

CBR Currents

Newsletter of the Centre for Brain Research, IISc

WAVE 4

SEPTEMBER 2023



CBR-SANSCOG:
Many disciplines, one mission

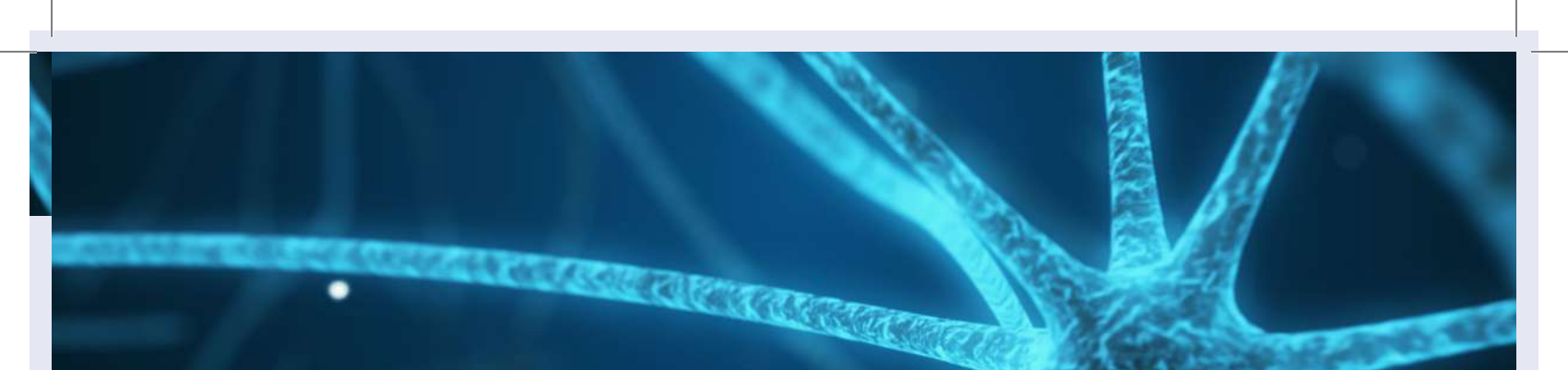
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A microscopic view of neurons, showing a central cell body with multiple long, branching processes extending outwards. The image is rendered in shades of blue and cyan, giving it a scientific and futuristic appearance. The neurons are set against a dark background, making the glowing structures stand out.

EDITORIAL

CBR-SANSCOG: The Pride of CBR

The CBR-SANSCOG study (Srinivaspura Aging, Neurosenescence, and COGntion Study) stands as a pioneering research endeavour in India. It has the distinction as one of the world's most extensive longitudinal investigations on the aging brain, centered on the rural aging populace. This is a forward-looking, groundbreaking project for CBR and entails a community-rooted, cohort study involving as many as 10,000 healthy individuals (aged 45 years and above)



drawn from the villages of Srinivaspura taluk in the Kolar district of Karnataka, India (about 100 km from Bangalore). The core objective of the study is to discern risk factors as well as protective factors for neurodegenerative disorders of the elderly population. The findings of the study will facilitate the development of targeted interventions, aimed at either preventing or postponing the onset of dementia, thereby fostering an enhanced quality of life for an important part of our society, namely the elderly population.

The CBR-SANSCOG project is generously supported by the Pratiksha Trust, established by Mr. Kris Gopalakrishnan and Mrs. Sudha Gopalakrishnan. This initiative is focused on a rural community, representing the typical Indian rural conditions in terms of income, literacy, and agriculture. Managing the logistical aspects of conducting comprehensive assessments for numerous baseline and follow-up cases each month is a complex and mammoth task, requiring a dedicated team of around 30 members, including faculty, medical professionals, nurses, and field workers. The CBR team has implemented a well-organized process to handle these intricate logistics and is actively striving for operational excellence through innovative technological approaches.

The wealth of multi-modal data generated from both baseline and follow-up cases is proving to be invaluable in

terms of the precious insights it offers. Once fully leveraged, this data has the potential to provide fresh perspectives and novel approaches to addressing neurodegenerative disorders. This project is poised to position CBR at the forefront of global leaders in such studies, undoubtedly enhancing its reputation. CBR-SANSCOG is a true source of pride for the entire CBR community.

In this edition of *CBR Currents*, we are excited to guide our readers through the fascinating facets of this study and share some of the insightful findings we have already uncovered. We offer glimpses of events that have kept CBR bustling with activity and excitement. We are pleased to have embarked on several exciting collaborative research and innovation projects in partnership with various departments and centres of IISc. Another highlight is the lively interview with Prof. K Srinath Reddy, esteemed Chair of the CBR Scientific Advisory Committee, whose wisdom and guidance continue to benefit us immensely.

We hope you enjoy reading this edition and, as always, look forward to your comments and suggestions; please write to director.cbr@iisc.ac.in.

Y. Narahari, Director



CBR-SANSCOG: A Flagship Project to Understand Aging and Dementia in Rural India

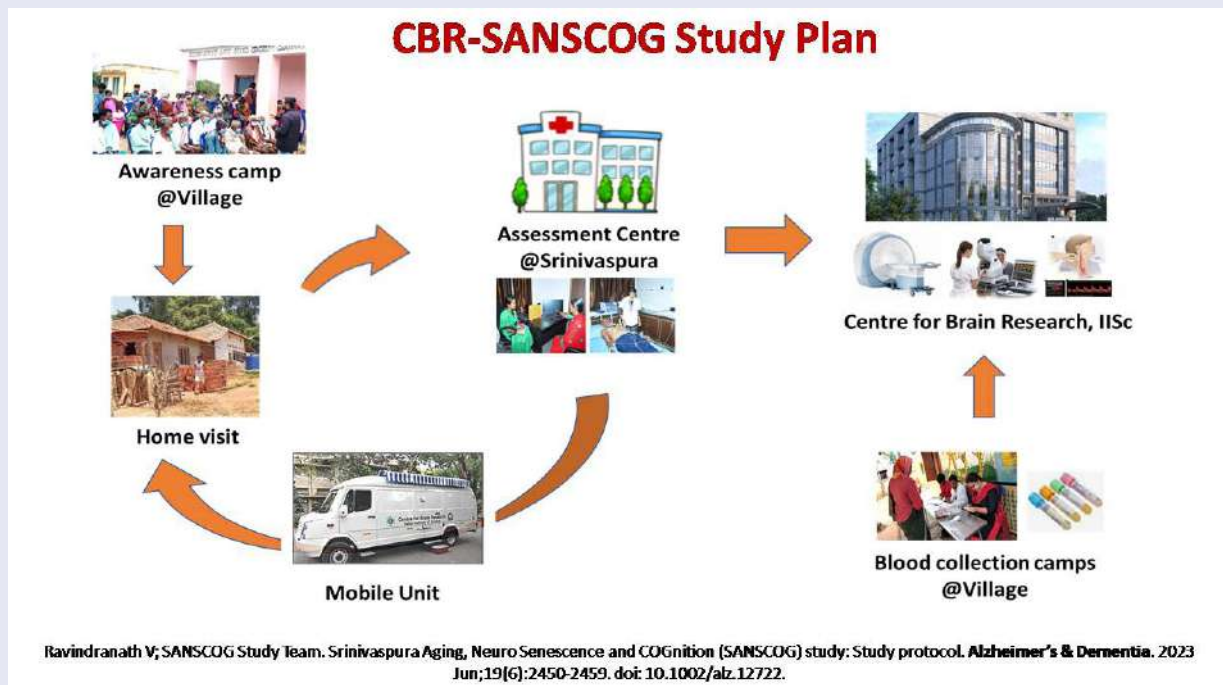
In the coming years, aging citizenry will be one of the biggest challenges for India. Based on a report by the United Nations, India is projected to have an increase in its elderly population by almost 19%. Given the unique geographical, socio-cultural, linguistic, and genetic diversity of Indians, it is essential to understand the underpinnings of aging-related disorders such as dementia in the Indian population. Therefore, a prospective, large-scale study can lead to significant breakthroughs, with emphasis on the rural population which is generally the understudied group.

Srinivasapura Aging, Neuro Senescence and Cognition (CBR-SANSCOG) study in Srinivasapura, Karnataka commenced under the aegis of the Centre for Brain Research (CBR), Indian Institute of Science along with the National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru and Sri Devaraj Urs Academy of Higher Education (SDUAHER), Kolar. A one-of-its-kind study, CBR-SANSCOG is one of the flagship projects spearheaded by CBR. The goal is to recruit 10,000

rural participants comprising cognitively healthy individuals, above the age of 45 years. Another project, Tata Longitudinal Study of Aging (CBR-TLSA), funded by the Tata Trust, was launched with an aim to recruit 1,000 elderly subjects from areas in and around Bengaluru and follow them up periodically. Both these projects focus on evaluating the risk and protective factors associated with cognitive changes due to normal aging, dementia, and other related disorders.

Participants, from both rural and urban areas, undergo detailed assessments of clinical, neurocognitive, lifestyle, anthropometric, biochemical, genetic, and multi-modal neuroimaging measures, to follow their trajectories of aging – both normal and pathological. To say that urban and rural populations are similar would be a gross exaggeration. Hence, assessments are harmonised between the two studies, so that useful comparisons can be made between the two contrasting population groups.

The CBR-SANSCOG study is unique in several ways. First, it is an unprecedented large-scale study of aging in rural India. Second, the study uses a comprehensive range of assessments to measure risk factors for dementia, along with automatic digital output for ECG data, through the Smart View ECG software. Third, the study follows participants over time to track changes in cognitive function and dementia risk. Here, the ultimate goal is to provide insights into the risk factors (that contribute to the pathogenesis and progression of dementia) and




protective factors. Eventually, the insights could facilitate the development of interventions to prevent or delay the onset of dementia, and therefore, improve the quality of life of the elderly.

Conducting a large-scale research project involving human subjects in a rural setting in India is a challenging undertaking. The CBR-SANSCOG study team has adopted unique recruitment and cohort engagement strategies for the same. Prior to the recruitment of participants, the CBR-SANSCOG study team liaised with the local public health officials and worked closely with the grassroot level leaders and community health workers, to build better connections with the community and to create awareness about the study.

For the rural participants, the first visit happens at their home, during which socio-demographic data and written consent to participate in the study are obtained. The second visit is at the CBR-

SANSCOG project office in Srinivaspura or in the mobile unit, where detailed clinical and neurocognitive assessments are done. Biochemical and genetic tests are done through periodic blood collection camps in the village itself. The third visit involves neuroimaging, where a subset of the cohort undergoes brain MRI investigation at the IISc or NIMHANS. Experts from different fields such as basic scientists, geneticists, clinicians, cognitive psychologists, social workers, etc., are involved in the project, thus leveraging diverse perspectives and comprehensive skill sets.

The field data collectors (FDCs) maintain periodic contact with participants through telephone or in-person house visits at least twice a year. They also actively engage the cohort through activities like general health awareness camps, street plays, and sports events, during which participants are provided food. In addition to providing support and engaging with the participants, the FDCs also collect data on cardiovascular risk factors.



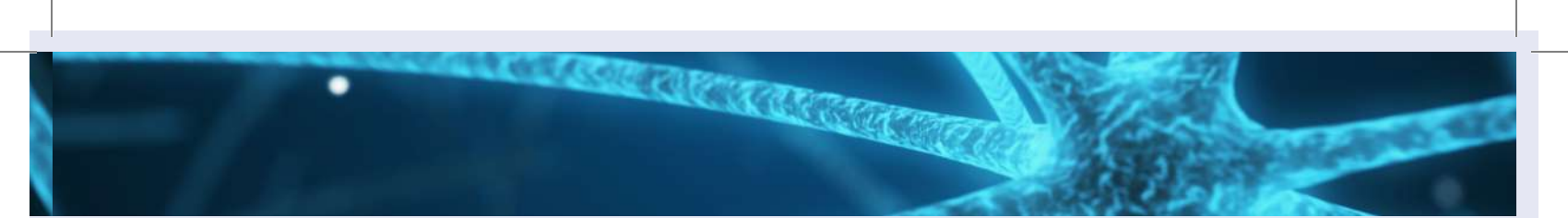
Cardiovascular disease (CVD) is a major risk factor for dementia. Studies have shown that people with CVD are more likely to develop dementia, even after controlling for other risk factors such as age, genetics, etc. This is likely because CVD can damage blood vessels in the brain, leading to cognitive decline. The CBR-SANSCOG study has found that the prevalence of cardiovascular risk factors is different in rural and urban India, with the urban cohort having a higher prevalence. The study team also assesses the impact of lifestyle-related risk factors on cognitive functions. For example, they have studied the impact of sleep and physical activity on cognitive functions. They have also recently initiated efforts to study the role of cardiac autonomic dysfunction in dementia risk.

Addressing the impact of the COVID-19 pandemic is also important. One of the studies by the CBR-SANSCOG team found that the pandemic led to an increase in the prevalence of modifiable risk factors for dementia, such as obesity, dyslipidemia, and depression. Another study found that the pandemic led to an increase in the prevalence of psychological distress, such as depression, in older adults in rural India. Both studies suggest that the pandemic has adversely impacted the physical and psychological health of this marginalized, rural Indian population.

We have also conducted studies on middle-aged and older adults in rural India to assess the impact of social networking

on specific cognitive domains. People with more diverse social networks, larger social networks, and more embedded networks had better cognitive function, even after controlling for other factors such as age, education, and health status. These findings provided evidence that social networking is an important contributor to maintaining cognitive health in older adults. It suggests that interventions that can help people build and maintain strong social networks may be beneficial for cognitive health. With regards to genetic factors, a study focusing on APOE4 was conducted since APOE4 is a gene mostly associated with the risk of dementia. Findings showed that though ApoE-ε4 alone was not associated, it interacted with age, gender, and education to affect attention function in the rural Indian population.

Further, we have tried to throw light on the number of people with dementia who are undiagnosed and untreated in rural and urban India. The data suggests that there are more undiagnosed people in the rural population than in the urban population. Likewise, a higher count of people who have not received treatment is again more prevalent in the rural cohort. A comparison of the baseline clinical data from the TLSA and SANSCOG studies also found a higher prevalence of cognitive impairment in rural populations in the age groups of 55-64 years and 65-74 years. Additionally, the prevalence of cognitive impairment was higher in females who were aged between 55 and 64 years. Likewise, depression was also more prevalent in rural participants,



with a female preponderance in both groups. Early-life stressors (childhood parental death) and head injury were also more prevalent in rural than urban participants.

All these findings point out the stark difference between the two populations and its importance in developing strategies to increase awareness of dementia and improve access to care for people with dementia in rural India. We also noted some potential protective factors against dementia, namely, physical activity, social engagement, and a healthy diet which have been shown to improve cognitive function and delay the onset of dementia. Another significant protective factor is education. A likely reason could be that education helps to build up cognitive capacity, which is the brain's ability to withstand the effects of aging and disease. Thus, it was observed as a protective factor.

Besides the research efforts mentioned above, the CBR-SANSCOG study team plans to conduct research on sleep and autonomic activity. Data collection for this study will begin in the near future and the ensuing investigations are expected to serve to address CBR's multipronged mandate of better understanding the aging brain, preserving cognitive functions in aging, and reducing the risk and burden of aging-related, neurodegenerative disorders.

Recently, we have expanded our study

team by recruiting additional members and setting up a new assessment unit, where an independent assessment team will carry out clinical and cognitive assessments at the CBR-SANSCOG project office. Dr. Jonas S. Sundarakumar, Principal Investigator of CBR-SANSCOG, said, "We are committed to providing the highest quality of research, and we believe that these new additions to the team will foster significant progress. This will surely increase the number of daily assessments and enable us to reach our baseline as well as follow-up assessment targets".

Another endeavor is to start the data analysis work in collaboration with the IISc and ISI faculty so as to include additional cerebrovascular assessments such as MR-Angiography (MRA) and perfusion-weighted MRI using arterial spin labelling (ASL). This research will not be an end in itself but serve as a gateway for future, large-scale research in this direction.

Overall, it is highly likely that the ongoing research and future efforts under CBR-SANSCOG will lead to fruitful results. The CBR-SANSCOG study is an important step forward in the fight against dementia, and it is a testament to the dedication and hard work of the research team. With the collaborative efforts of all the like-minded stakeholders involved, we can develop effective prevention and treatment strategies for dementia. Consequently, this will make a real difference in the lives of people with dementia.

Events @ CBR

Since the last Wave of *CBR Currents*, it has been an extraordinarily busy and exciting time at the Centre. This section captures highlights of some of the most significant events.

Collaboration Explorations with IISc

CNS-CBR Workshop

CBR hosted a workshop on 15th May 2023 to explore synergistic collaborations with the Centre for Neuroscience (CNS), IISc. Faculty members from CBR and CNS engaged in focused discussion to identify themes of common interest and potential partnership avenues wherein complementary skills could be capitalised upon. It was agreed that ongoing and future organically evolving collaborative projects involving the Centres could be nurtured through avenues such as joint PhD supervision and using opportunities like the CBR-FABRIC program as well as extramural sources of funding.






BSSE-CBR Workshop

On 24th August 2023, CBR had the pleasure of hosting faculty members from the Centre for Biosystems Science and Engineering (BSSE), IISc. The meeting entailed presentations outlining the research interests and initiatives of the Centres and brainstorming to narrow down potential collaborative projects that could benefit from the research interests and collective expertise of the Centres and strongly aligned with the mandate of CBR. The attendees concurred on the scope for exciting partnerships and expressed interest in delving into these areas through suitable enabling mechanisms.

Accreditation of the CBR Biobank

The CBR Biobank catalogues and stores valuable DNA, plasma, and serum samples pertaining to the flagship research projects. With the aim of establishing a robust Quality Management System (QMS) and enhancing the quality of both the biological materials and associated data, an accreditation initiative has been initiated in partnership with the Centre for Laboratory Accreditation (CLA), a subsidiary of the Quality Accreditation Institute (QAI), that confers ISO 20387 certification for biobanks.





The accreditation process involves three phases: personnel training, submission of Standard Operating Procedures (SOPs) and related documents using a self-declared assessment tool, and an onsite inspection by auditors. CBR Biobank staff (a team of 12 members, including 2 faculty members and 2 scientific officers) underwent rigorous training (online) from 15th to 17th June 2023. The training program, led by Prof. B.K. Rana (CEO, QAI), covered various topics such as the general and structural prerequisites of biobanks, with a special focus on data documentation, safety, confidentiality, impartiality, and different aspects of QMS according to ISO 20387 standards. The training concluded with an examination and successful procurement of certificates by all the attendees. Completion of the remaining phases of the accreditation process will strengthen the biobank's capacity and operations, foster the sharing of biospecimens and data with the research community, and thereby contribute to the advancement of scientific research.

Expression of Gratitude to CBR-TLSA Volunteers

On 7th July 2023, CBR hosted a special interactive session for volunteers of the Tata Longitudinal Study of Aging (CBR-TLSA). The in-person event was attended by over 230 study participants and their families. The CBR-TLSA team provided detailed updates on the progress of the study and the major outcomes thus far. Plans for the near and far future were outlined. An elaborate interactive session, moderated by Prof. Narahari, provided an opportunity for the attendees to share their expectations and feedback on their unique experiences as participants of CBR-TLSA. The session also enabled the discussion/clarification of specific queries regarding enrollment and assessments and general questions related to healthcare, dementia prevention and management, and



caregiver support. Volunteers with longstanding involvement in the study were specially thanked and felicitated. On behalf of the funder, Ms. Daphne Vallado (Program Coordinator, Tata Trusts) affirmed continued support and commended the progress of the study and CBR's initiative to strengthen engagement with the volunteers.

Evening of Stories

CBR organised an event titled 'Evening of Stories' on 21st July 2023 to host a book talk by Ms. Nandita Jayaraj, journalist and co-author of 'Lab Hopping: A Journey to Find India's Women in Science'. She provided an overview of her motivation to co-author the book and her experience interviewing multiple stakeholders to gauge the issue of gender gap in the Indian academic research ecosystem and other hurdles faced by women scientists. The talk was followed by a panel discussion (moderated by Dr. Shweta Ramdas, Assistant Professor, CBR) with Prof. Bhavana Kanukurthi (Department of Computer Science and Automation, IISc), Prof. Hiya Ghosh (National Centre for Biological Sciences), and Dr. Reshma SV (PES University). The panelists shared their stories of persistence and gave tips on what it takes to build a successful career in academia in India. The talk and panel discussion were well-received by not only the CBR fraternity but also young scientists from various departments and centres of IISc. Prior to this session, CBR students had the opportunity to interact online with Ms. Aashima Dogra, co-author of the said book.

Centre for Brain Research
Indian Institute of Science campus, Bengaluru

Join us for an
Evening of Stories

Stories of persistence
Stories of breaking stereotypes
Stories of our women scientists

Book Talk by
Nandita Jayaraj,
Journalist and Co-author of
'Lab Hopping: A Journey to Find
India's Women in Science'

followed by a panel discussion with
Bhavana Kanukurthi, IISc
Hiya Ghosh, NCBS
Reshma SV, PES University

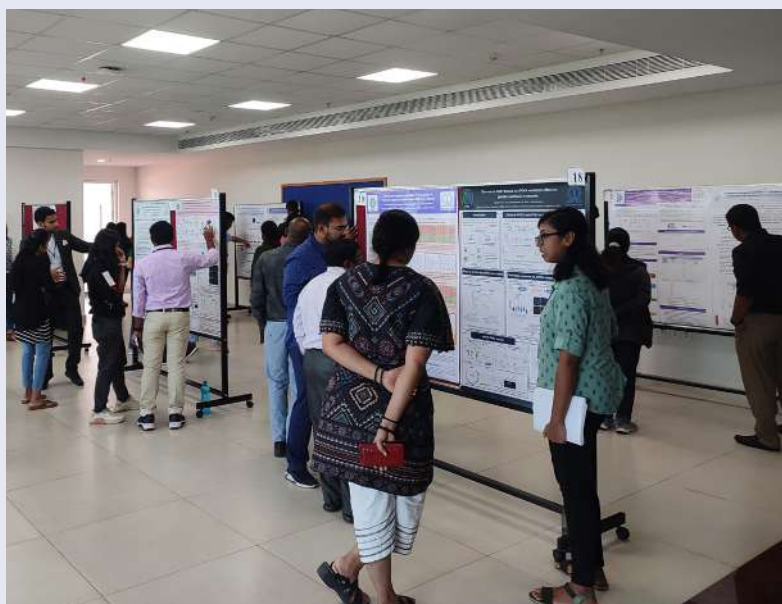
CBR Auditorium | July 21, 2023 | 4:45 - 6 pm
Goodies available - Chai, snacks, and lots of inspiration

Registration link: <https://forms.office.com/r/wyjmE30u2q>



Poster Symposium for Research Interns

On 31st July 2023, CBR organised a CBR poster symposium wherein research interns enthusiastically showcased their learnings and accomplishments at CBR. The event was also attended by external experts (scientists and students from institutions like IISc, NIMHANS, InStem, JNCASR, and MAHE) who actively interacted with the interns and offered feedback on their posters. The attendees appreciated the motivation levels of the interns and their contributions to the ongoing research endeavours of CBR. Based on the recommendations by a panel of external experts, poster prizes were awarded.



Pursuit of a Partnership with SGBC

As a follow-up to the CBR faculty members' visit to Sudha Gopalakrishnan Brain Centre (SGBC), IIT Madras, in April 2023, a team of researchers from SGBC visited CBR on 11th August 2023. They had a tour of the facilities and interacted with the faculty members. Potential topics of collaboration (involving aspects like vascular dementia, sex differences in AD pathology, early molecular events associated with AD, and brain imaging) identified earlier were discussed in greater detail. It is expected that the conversations will lead to innovative joint research proposals built on both the Centres' complementary infrastructure and collective expertise.



Distinguished Visitors to CBR

CBR had the pleasure of hosting many distinguished visitors and invitees, who are well-wishers and potential partners in our research endeavours.

The list includes:

- Prof. Siddhartha P. Sarma, Molecular Biophysics Unit, IISc
- Dr. Uma Nambiar, Consultant, Bagchi Parthasarthy Hospital & IISc Medical School
- Dr. Usha Narayan, Global Commercial Strategy, Merck Life Science
- University of Cote d'Azur President's delegation
- Prof. Vyjeyanthi Periyakoil, Founding Director, Stanford Aging, Geriatrics and Ethnogeriatrics Transdisciplinary Collaborative Research Center, Stanford University
- Prof. LS Shashidhara, Director, National Centre for Biological Sciences
- Delegates from Vayah Vikas, a not-for-profit organisation working for the well-being of senior citizens
- Prof. Gilles Mithieux, Director, Centre National de la Recherche Scientifique, Lyon
- Dr. H Paramesh, Visiting Professor, Divecha Centre for Climate Change, IISc
- Delegates from EDM2023, the 16th International Conference on Educational Data Mining organised in IISc
- Prof. Sathees Raghavan, Department of Biochemistry, Chair – Central Animal Facility, IISc.

Looking Back, Looking Ahead


In conversation with Prof. K Srinath Reddy, Chair, CBR Scientific Advisory Committee

In an attempt to bring some of CBR's inspiring well-wishers and stakeholders closer to our readers, *CBR Currents* will feature a series of interviews, launched here by a lively conversation with Professor Srinath Reddy, Chair of the CBR Scientific Advisory Committee (SAC). Please read on for a better appreciation of the role of the SAC and his thoughts on the strengths and potential of CBR.

In your role as the Chair of the Scientific Advisory Committee, you have been making exemplary contributions to setting CBR's research goals and monitoring the efforts towards these goals. It has not been long since its inception, but could you please comment on how the Centre has evolved over the years?

Thanks for inviting me to have this conversation. Let me start by clarifying my role. The goals of research at CBR are set collectively. Initially, the overall mission was set by the leadership of IISc, the founding Director of CBR Prof. Vijayalakshmi Ravindranath, and Mr. Kris Gopalakrishnan whose generous support helped to establish the centre. That is an inspiring mission, to study the structural and functional changes in the brain which occur with aging, identify their driving biological processes and social determinants, and to enable us to decipher their relationship to a decline in cognition and onset of dementia. This investigation spans from study of genomics and animal research in the brain's structure and functions to population-based epidemiology and clinical correlates. Mapping the mystery of the mind, with the aim of preventing aging-related decline in cognitive functions and the onset of dementia is a very laudable objective. The fact that CBR was established to study this in the Indian context, to identify the determinants, drivers, and dynamics of aging-related cognitive changes in the world's largest population, recognises the strength of Indian science. It will also enrich science everywhere by providing deeper insights into brain functions and expanding the knowledge pool on their age-related changes, for global application.





The role of the Scientific Advisory Committee (SAC), which I have the honour of chairing, is to review the progress of research projects which are attempting to advance this mission and suggest ways by which the research can be sharpened in focus, strengthened in methodology, and streamed towards potential applications. This is a collective effort, of all members of SAC and the many scientists working at CBR. Apart from refining ongoing research to impart more vigour and rigour, new ideas too are discussed, fresh research questions are generated, and their path is charted from purpose to process and then on to potential products. It is the collective intellect of CBR's scientific community and the SAC which defines and refines the quest for new knowledge on the intricate relationships of aging and brain function.


A major strength of CBR's SAC is that it provides a confluence of many disciplines from biomedical sciences and statistics to clinical medicine and public health. This provides great strength in investigating complex scientific issues through interdisciplinary approaches. I have greatly benefited from the expertise and wisdom of the SAC members, in improving my own understanding of neuroscience and many other relevant scientific disciplines. I was probably inducted into the SAC as an epidemiologist, to assess and assist the Srinivaspura Aging, Neurosenescence and COGnition study (SANSCOG) in a rural population. However, the role has offered me a rare opportunity to avidly learn from eminent experts in many other disciplines and to continually keep the synapses in my own aging brain buzzing with acquisition of new knowledge.

I believe CBR has evolved very well over the years, with the addition of the Tata Longitudinal Study of Ageing (TLSA) in an urban population and the GenomeIndia project which seeks to provide an extensive genomic mapping of the highly diverse Indian population. There are also several faculty-initiated projects which involve studies of neuronal metabolism and synaptic dysfunction, the relationship of Locus Coeruleus to dementia, the pathways of vascular dementia, dysfunctional impact of disruption in cross-hemispheric circuits and the diagnostic as well as the predictive role of blood biomarkers related to risk of or protection against dementia. All of these studies are propelling CBR's research agenda towards its scientific and public health goals.

What are some unique features of CBR and what impact do you expect in the time ahead?

CBR has a highly relevant and well-focused scientific mission, which is linked to a social purpose. It seeks to generate knowledge that can protect and even promote brain function, as people age. For pursuing that mission, it brings the strength of interdisciplinary enquiry into questions related to a highly complex adaptive system - the human brain. The research truly connects cell to society. I expect CBR to advance knowledge to application with significant impact on public health policies and clinical practice.

What, according to you, are areas in which CBR must attempt to focus to emerge among the global leaders in aging brain research?



CBR must retain its strong focus on opening the path to impactful application, while positioning the study of brain's biology in the context of ongoing social, demographic, economic, environmental, and behavioural transitions in our diverse population. In its scientific investigation, it must expand the study of genomics to elucidating the role and potential intervention levers of epigenomics. These should include both social epigenomics and environmental epigenomics. Existing birth cohorts in India can also be partnered, to study the epigenetically mediated effects of early life influences on adult disease, as relevant to brain health.

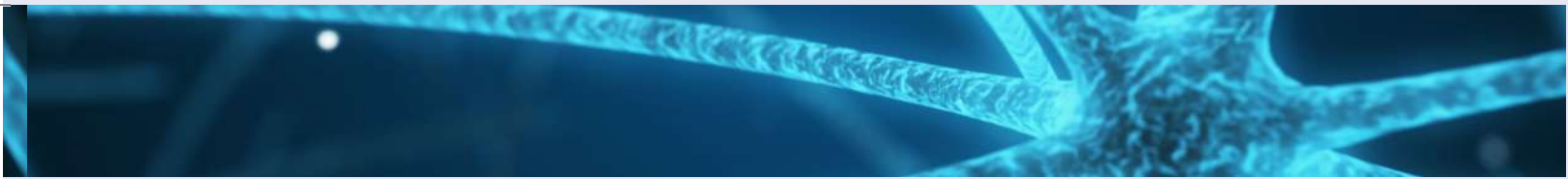
CBR should also take advantage of the large number of healthcare facilities in India, from community-based primary health centres to advanced tertiary care hospitals, to chart the natural history of aging-related cognitive changes and derangements of brain function. Subsequently, these links to the health system will provide the settings for the evaluation of public health and clinical interventions. While developing these partnerships, CBR should develop capacity for collation and analysis of Big Data, gathered from multiple data sources.

To enhance the quality of its scientific enterprise and achieve greater impact, CBR must build partnerships with other institutions, in the region, across India and engage valuable global partners. To be recognised as a global leader in the field,

CBR must not only unravel the effects of aging on the brain under different living conditions but also point the ways to protect brain health. Cerebral functions need not recede as the chronological clock of our lifetime advances. We, in India, are very well positioned to advance this knowledge given the huge diversity of gene-environmental interactions in our geographically dispersed, culturally variegated, and socio-demographically stratified population. Our ability to harness both modern science and traditional systems of healing gives us a broad avenue for advancing holistic understanding of health and an integrated approach to healing. CBR should utilise these opportunities to solve the complex crossword puzzles posed by aging brains.

You are a visionary institution builder who has steered and overseen numerous public health projects. Based on this rich experience, could you kindly share suggestions for CBR's community outreach and public engagement initiatives?

You are far too generous in your assessment of my contributions. I have always believed that science is sterile if it lacks social relevance. Community engagement constantly reminds us of that purpose. It also enrolls the community as an active partner in conducting research and successfully delivering a programme - by identifying needs, setting priorities, designing ethically sound and contextually feasible research, participating in or



monitoring progress of implementation of a programme, and facilitating multi-sectoral engagement. Even to influence behaviours that enable protection of brain health and to discourage behaviours which erode it, an informed and engaged community is needed. In projects like CBR-SANSCOG and CBR-TLSA, wider participation of persons from the rural and urban communities will make the studies more representative and enhance the external validity (generalisability) of the studies.


With regard to public engagement, through awareness-enhancing interactions, the value lies not only in increasing the profile of CBR and providing a greater understanding of its work but also in providing information which enables people to protect, preserve and promote their overall health in general and brain health in particular. A clear message we must convey is that brain health is not separate from general health, as many of the risk-enhancing and protection-conferring factors are the same. By educating people on brain health, we can prevent many other diseases too - like cardiovascular diseases, diabetes, and cancers.

Armed with medical degrees and formal training in epidemiology, you have served as Advisor on Health to several governments and as physician to two Prime Ministers of India, besides being a research stalwart. Professional trajectories

like yours are truly exceptional and hard to come by. What measures could be taken to strengthen the clinical research ecosystem in the country?

Again, you are being far too kind in your profiling of my stature. To answer your question, I would like to place great emphasis on creating a conducive environment for interdisciplinary research. Whether in basic research, clinical research, or public health research, siloed approaches will not work. Complexity defies linear models. We are now dealing with many complex adaptive systems which coexist and often coalesce. It requires the confluence of many disciplines to discover causal pathways and design effective interventions. This is true of clinical medicine too. Can we only prescribe a medicine, without understanding the behavioural and economic determinants of adherence to therapy or adopt the tunnel vision of a single organ specialist while dealing with an elderly person suffering from multiple co-existing chronic conditions?

We must also recognise that clinical research on major questions will require large sample sizes. That is why large, simply designed, collaborative clinical studies are being promoted in recent years, especially in the area of clinical trials. We need to build inter-institutional collaborations in our country, to undertake high-quality studies of this nature. We must also harness our growing strength in digital health for improving the efficiency and quality of our research enterprise. Our research funding agencies and evaluation processes for academic promotions should give greater weightage to problem-



solving interdisciplinary research. We need to train clinical researchers for adopting methodologically sound and ethically unimpeachable research methods. Even if they are not actively undertaking clinical research themselves, they must be sufficiently conversant with good research methodology to critically appraise the quality and generalisability of published research before they incorporate the findings into their practice.

Lastly, are there any words of advice for students considering career paths in clinical/life sciences research?

I will try to keep my advice simple. Research is both a deeply satisfying enterprise and a highly demanding endeavour. You must undertake it with unwavering enthusiasm and undimmed commitment. All along the way, remind yourself of the advice Louis Pasteur gave his young research fellows: “Keep your enthusiasm but keep strict verification as its constant companion”. It has been rightly said that science is ‘organised scepticism’. To perform well in that arena, with elan and efficiency, a researcher must train well in research methodology and keep updating that knowledge.

In research, enthusiasm must always be combined with objectivity. I believe that Karl Popper’s dictum of earnestly attempting to refute your own hypothesis is the canon of objectivity. Intellectual honesty must always triumph over

yearning for applause and honours. The process of critical peer review must commence in the researcher’s own mind, and within the research team, before it proceeds to an independent review by others.

Whether in life sciences or clinical sciences, research should ultimately lead to public good and societal advancement. The immediate products of research may not always yield such beneficial applications but must open the road to potential products that improve human health and well-being. The purpose of public health and clinical research should be to provide evidence-informed, context-relevant, resource-optimising, culturally adaptive, and equity-promoting recommendations for policy and practice. Life sciences research illuminates that path by providing a wealth of knowledge that has the potential for translation into public health and clinical applications.

In this era of Team Science, very few researchers can be ‘lone rangers’. Interdisciplinary research too demands purpose-driven, productive, and pleasant collaborations. While a solitary maverick can indeed sometimes provide the spark to ignite a very innovative scientific quest, teamwork is the fuel that is needed to keep that vehicle running smoothly and swiftly towards its goal of societal benefit. So, researchers in life sciences, clinical medicine, and public health must develop into T-shaped personalities, with depth of expertise in their chosen area and breadth of familiarity and respect for other disciplines which may contribute to collaborative research.



New Addition to Team CBR

CBR has been delighted to welcome and induct Prof. Neelam Sinha, who joined as an Associate Professor on 17 July 2023.

Prof. Neelam Sinha's interests lie in applying machine learning techniques for multi-modal neuroimaging.

She completed her PhD in Signal Processing from the Department of Electrical Engineering, IISc, in 2008. Her thesis involved the reconstruction of magnetic resonance (MR) images from under-sampled data. Before joining CBR, she worked as a faculty member at the International Institute of Information Technology (IIIT) Bangalore, wherein she focused on problems such as infiltrator cell detection, glioma grading, age estimation, and Parkinsonian disorder classification – all using MR acquisitions. Besides, she also has experience working on EEG time series for problems such as PD detection, signatures of mathematical cognition, startle response, and assessment of creativity in tasks being performed.

"I am quite excited about setting up a 'Multi-modal Neuroimaging Lab' at CBR", she says. "The primary objective of the lab is to bring together inferences from different imaging modalities to better understand neurodegenerative disorders among the elderly." Her research group will explore techniques such as Deep Learning frameworks, Interpretable AI, and Causal Models, that have proven to be successful across domains. Some of the sub-tasks towards the grand goal are (i) Cognitive deficit estimation (ii) Localization of causes (iii) Measuring goodness of interventional mechanisms and (iv) Identification of early biomarkers.

Besides research and teaching, she enjoys being amazed by the infinitude of lovely patterns in nature – flowers, leaves, twigs, spider webs, mushrooms – abundantly present in our lovely campus.





Recent publications by Prof. Sinha

- “Measuring deviation from stochasticity in time series using autoencoder-based time-invariant representation: Application to black hole data”, Chaka SaiPradeep, Neelam Sinha and Banibrata Mukhopadhyay, in proceedings of 48th IEEE Conference on Acoustics, speech and signal processing (ICASSP 2023)
- Simultaneous segmentation of multiple structures in fundal images using multi-tasking deep neural networks”, Sunil Kumar Vengalil, Bharath K and Neelam Sinha, in Frontiers of Signal Processing 2:71, Dec 2022
- “An investigation of the multidimensional (1D vs 2D vs 3D) analyses of EEG signals using traditional methods and deep-learning based methods”, Shah D, Gopika K. G, and Neelam Sinha, in Frontiers of Signal Processing 2:93760, July 2022.

For more information, please visit <https://cbr.iisc.ac.in/people/neelam-sinha/>


Putting the 'Work' in 'Networking', the fun way

Having earned coveted recognition as one of the 30 ISTAART Ambassadors from 14 countries, **Ms. Rajitha Narayanasamy**, a psychologist in the CBR-TLSA team, shares her memorable experience at AAIC 2023.



The ISTAART Ambassador program (<https://istaart.alz.org/>) aims to connect early researchers across the globe with year-round leadership and networking opportunities. As one of the many benefits of being an ISTAART Ambassador, I was able to volunteer at the Alzheimer's Association International Conference (AAIC '23), one of the world's largest annual dementia conferences, held in Amsterdam in July 2023; this volunteering enabled invaluable experiences.

My responsibilities at AAIC '23 included monitoring sessions, engaging with session chairs and speakers, aiding the Alzheimer's Association booth, and assisting in workshops and receptions. These activities gave me a chance to interact with celebrated leaders in the field which would have been otherwise impossible. I seized opportunities to attend sessions pertaining to my research interests and to forge connections with speakers. Further, I could also participate in a few pre-conference events such as an



interactive workshop on 'Cognitive Assessment in Low- and Middle-Income Countries'. It was fun to learn from researchers across the globe working on cross-cultural adaptation of neuropsychological assessments. I was fortunate to interact closely with eminent speakers such as Dr. Paulo Caramelli, and Dr. Michael Hornberger, and share insights about Indian initiatives.

A workshop titled 'Grant Opportunities & Tips and Tools to Writing Applications for Success' imparted grant-writing skills and provided a roadmap to funding avenues for budding researchers. Poster presentations enabled productive exchanges with like-minded researchers and helped me gain valuable feedback from esteemed experts. Post-conference events such as welcome receptions and networking events extended the conference experience beyond the stage by fostering meaningful discussions and nurturing collaborations in less formal settings. I was able to take part in the 'Alliance of Women Alzheimer's Researchers (AWARE)' panel discussion and imbibed interesting perspectives on overcoming challenges and fostering mutual support.

Finally, a key highlight was the lasting friendships I formed within the ISTAART ambassador community. Despite our diverse research interests and geographical origins, we bonded over shared laughter, heartfelt moments, tired feet, and a mutual passion for dementia research and care.

Overall, the ambassadorship has been truly enlightening, exposing me to the myriad of opportunities that lay ahead in the field of dementia research. I am grateful for CBR's support in making this once-in-a-lifetime experience possible.



Infrastructure @ CBR

CBR's state-of-the-art infrastructure, which enables advanced research on the aging brain and related disorders, has been made possible with generous core funding from the Pratiksha Trust and support from other organisations (governmental and private) like DBT, DST, Tata Trusts, SKAN Research Trust, India Alliance, and Fidelity Foundation. Through this section of *CBR Currents*, we hope to inform our readers of the sophisticated research facilities available at the Centre.

Histology and Microscopy

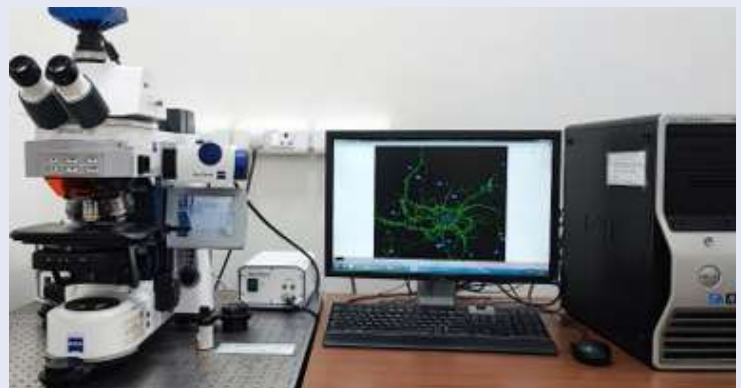
Cellular and molecular neuroscience research at CBR focuses on understanding the neural circuitry at different levels of organization ranging from molecules to behaviour using appropriate experimental models. To this end, the infrastructure encompasses a state-of-the-art facility that caters to different research groups at CBR. This includes a dedicated histology room to section animal brain tissue specimens followed by a high-end imaging facility.



Using the Leica CM 1520 Cryostat, tissue sections as thin as 30 micrometres can be cut at -20 degree Celsius.

Zeiss Apotome

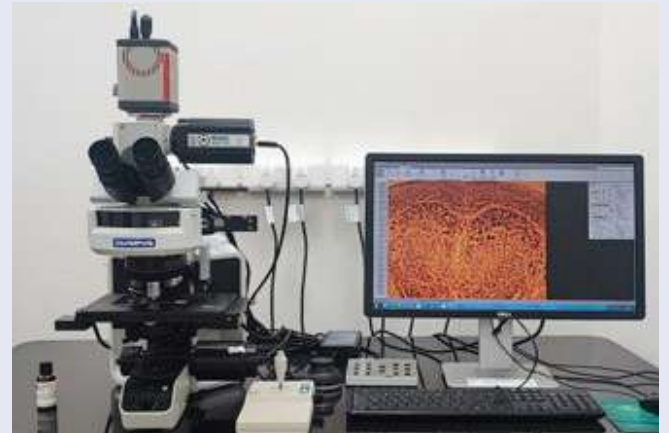
CBR houses a widefield fluorescence microscope to image 2D and 3D structures from fixed tissues and cells. This device is widely used to image cultured neurons, endothelial cells, pericytes, microvessels, etc. Images are taken for further offline quantification.



Cultured neuron showing phalloidin staining for actin filaments

Olympus BX53 with Neurolucida and Stereo Investigator system

This system helps study neuronal structures by generating quantitative morphometric data and unbiased quantification of subcellular structures.



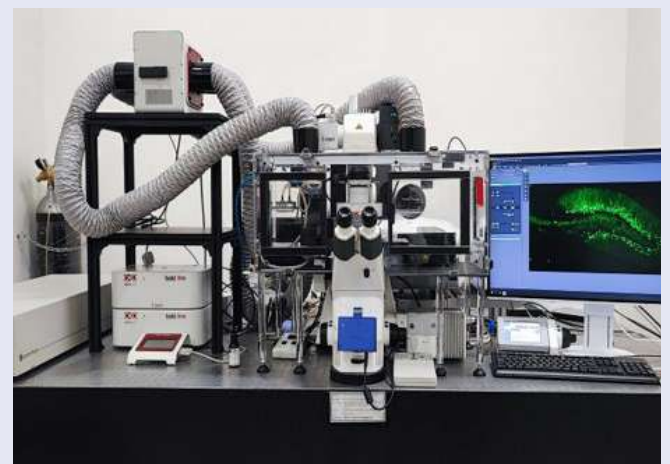
Mouse coronal showing Golgi Cox staining of neurons

Confocal Microscopes

The microscopes with the detection range of 400-700 nm are used for fluorescence imaging to generate high-resolution images. CBR's confocal microscopes are currently used for imaging axonal terminals and for studying the morphology of astrocytes, vascular structures, etc. The microscopic system does have an option for live cell imaging including Fluorescence Resonance Energy Transfer (FRET) and Fluorescence Recovery After Photobleaching (FRAP) methods to study the synaptic function.

Zeiss LSM 780

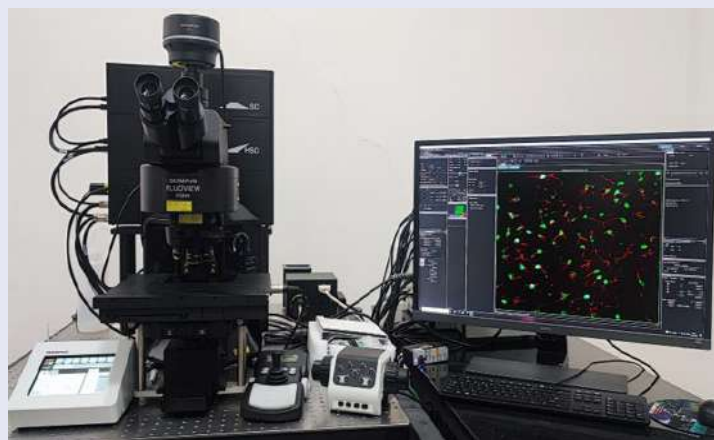
The Zeiss LSM 780 is a highly sophisticated, visible light confocal laser scanning microscope equipped with a 34-channel spectral array. It is inverted and is equipped with an incubation chamber for regulating temperature for live cell imaging. It possesses a motorized stage and software for tile imaging which facilitates very high-resolution files from large fields of view.



Mouse hippocampal section GFP expression under Thy 1 promoter

Olympus FV3000

Olympus FV3000 is a laser-scanning confocal microscope that generates high-resolution, high-contrast images of samples. It scans samples point by point, resulting in precise 3D fluorescence images. Among other features, it has a motorized XYZ stage for easy transition between macroscopic to microscopic imaging. It has 6x solid-state diode lasers and a fully enclosed environmental chamber for live cell imaging.



Mouse hippocampus showing astrocytes stained with glial marker (GFAP)





