* **eClinicalMedicine**, 2022;47:101395. doi:https://doi.org/10.1016/j.eclinm.2022.101395.
11. Sundarakumar JS, Raviteja KV, Muniz-Terrera G, Ravindranath V. *Normative data for three physical frailty parameters in an aging, rural Indian population.* **Health Science Reports**, 2022;5(e567). doi:10.1002/hsr2.567.
12. Sundarakumar JS, Shahul Hameed SK, SANSCOG Study Team, Ravindranath V. *Burden of Vitamin D, Vitamin B12 and Folic Acid Deficiencies in an Aging, Rural Indian Community.* **Frontiers in Public Health**, 2021;9:707036. Published 2021 Sep 3. doi:10.3389/fpubh.2021.707036.
13. Murty DV, Manikandan K, Kumar WS, Ramesh RG, Purokayastha S, Nagendra B, Menesgere AL, Balakrishnan A, Javali M, Rao NP, Ray S. (2021). *Stimulus-induced gamma rhythms are weaker in human elderly with mild cognitive impairment and Alzheimer's disease*. **eLife**, 10, e61666. https://doi.org/10.7554/eLife.61666

Manuscripts Accepted

1. SANSCOG Collaborators. *Srinivaspura Aging, Neuro Senescence and COGnition (SANSCOG) study: Study Protocol.* **Alzheimer's & Dementia**, 2022.
2. Sundarakumar JS, Hameed SKS, Dilip B, Deepak S, BR Vinaykumar, Ravindranath V. *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**, 2022.
3. Sundarakumar JS, Hameed SKS, Menesgere AL, Jain S, SANSCOG & TLSA Study Teams, Ravindranath V. *Prevalence of neuropsychiatric conditions and cognitive impairment in two parallel, aging study cohorts from rural and urban India.* **Alzheimer's & Dementia**, 2022.
4. Menesgere AL, Sundarakumar JS, SANSCOG & TLSA Study Teams, Ravindranath V. *Comparison of Risk Factors for Dementia among Rural and Urban Elderly Adults: Data from two cohort studies in India.* **Alzheimer's & Dementia**, 2022.
5. Kahali B, Balakrishnan A, Muralidhara SD, Muniz-Terrera G, Ritchie K, SANSCOG study team, Ravindranath V. *COGNITO (Computerized assessment of adult information processing): Normative data for rural Indian population from SANSCOG study.* **Alzheimer's & Dementia**, 2022.

Manuscripts under Review

1. Kommaddi RP, Verma A, Graciela MT, Tiwari V, Chithanathan K, Diwakar L, Gowaikar R, Karunakaran S, Graff-Radford NR, Day GS, Laske C, Schofield PR, Vöglein J, Nübling G, Ikeuchi T, Kasuga K, the Dominantly Inherited Alzheimer Network (DIAN), Ravindranath V. *Sex difference in evolution of cognitive decline: Studies on mouse model and the Dominantly Inherited Alzheimer Network cohort.* 2022. **Translational Psychiatry**, 2022.
2. Menesgere A, Kommaddi RP, Giridhar V, Ravindranath V. *Role of APOE ε gene in cognitive performance among cognitively healthy participants of TLSA cohort.* **Journal of Alzheimer's Disease**, 2022.
3. Verma A, Kommaddi RP, Gnanabharathi B, Hirsch EC, Ravindranath V. *Genes critical for development and differentiation of dopaminergic neurons are downregulated in Parkinson's disease*. **Scientific Reports**, 2022.
4. Hermon SJ, Karunakaran S. (2022). *Duality in recognition memory deficits in APPswe/PS1dE9 mice.* **Behavioural Brain Research**, 2022.
5. Tiwari V, Viswamitra S, SANSCOG & TLSA Study Teams, Ravindranath V. *Structural and Microvascular pathologies with aging: In vivo MRI findings from TLSA and SANSCOG cohorts of India.* **Alzheimer's & Dementia**, 2022.

6. de Erausquin GA, 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, Ole Mors NP, 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 V, Majid A, Sundarakumar JS, 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,** (N Y) 2022.
7. Lukose A, Rahul KV, Joseph MS, Sivakumar PT, Rao GN, Gangadhar BN, Ritchie K, Balakrishnan A, Ravindranath V, Rao NP. *Cross-cultural adaption of the Computerized Assessment of Information Processing battery (COGNITO) for an Indian longitudinal study on rural elderly.*
8. Sundarakumar JS, Hameed SKS, Menesgere AL, Jain S, SANSCOG & TLSA Study Teams, Ravindranath V. *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.* **Brain and Behavior**, 2022.
9. Menesgere AL, Giridhar V, Bota R, Ravindranath V. *Role of Vitamin D on cognitive performance among healthy volunteers of SANSCOG cohort.* **Journal of Nutrition Education and Behavior**, 2022.

V. Events

Scientific Advisory Committee Meeting

The Scientific Advisory Committee meeting was held online on 1st October 2021. The Committee reviewed the ongoing research projects and provided feedback and valuable suggestions. New projects proposals were also considered during this meeting. The Committee appreciated the overall progress made in the activities of the Centre.

VI. Building

The building which was under construction in the land identified for CBR at IISc Campus has been completed in all respects. CBR has been functioning from this building since October 2021. The built-up area is 1,10,000 sq.ft in a configuration consisting of basement + ground + 5 stories, totaling 7 stories. It has provision to position the brain and DNA bank in the basement. The ground floor of the facility is used for research work related to human subjects including clinical, cognitive evaluation, EEG etc. It also has the Administrative Office, a cafeteria, and a lounge for the volunteers who have agreed to participate in the research. Wet labs for genetics and basic biology, informatics, cognitive science and related research are provided on the 2nd, 3rd, 4th, and 5th floors. The 1st floor has the services and an auditorium. It is a centrally air-conditioned building.

The cost of the building is INR 57 Crores and is generously funded by the Pratiksha Trust. We are grateful to the Pratiksha Trust for funding the construction of the building.

A letter was sent to the Honourable Prime Minister inviting him and seeking his time for the formal inauguration of the building. It is heartening to report that Honorable Prime Minister Shri Narendra Modi visited the campus on June 20, 2022 and inaugurated the CBR Building.

A Construction Committee, consisting of the following members, monitored the activities.

Prof. H. P. Khincha	: Chair
Prof. Vijayalakshmi Ravindranath, Director, CBR	: Member
Prof. A. Sridharan	: Member
Prof. B.R. Srinivasamurthy	: Member
Prof. B.K. Raghuprasad	: Member
Prof. G. Rangarajan	: Member
Prof. Y. Narahari	: Member
Mr. R. Mohan Das, Special Officer, CBR	: Member

VII. Finance

The total receipts for the year 2021-22 were INR 3,575.38 Lakhs and the total payments for various activities of the Centre were INR 5,653.80 Lakhs.

The details of receipts and payments for the year 2021-22 are as follows.

Sl. No.	Particulars	Receipts (in Lakhs)	Payments (in Lakhs)*
1	Donations from Pratiksha Trust towards Activities Account	1555.00	2023.29
2	Other Receipts	50.50	0.00
3	Donations from Pratiksha Trust towards the construction of new building	300.00	1343.65
4	Funds from External Agencies	1669.88	2286.87
	Total	**3575.38**	**5653.80**

* The excess payment over receipt, is due to carried forward liability and from the balance carried over.

Funds received from external agencies during 2021-22					
			Funds received during 2021-22		
Project	**Funding agency**	**Total amount sanctioned (in lakhs)**	**Existing projects (in lakhs)**	**New projects (in lakhs)**	**Total Funds Received (in lakhs)**
NSM Project - Dr Bratati Kahali	National Supercomputing Mission (NSM)	26.31	-	26.31	26.31
DST Inspire Program - Dr Suresh S N	Department of Science & Technology	112.40	21.34	-	21.34
SERB Project - Dr Bratati Kahali	Science & Engineering Research Board	37.44	6.50	-	6.50
SPM Fellowship - Contingency Grant	Council of Scientific & Industrial Research	0.60	0.60	-	0.60
SKAN Project	M/s Ashok Soota Medical Research LLP	2000.00	-	500.00	500.00
INSACOG Project - Dr Bratati Kahali	Department of Biotechnology	211.81	-	55.11	55.11
Fidelity Foundation	Fidelity Bermuda Foundation	265.72	-	265.72	265.72
Alzheimer's Disease Data Initiative	Alzheimer's Disease Data Initiative	59.61	-	59.61	59.61
Tata Project	JTTO	1,090.77	19.25		19.25
Tata Education Trust	TATA Education Trust	3,713.20	-	715.44	715.44
Total		**7,517.85**	**47.70**	**1,622.18**	**1,669.88**

VIII. 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, 2022, are the following.

Prof. G Rangarajan, Director, IISc (*Ex officio*) : Chair
Chair, Governing Council, IISc, (*Ex officio*) : Member
Chief Secretary to Government of Karnataka (*Ex Officio*) : Member
Additional Chief Secretary to Government of Karnataka (*Ex Officio*) : Member
Principal Secretary (Finance) Government of Karnataka (*Ex Officio*) : Member
Secretary, Dept. of IT & BT, Government of Karnataka (*Ex Officio*) : Member
Prof. Vijayalakshmi Ravindranath, Director, CBR : Member
Shri. Kris Gopalakrishnan, Co-Founder, Infosys : Member
Mrs. Sudha Gopalakrishnan : Member
Shri. Dinesh Krishnaswamy : Member
Shri. S D Shibulal : Member
Prof. Y Narahari, Department of Computer Science and Automation, IISc : Member
Prof. Navakanta Bhat, Dean, Division of Interdisciplinary Sciences, IISc : Member
Prof. D N Rao, Dept of Biochemistry : Member
Prof. Usha Vijayraghavan, Dean, Division of Biological Sciences, IISc : Member
Prof. H P Khincha, Dept. of Electrical Engg. (Retd), IISc : Member
Dr. Ramesh Babu : Member
Dr. Girija Ramesh Babu : Member
Prof. Anurag Kumar, Dept. of Electrical Communication Engg., IISc : Member
Prof. N Balakrishnan, Supercomputer Education and Research Centre, IISc : Member
Dr. P Satish Chandra : Member
Dr. K Kasturirangan, Raman Research Institute, Bangalore : Member
Prof. P Kondaiah, Dept. of MRDG, IISc : Member
Prof. S Mayor, Director, NCBS, Bangalore : Member
Mrs. Sudha Murty : Member
Dr. U B Muthane : Member
Prof. G Padmanabhan, Emeritus Professor, Dept. of Biochemistry, IISc : Member
Mr. S V Ranganath : Member
Prof. M R S Rao, JNCASR, Bangalore : Member
Dr. M S Valiathan : Member
Justice M N R Venkatachaliah : Member
Mr. Ashok Soota : Member

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, 2022, is as follows:

Prof. G Rangarajan, Director, IISc (*Ex officio*) : Chairperson
Shri. Kris Gopalakrishnan, Co-Founder Infosys : Member
Shri. Dinesh Krishnaswamy : Member
Shri. S D Shibulal : Member

Mrs. Sudha Gopalakrishnan : Member
Prof. Y Narahari, Dept of Computer Science and Automation, IISc : Member
Prof. Navakanta Bhat, Dean, Interdisciplinary Sciences Division, IISc : Member
Prof. Usha Vijayraghavan, Dean, Biological Sciences Division, IISc : Member
Prof. H P Khincha, Dept. of Electrical Engg, (Retd) IISc : Member
Prof. D N Rao, Dept of Biochemistry, IISc : Member
Prof. Vijayalakshmi Ravindranath, Director, CBR : Member- Secretary

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, 2022, are:

Prof. G Rangarajan : Chair
Prof. Vijayalakshmi Ravindranath : Member
Mr. K C Ganesh : Member
Prof. P S Anilkumar : Member
Prof. Navakanta Bhat : Member
Mr. R Mohan Das : 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, Aster RV Hospital, Bangalore : Chair
Prof. D N Rao, Dept. of Biochemistry, IISc : Member
Prof. K N Balaji, Dept. of MCBL, IISc : Member
Dr. Kiran Khanapure, Vikram Hospital, Bangalore : Member
Dr. Girish Baburao Kulkarni, NIMHANS Bangalore : Member
Adv. Arvind Moorchung, Sr Consultant : Member
Prof. Anitha Kurup, NIAS Bangalore : Member
Mr. Alaganandan Balaraman : Member
Dr. Jonas S Sundarakumar, Scientific Officer Grade I, CBR : Member Secretary

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 : Member
Prof. Maria Corrillo, Chief Science Officer, Alzheimer's Association : Member
Prof. Stanley Fahn, Columbia University : Member
Prof. Vijayalakshmi Ravindranath, Director, CBR : Member
Prof. Sudha Seshadri, UT Health Science Center at San Antonio : Member
Prof. Carla Shatz, Stanford University : Member
Prof. Mary Ganguly, Pittsburgh : Member
Prof. Srinath Reddy, PHFI, New Delhi : Member
Prof. B N Gangadhar, NIMHANS, Bangalore : Member
Prof. Bart D Strooper, Director, UK Dementia Research Institute : Member
Prof. Stacie Weninger, President of FBRI, USA : Member
Prof. Vasant Honavar, Penn State University : Member

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)	: Chairman
Prof. Ramesh Hariharan (CEO, Strand Genomics, Bangalore)	: Member
Prof. Ravindra M Pandey (AIIMS, New Delhi)	: Member
Prof. Anurag Agrawal (IGIB, New Delhi)	: Member
Prof. K Thangaraj (CDFD, Hyderabad)	: Member
Prof. Vidita Vaidya (TIFR, Mumbai)	: Member
Prof. Pratima Murthy (NIMHANS, Bangalore)	: Member
Prof. Vijayalakshmi Ravindranath (Director, CBR)	: Member

Internal Committee against Sexual Harassment

Dr. Bratati Kahali, Assistant Professor, CBR	: Chair
Dr. Khader Valli Rupanagudi, Scientific Officer, CBR	: Member
Dr. Latha Diwakar, Senior Scientific Officer, CBR	: Member
Ms. Pragati Shukla, Advocate	: Member
Mr. P Manivannan, Finance Officer, CBR	: Member

Institutional Biosafety Committee

Prof. Vijayalakshmi Ravindranath, Director, CBR	: Chair
Prof. Anita Mahadevan, NIMHANS, Bangalore	: DBT Nominee
Dr. Jonas S Sundarakumar, Scientific Officer, CBR	: Biosafety Officer
Dr. Ravi Manjithaya, JNCASR, Bangalore	: Outside Expert
Dr. Ravi Muddashetty, Associate Professor, CBR	: Member
Dr. Bratati Kahali, Assistant Professor, CBR	: Member
Dr. Latha Diwakar, Senior Scientific Officer, CBR	: Member
Dr. Khader Valli Rupanagudi, Scientific officer, CBR	: Member
Dr. Smitha Karunakaran, Assistant Professor, CBR	: Member Secretary

Faculty and Staff at CBR

Academic Staff

Prof. Vijayalakshmi Ravindranath, Director
Dr. Ravi Muddashetty, Associate Professor
Dr. Bratati Kahali, Assistant Professor
Dr. Smitha Karunakaran, Assistant Professor
Dr. Vivek Tiwari, Assistant Professor (up to 31st August 2021)
Dr. Rahul Kumar, Assistant Professor (up to 30th September 2021)
Dr. Suresh S N, INSPIRE Faculty (up to 16th August 2021)

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

Scientific Staff

Dr. Latha Diwakar, Senior Scientific Officer
Dr. Kommaddi Reddy Peera, Senior Scientific Officer
Dr. Jonas Sundarakumar, Scientific Officer Grade I
Dr. Khader Valli Rupanagudi, 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. Karru Venkata Ravi Teja, Clinical Research Associate
Dr. Albert Stezin Sunny, Clinical Research Associate
Dr. Ragasudha Botta, Clinical Research Associate
Dr. Sandeep Kumar Barodia, Research Associate
Dr. Gowdham Manivel, Post-doctoral Fellow
Dr. Rajesh Kumar Gazara, Post-doctoral Fellow
Dr. Naveen Kumar Gowda, Post-doctoral Fellow
Ms. Sree Vishmaya V, Project Associate I
Mr. G Goutham Kumar, Project Associate I
Mr. Aditya Yinaganti, Project Associate II
Mr. Virender Kumar Pal, Project Associate II
Dr. D M Parimala, Veterinarian
Ms. Disha Awasthy, Project Scientist
Mr. Shubham Jain, Project Scientist I
Mr. Kambadur Gundu Ananthamurthy, Project Assistant
Ms. Ankita Talukdar, Project Assistant
Ms. Medha Sharma, Project Assistant
Mr. Vishak Madhwaraj Kadambalithaya, Project Assistant
Ms. Yashna K Praveen, Project Assistant
Ms. Pavani R, Project Assistant
Ms. Anupriya Sadashivam, Project Assistant
Ms. Varsha Giridhar, Project Assistant
Ms. Sarayu Ramakrishna, Senior Research Fellow
Mr. Sheldon D Silva, Senior Research Fellow
Ms. Bharti Nawalpuri, Senior Research Fellow
Ms. Santoshi Kashyap, Junior Research Intern
Ms. Varsha H J, Junior Research Intern
Ms. Sneha Sadanand Palekar, Junior Research Intern
Ms. Rachana Navaneetha, Junior Research Intern
Ms. Rajitha Narayanasamy, Junior Research Intern

Ms. Meghana R, Junior Research Intern
Ms. Varshini M V, Junior Research Intern
Dr. Divya N M, Medical Officer
Dr. Venkatesh S, Medical Officer
Dr. Harshini Sankala R, Medical Officer
Dr. Babu Dilip, Medical Officer
Dr. Vinay Kumar B R, Medical Officer

Ph.D. Students

Ms. Krithika S
Ms. Haseena P A
Mr. Akhilesh Shailendra Khamkar
Ms. Bindushree K R
Ms. Srishti Kushwaha
Ms. Mayank
Ms. Shreya Chakraborty
Ms. Nimisha B
Ms. Nisa Manzoor Shah
Ms. Rupsa Roy Choudhury

Technical Staff

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
Ms. Rehab Hussain, Junior Technician
Mr. Divakar A, Lab Technician
Mr. Vinayak Hosawad, Technical Assistant
Mr. Victor Arul Raj, Technical Assistant
Mr. Anees N K, Technician
Mr. Goutham V, Optometrist
Mr. Mohana C, Lab Assistant
Mr. Rajesh G, Lab Assistant
Ms. Pavithra D P, Lab Assistant
Ms. Rupanagudi Sunitha, Lab Assistant
Mr. Manjunatha G M, Lab Assistant
Mr. Prashant Deora, Lab Technician
Mr. Naveenan S, Data Analyst
Ms. Ankita Khan, Data Analyst
Ms. Mehak Chopra, Data Analyst
Ms. Swetaleena Satpathy, Data Analyst

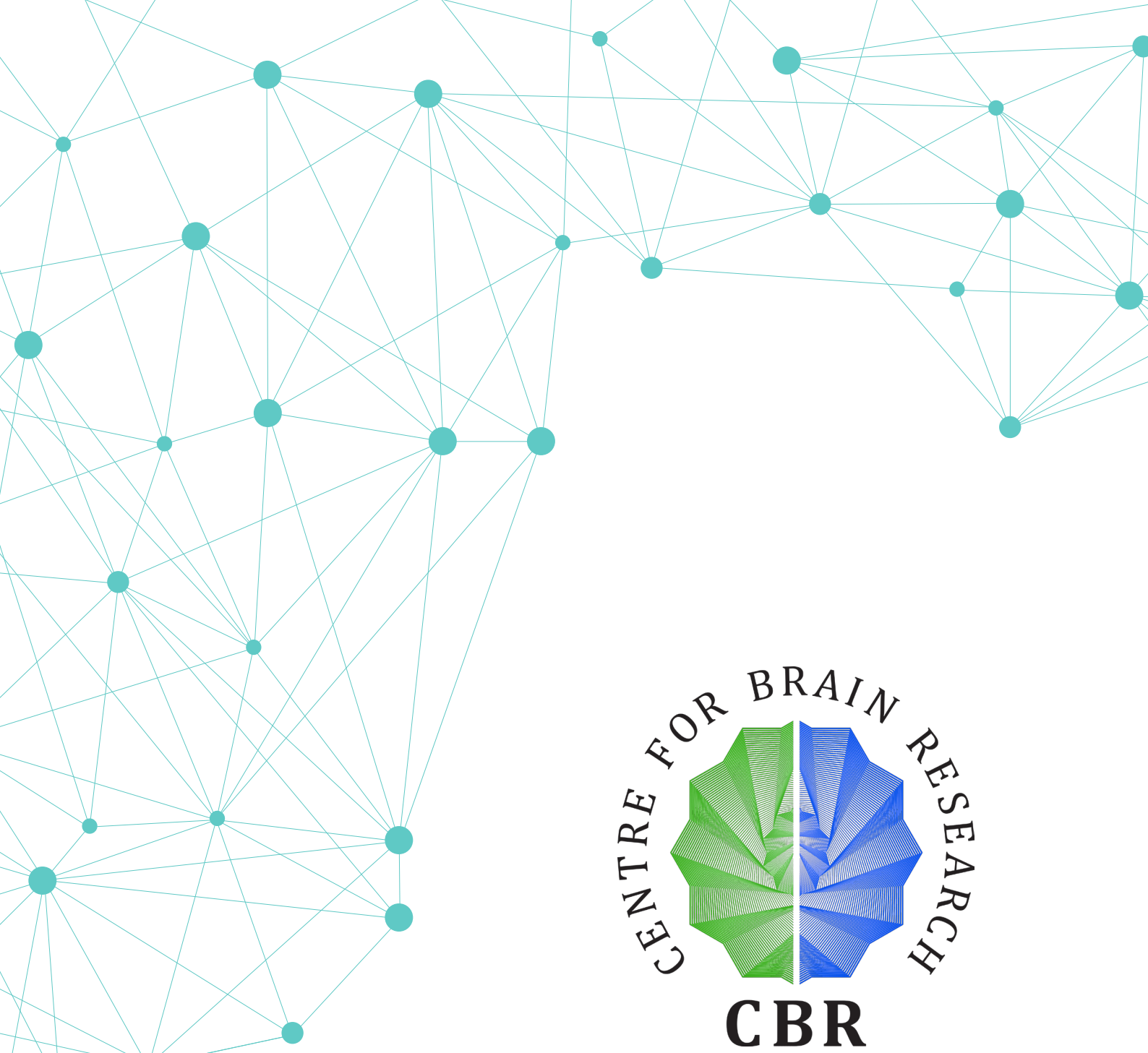
Field Staff

Mr. Ramesh K, Office Manager
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. Hari Kumar, Field Data Collector
Mr. Sreedhara N, Field Data Collector
Mr. Madhuresha, Field Data Collector
Mr. Nagesha C, Field Data Collector
Mr. Shankarappa N, Field Data Collector
Ms. Sunitha H S, Nurse
Ms. Shyalashree 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

Administrative Staff

Mr. R Mohan Das, Special Officer
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. Rahul Dev, Administrative Assistant
Ms. Chaithra B L, Administrative Assistant
Ms. Roopa R, Administrative Assistant
Mr. Ravikumar K L, Executive Assistant
Ms. Triveni, Front Office Executive
Mr. Sudarshan Rao N, Project Engineer
Mr. M R Chandrashekar, Security Advisor



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