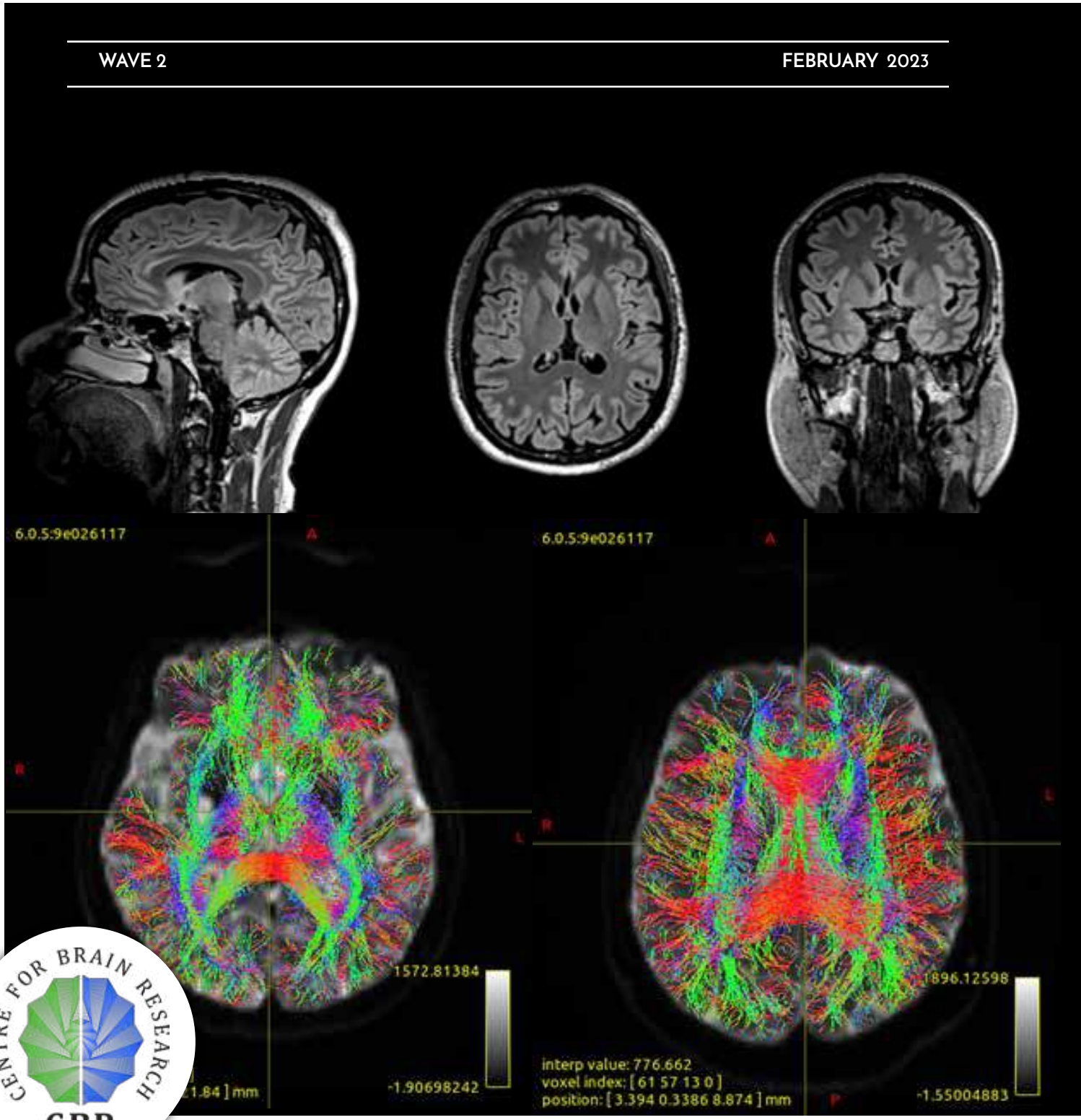
CBR Currents

Newsletter of the Centre for Brain Research, IISc

WAVE 2 FEBRUARY 2023



CENTRE FOR BRAIN RESEARCH
CBR

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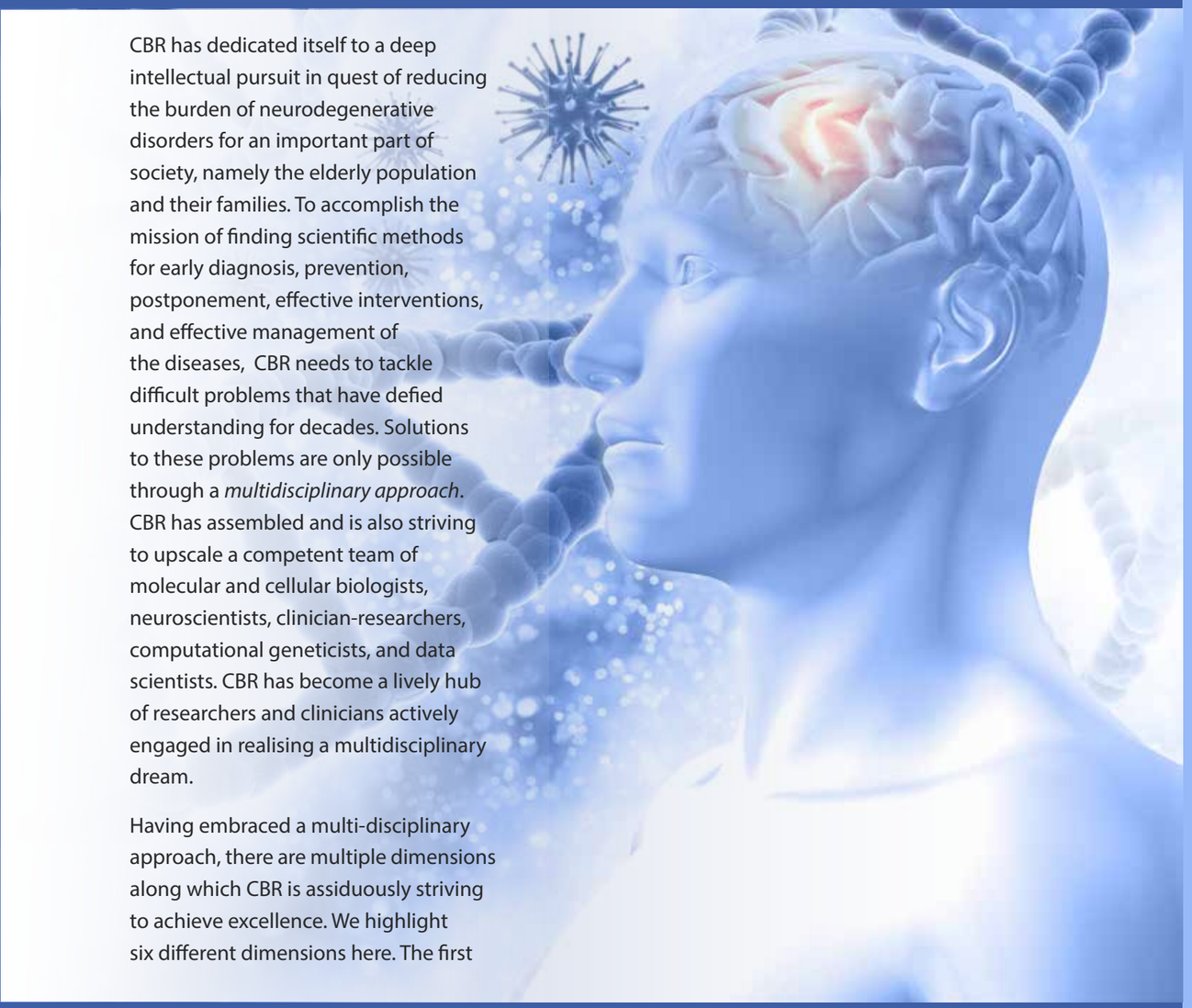
Neuroimaging:
A picture is worth a thousand words

EDITORIAL

CBR: A Multi-Disciplinary, Muti-Dimensional Dream



CBR has dedicated itself to a deep intellectual pursuit in quest of reducing the burden of neurodegenerative disorders for an important part of society, namely the elderly population and their families. To accomplish the mission of finding scientific methods for early diagnosis, prevention, postponement, effective interventions, and effective management of the diseases, CBR needs to tackle difficult problems that have defied understanding for decades. Solutions to these problems are only possible through a *multidisciplinary approach*. CBR has assembled and is also striving to upscale a competent team of molecular and cellular biologists, neuroscientists, clinician-researchers, computational geneticists, and data scientists. CBR has become a lively hub of researchers and clinicians actively engaged in realising a multidisciplinary dream.

Having embraced a multi-disciplinary approach, there are multiple dimensions along which CBR is assiduously striving to achieve excellence. We highlight six different dimensions here. The first dimension is for CBR to become an international centre of excellence in the scientific study of normal and pathological aging of the brain to unravel the mysteries of neurogenerative disorders of the elderly population.

Longitudinal studies involving muti-modal assessments in carefully selected cohorts of human subjects are key to a thorough understanding of the aging brain. The second dimension for CBR excellence is to assume a leadership role in scientific conduct of longitudinal studies of rural and urban cohorts in India and abroad.

Expert use of Artificial Intelligence and Machine Learning techniques on neuroimaging and other modes of data is proving to be a game changer in aging brain research and innovation. The third dimension is for CBR to be a front runner in the creative use of these techniques.

World over and particularly in India, a massive socio-economic crisis could break out if neurodegenerative diseases are not tackled effectively. The fourth dimension of excellence for CBR is to be a policy advisor to the Government in public health initiatives connected with neurodegenerative diseases and shape the policies for the effective management of neurogenerative conditions.

The fifth dimension for CBR is to bridge the science-society gap in the area of neurodegenerative diseases. CBR will spearhead India's efforts to reach out to the different sections of the society to dispel misconceptions about neurodegeneration and to educate everyone on the tremendous scientific and technological advances in the area.

The sixth dimension where CBR must make a mark is translational research. CBR would work towards bench-to-bedside translation by engaging in collaborations with leading research groups, global industry, and the startup ecosystem.

In the coming years, CBR will strive to achieve excellence in all the six dimensions and beyond, through a multi-disciplinary approach and offer its services to the society and the nation.

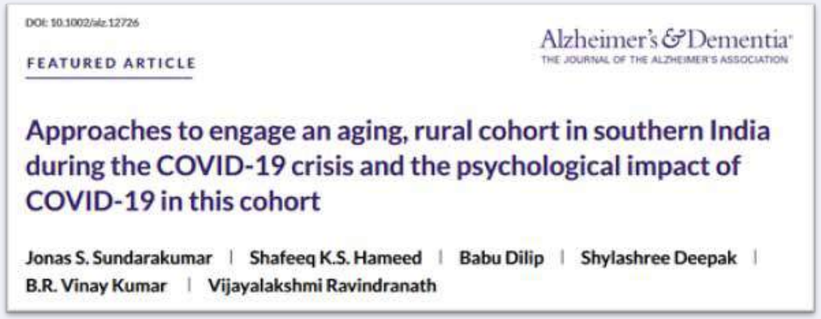
The first wave of "CBR Currents" was received with overwhelming enthusiasm. We are delighted to present Wave 2. This issue contains several highlights of recent research in CBR. In the past three to four months, CBR has successfully conducted several scientific and outreach events. You will find an overview of these events in this issue. We also had several distinguished researchers visiting CBR in recent times and delivering state-of-the-art talks. These are covered as well. We are starting a series of snapshots of the scientific and computing infrastructure in CBR, with an overview of the computational data centre in CBR. The cover page has MRI images taken at the JN Tata MRI Centre as part of the multimodal assessments that are central to our longitudinal studies and represents interesting research findings emerging from these assessments.

We hope you enjoy reading this issue and look forward to your comments and suggestions; please write to **director.cbr@iisc.ac.in.**

Y. Narahari,* *Director

Cover Story

Some Research Highlights from SANSCOG study and TLSA



We envisage that such engagement strategies would improve subject rapport and cohort retention, and thus, could be adopted by similar cohort studies across the world. This marginalized, rural Indian community had severe, adverse psychological impact in this pandemic. Urgent public health measures are needed to mitigate this impact and develop appropriate preventive strategies.

During COVID first wave, 28.8% and 5.5% had depression and anxiety, respectively in the rural cohort. Corresponding figures in the urban cohort were 6.5% and 1.7%. During second wave, 28.8% of rural subjects had depression and 3.9% had anxiety, whereas corresponding figures in urban subjects were 13.1% and 0.66%. During the above-mentioned four time periods, proportions of depression were: rural—8.3%, 28.8%, 16.6%, 28.8%; urban—12%, 6.1%, 8.8%, 13.1%. Multi-fold increase in depression among aging, rural Indians during first and second waves, with high depression among subjects ≥65 years and those with comorbidities during the first wave, is concerning. Urgent public health measures are needed to address this added mental health burden and thereby, prevent further potential adverse consequences.

The rural cohort is younger and less educated than the urban cohort. The chi-square test showed that the proportion of participants with hypertension, diabetes, and obesity was lower in the rural cohort, whereas physical inactivity was higher in comparison with the urban cohort; however, the proportion of high-risk CAIDE scores was higher in the rural cohort. Despite the rural cohort having a smaller proportion of participants with hypertension, diabetes, and obesity, the overall CAIDE score was higher—the main reason for this is low educational level.

Study subjects in rural India recruited into the Srinivaspura Aging, Neuro Senescence and Cognition (SANSCOG) study were administered the COGNITO battery of tests, which traverse cognitive domains of attention, memory, language, and visuospatial abilities. Percentile norms based on age and education stratification were derived for the above cohort.

Percentile norms are commensurate with literacy levels in this population. The percentile scores for the cognitive tests show a decline for the individuals aged 75 years and above indicating lower cognitive functioning in this age group. This is the first-ever study reporting norms for diverse cognitive domains for illiterate, literate, low-literate individuals enrolled in a large-scale community-based cohort study in rural India.

CBR welcomes New Faculty member on board!

CBR has been delighted to welcome and induct Dr. Shweta Ramdas, Assistant Professor, who joined its faculty on 19 January 2023.

Dr Shweta Ramdas

Dr. Ramdas is an expert in human genetics and genomics, epigenetics, and bioinformatics. She completed her B.S. in Computational Biology at the National University of Singapore. Working in the research group of Prof. Jun Li at the University of Michigan, she earned her Ph.D. in Bioinformatics and an M.A. in Applied Statistics. Her Ph.D. thesis was on the genetics of complex traits with a focus on bipolar disorder and aerobic capacity. She pursued postdoctoral research (on regulatory genetic variation in human diseases) at the Department of Genetics, University of Pennsylvania. She had an Assistant Professorship stint at Azim Premji University prior to joining CBR. She has rich experience working with several multi-institutional genetics consortia to identify trait-associated genes and signals.

At CBR, Dr. Ramdas continues to be interested in human genetic variation and its biological function. Using sophisticated bioinformatic and statistical approaches, her lab will investigate how genetic variation is shaped by evolution and population history and will explore the functional role of this variation in regulating gene expression and human disease. She also seeks to ask and answer novel biological questions based on inferences from mining publicly available data. She has a flair for teaching courses in genomics, genetics, quantitative biology, and programming.

"I'm thrilled to have joined CBR and to be a part of this vibrant community. I'm looking forward to starting some projects on the role of genetic variation in neurodegeneration and aging, and to build connections (scientific and otherwise) with the folks at CBR to answer exciting questions", she says.

Besides research and teaching, she has devoted time to conducting resilience skills workshops for undergraduate students to help them deal with stress and adversity. She is passionate about science communication and outreach and is the co-creator of 'A Burst of Science', a series of science podcasts in Hindi and Kannada.

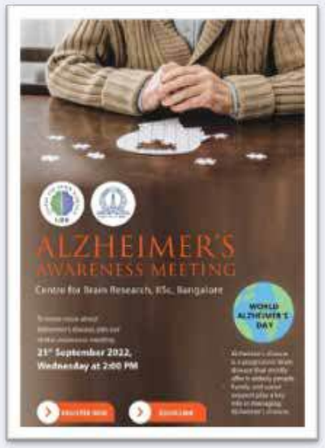
Recent publications

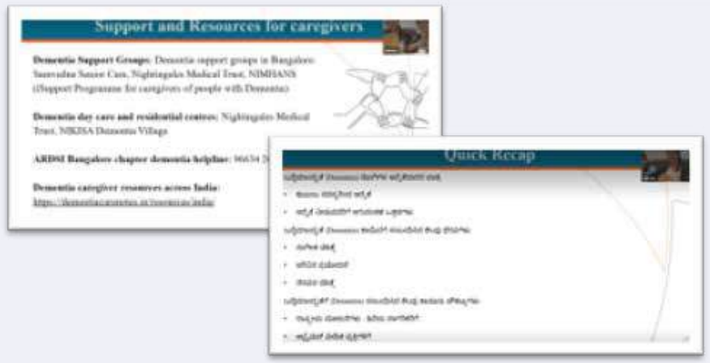
- Kanoni S*, Graham SE*, Wang Y*, Surakka I*, Ramdas S*, Zhu X* et al. (2022). Implicating genes, pleiotropy and sexual dimorphism at blood lipid loci through multi-ancestry meta-analysis. Genome Biology 23, 268 (2022).
- Ramdas S*, Judd J*, Graham SE*, Kanoni S*, Wang Y*, et al. (2022). A multi-layer functional genomic analysis to understand noncoding genetic variation in lipids. American Journal of Human Genetics 109(8):1366-1387.
- Vujkovic M*, Ramdas S*, et al. (2022) A multiancestry genome-wide association study of unexplained chronic ALT elevation as a proxy for nonalcoholic fatty liver disease with histological and radiological validation. Nature Genetics 54, 761–771 (2022).

For more information, please visit https://www.cbr.iisc.ac.in/people/shweta_ramdas/ and https://shwetaramdas.github.io/; follow Dr. Ramdas on Twitter @shramdas.

Events @ CBR

The past few months saw CBR bustling energetically with activity. Highlights of some of the most notable events are captured in this section.



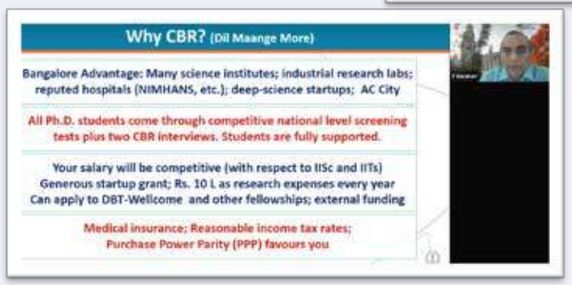


Alzheimer's Awareness Meeting, 21 September 2022

As a way of commemorating World Alzheimer's Day and furthering its mission to strengthen public engagement in health research, CBR organized an Alzheimer's Awareness Meeting on 21 September 2022. This online session benefitted over 200 attendees (including the families of current and potential participants of the Tata Longitudinal Study of Aging) from in and around Bangalore. The topics addressed at the 2.5 hour-meeting ranged from types of dementia to early signs, currently available therapies, caregiving and associated issues, and the indispensability of longitudinal studies of aging. To amplify the reach, the presentations were made in English and Kannada. Dr. Kris Gopalakrishnan, Chair, Governing Council, IISc, and Prof. Govindan Rangarajan, Director, IISc, graced the occasion with their kind participation, lucid thoughts on aging brain research in India and CBR's vantage point in this context, and warm words of felicitation.

Visit by NIAS delegation, 19 October 2022

The National Institute of Advanced Studies (NIAS), located on the IISc campus, organized a residential week-long training program (17 to 21 October 2022) for women scientists and technologists from many parts of India. This course, supported by the Department of Science and Technology (DST), Government of India, was under the banner of the continuing 'DISHA Programme for Women in Science' initiative. It was aimed at empowering mid-career women scientists by imparting motivation for their professional lives and enabling interdisciplinary training and networking. The course included invited lectures by experts, group discussions, presentations by the participants, technical visits, and cultural events. As part of the program, the participants spent the afternoon of 19 October 2022 at CBR, touring its facilities and interacting with its research staff. They also received an overview of CBR's vision, mission, and various initiatives. The delegation was excited to get a glimpse of the Centre's unique role in addressing health challenges affecting the country's elderly population.



Young Researchers Meetings, 29 and 31 October 2022

CBR is on the lookout for bright and enterprising faculty and postdoctoral candidates in its focus areas. As an attempt to attract talent, CBR organized online Young Researchers Meetings (YRMs) in late October. The meetings were attended by over 120 aspirants from across the globe. One of the two meetings catered specially to clinician-researchers. Dr. Kris Gopalakrishnan and Prof. Sudha Seshadri (Member, CBR International Scientific Advisory Board) added immense value to the YRMs by kindly providing an overview of CBR's vision and flagship research projects. The meetings included presentations (by the Director and faculty members) on CBR's major research activities and interactive Q&A sessions covering diverse aspects related to kickstarting a research career at CBR. The YRMs, particularly the interactive sessions, were quite well-received by young researchers motivated to know more about and partake in CBR's mission.

Visit by Professor Margaret Martonosi, 06 January 2023

CBR had the privilege of briefly hosting Prof. Margaret Martonosi, the US National Science Foundation's (NSF) Assistant Director for Computer and Information Science and Engineering (CISE). She is an internationally acclaimed expert in mobile computing and computer architecture in classical and quantum systems. During her CBR visit, kindly facilitated by Prof. R. Govindarajan of the Division of Electrical, Electronics, and Computer Sciences (EECS), IISc, Prof. Martonosi was accompanied by Dr. Cate Flanley, Science Analyst, NSF, and Mr. Vikram Joshi from the US Consulate. The team was introduced to the research-related and other goals of CBR and its endeavours in those directions. It acknowledged the pertinence of these efforts in the context of senior citizen well-being and was deeply appreciative of how CBR is envisioned to be an inspiration for philanthropic funding in biomedical research in India. Prof. Martonosi's visit, like that of NSF Director Prof. Panchanathan's visit and encouragement in August 2022, has served to propel CBR's resolve to tackle the neurodegenerative disease burden facing the country.

CBR Session in BCL Workshop, 10 January 2023

There couldn't have been a more exciting start to the new year: CBR had the privilege of actively contributing to Edition IV of the Brain, Computation, and Learning Workshop (BCL 2023) in early January 2023. Sponsored by IISc and a generous endowment from the Pratiksha Trust, this highly sought-after interdisciplinary event has been instrumental in facilitating cross-learning, productive brainstorming, and innovative collaborations among computer scientists, neurobiologists, and research students from across the country. The list of speakers and research topics covered at this year's workshop is available at https://bcl.iisc.ac.in/.

The half-day session on 10th January, orchestrated by CBR faculty members and research staff, touched upon a wide range of pertinent topics such as neurocognitive assessment, non-invasive brain stimulation, and the genetic architecture of human cognition. Prof. Thomas Gregor Issac, Associate Professor, gave an overview of CBR's mandate and flagship research projects. Dr. Jonas S Sundarakumar, Assistant Professor, laid out the definitions and explained the value of neuropsychological assessment, as a complementary tool to modalities like imaging, in aging brain research. Dr. Pooja Rai, Postdoctoral Fellow in Dr. Sundarakumar's group, elaborated on the design of neuropsychological assessments and the categories of commonly used assessment instruments. Ms. Rajitha Narayanasamy and Ms. Meghana R, Psychologists in the TLSA team, educated the audience about assessments pertaining to the cognitive domains of attention, executive function, visuospatial abilities, memory, language, and social cognition. This session included pre-recorded videos to demonstrate how such assessments are performed. Psychologist Ms. Meenakshi Menon discussed the considerations for evaluating, scoring, and interpreting neurocognitive tests. Medical Officers Dr. Ajith Partha and Dr. Amitha CM demonstrated the Hindi Mental State Examination (HMSE), a popular tool used for the assessment of cognitive impairment. This sub-session on clinical neurocognitive assessments was recapped by Scientific Officer Dr. Albert Stezin Sunny.

Dr. Chinnakkaruppan Adaikkan, Assistant Professor, began his session with an outline of the basics of neurodegenerative disorders; he shared data on how brain stimulations administered at gamma frequency improve episodic memory and impact neural oscillations and sleep. He also briefly conducted a practical tutorial on non-invasive brain stimulation. Prof. Bratati Kahali, Associate Professor, shared key insights based on her team's efforts to understand the shared genetic architecture and causal relationship between metabolic and neurodegenerative disorders. The faculty members then joined a dynamic panel that discussed opportunities, challenges, and various other aspects of research on the brain and computation.

Neuroimaging Workshop, 23 to 25 January 2023

To support training in the basic principles of neuroimaging, CBR successfully organized an introductory workshop on MRI and functional MRI (from 23 to 25 January 2023) for Ph.D. students and other young researchers. The coordination was led by Dr. Smitha Karunakaran, Assistant Professor, and Dr. Sadhana Singh, Research Scientist, in consultation with Visiting Faculty member Prof. S Senthil Kumaran (Department of NMR, All India Institute of Medical Sciences, New Delhi). The workshop was attended by CBR students and research staff and a few participants from IISc, NIMHANS, and St. John's Medical College. In order to facilitate close interactions among the mentors and trainees, only a limited number of participant slots was made available. The workshop was inaugurated by Visiting Faculty member Dr. Sanjaya Viswamitra (Department of Radiology, Sri Sathya Sai Institute of Higher Medical Sciences, Bangalore) who spoke about the history of MRI as a tool and its applications in clinical research. Over 3 days, there were theoretical lectures on a wide range of topics - basic principles of MRI, contrast mechanisms, safety guidelines of an MRI facility, MRI-based studies in animal models, structural and functional MRI data acquisition, analyses, and applications, to name a few. The workshop also included hands-on sessions, particularly on data analysis, at the J.N.Tata MRI Centre, IISc campus.

Besides the aforementioned experts, the list of speakers and tutors included Dr. Himanshu Joshi (NIMHANS), Mr. Victor Arul Raj (CBR), Dr. Priyanka Bhat (AIIMS, New Delhi), Dr. Albert Stezin Sunny (CBR), Dr. Jaladhar Neelavalli (Philips India Limited), Dr. Shweta Prasad (NIMHANS), Prof. Ganesan Venkatasubramanian (NIMHANS), and Dr. Manoj Kumar (NIMHANS).

Prof. Narahari, Director CBR, offered closing remarks and sought candid feedback from the trainers and trainees. Overall, the workshop was well-received. Most of the trainees found the workshop well-structured and the content relevant and comprehensive. Some of the trainees felt that the workshop could have been of longer duration with more dedicated time for practical learning. The encouraging, positive outcome of the workshop has motivated CBR to conceptualise similar training and capacity-building workshops periodically.

Mid-year Ph.D. Admissions

For the first time, CBR administered mid-year admission to its Ph.D. program, the announcement of which received an overwhelming response from life sciences students, undergraduate and postgraduate medical students, and computer science students. Following a rigorous selection process involving two rounds of interviews, the admitted students enthusiastically joined the Centre on 01 February 2023 thereby increasing the total Ph.D. student strength to 22. They attended a brief orientation session wherein the Director and Faculty members extended a warm welcome, explained the most salient features of the program, set the expectations, and wished them all the best for a great start. CBR looks forward to nurturing the vibrant research environment that is being augmented by its highly competent and ambitious student community.

Distinguished Visitors to CBR

CBR has had the pleasure of hosting several distinguished visitors and invitees who continue to be kind well-wishers and potential collaborators. Following is a non-exhaustive list of experts who visited CBR and interacted with the basic scientists and clinical research teams over the last few months.

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

Dr. Akshay Jagadeesh, Postdoctoral Fellow at Harvard University, gave a lecture on texture and object representations in human visual cortex and deep convolutional neural networks. He was accompanied by **Mr. B.V. Jagadeesh**, , a Silicon Valley-based serial entrepreneur who is the Founder and Managing Partner of KAAJ Ventures. (27 December 2022)

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

Dr. Sagar Kamarthi, is a Professor of Mechanical and Industrial Engineering and Director of Data Analytics Engineering Program at the Northeastern University, Boston. He is interested in research on machine learning models for personalized medicine and healthcare, among other areas. During his visit to IISc, he kindly spent time at CBR and gained an overview of its research and engagement initiatives. (30 December 2022)

Dr. Manoj Saranathani

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

Prof. Iracema Leroi and Prof. Mathew Varghese

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

Dr. Sourav Ghosh, Associate Professor of Neurology and Pharmacology at the Yale University School of Medicine, visited CBR and discussed potential collaborations. He also gave a talk on his group's animal-based studies aimed at deciphering the effect of the loss or gain of Axl (a member of the TAM subfamily of receptor tyrosine kinases) function on learning and memory deficits and long-term potentiation (LTP). The presented data had been garnered from sophisticated experiments such as behavioural testing in mice, electrophysiological assessment of LTP, and single nuclear RNA sequencing of brain cells. (27 January 2023)

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

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

Industrial Delegations

CBR was also pleased to host several industrial delegations appreciative of the Centre's research contributions and keen to identify and discuss promising avenues for innovative collaboration and cross-learning.

Infrastructure @ CBR

With generous core funding from the Pratiksha Trust and extramural support from agencies like Tata Trusts, SKAN Research Trust, Fidelity Foundation, DST, DBT, and India Alliance, CBR is home to world-class infrastructure for carrying out cutting-edge research on the aging brain and aging-related brain disorders. Through this section of CBR Currents, we aim to apprise our readers of the high-end equipment and research facilities available at the Centre.

The Information Technology (IT) unit at CBR manages the overall information and communications infrastructure to provide adequate support to the faculty, their research teams, and other staff members. The unit takes care of the heterogeneous network, data centre, cloud resources running in Microsoft Azure, application servers, software development, technical support to users, common computing facility, etc. Some of these services

Data Centre

The function of the data centre is to provide appropriate facilities for the critical and analytical application servers. The data centre is well-equipped with advanced technological features so all servers and network infrastructure can function efficiently without interruptions. The facilities in the data centre include Precision Air Conditioning (PAC) systems, uninterrupted power supply, backup power supply (DG set), CCTV, access control, and fire protection under Building Management System (BMS).

Network Connectivity

CBR is armed with 1-Gbps internet bandwidth from National Knowledge Network (NKN), the multi-gigabit nationwide network that serves as the National Education Research Network (NREN) of the country. This ensures a seamless browsing and download experience for the CBR staff, students, and faculty. A secondary internet service provider (ISP) with 100-Mbps bandwidth is available to pro-

vide immediate and adequate backup in case the NKN 1Gig link goes down. To provide secured connectivity (by means of protection from any attack/intrusion from outside the network), the Centre has deployed a high-availability Unified Threat Management (UTM) firewall which is effective in preventing unknown traffic.

High-Performance Computing Cluster (HPC)

The High-Performance Computing (HPC) system by Supermicro Sytems provides a powerful computing platform for the analysis of huge volumes of data obtained from human genome sequencing and magnetic resonance imaging (MRI) experiments. In this HPC cluster, there are two master nodes with 28 compute nodes each providing a total of 2088 cores and 11 TB of memory. It also consists of 2 NVIDIA GPU nodes with Tesla V100 SXM2 Nvidia Graphic Cards with 182 GB of memory per node.

Storage System

The 4 Petabytes SAN storage by Data Direct Networks (DDN) is an enterprise-class system that delivers a high-performance parallel file system, with GPFS (General Parallel File System, also known as IBM Spectrum Scale) for the HPC Cluster, and provides a central storage repository to CBR faculty and students for storing their lab/project data using Server Message Block (SMB)/ Network File System (NFS).

Backup System

The HPE StoreEver MSL6480 Tape Library serves as the backup storage system for the SAN Storage system. It performs daily incremental and full backups in line with the organisation's data protection policy and ensures data availability during any disaster/loss; the backup data is also moved to archival in order to meet long-term requirements.

CBR Currents - Wave 2

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