CBR Currents

Newsletter of the Centre for Brain Research, IISc

WAVE 5 FEBRUARY 2024

CBR-TLSA:
Towards Lessening Seniors' Affliction

cbr.iisc.ac.in

Unveiling New Horizons

As delighted as we are to bring to our readers the fifth Wave of *CBR Currents*, we are thrilled that **Professor K.V.S. Hari** has taken the helm as the Director of CBR, effective 01st January 2024.

Prof. Hari brings with him a wealth of experience in leadership in academia and industry, an unwavering dedication to excellence, and a deep commitment to advancing the frontiers of aging brain research. His illustrious career includes serving as a faculty member in the Department of Electrical Communication Engineering at IISc since 1992 and leading the department as Chair from 2015 to 2017. Prof. Hari's academic journey, spanning three decades, has extended across esteemed institutions such as Stanford University and KTH Royal Institute of Technology, where he held visiting faculty appointments. He has fostered impactful collaborations with reputed research groups worldwide. His primary research focus revolves around data science and the utilization of signal processing and wireless communication in addressing challenges within the domains of neuro science and medicine.

While we warmly welcome Prof. Hari to the CBR family, we also extend our heartfelt gratitude to Former Director **Prof. Y. Narahari** for his steadfast leadership and invaluable contributions since June 2022. Prof. Narahari's dedication and exemplary service have been instrumental in shaping the trajectory of the Centre, the foundation of which was meticulously laid by its visionary Founding Director **Prof. Vijayalakshmi Ravindranath**. As we embark on a new lap of this journey of discovery, innovation, and collaboration under Prof. Hari's stewardship, we look forward to building and thriving upon this foundation and making even greater strides in strengthening our understanding of brain aging. We remain immensely grateful to Pratiksha Trust and various other stakeholders for their relentless support in all our endeavours.

Prof. Narahari (right) passed the baton as CBR Director to Prof. Hari (left) in the gracious presence of Founding Director Prof. Vijayalakshmi Ravindranath, 01 January 2024

Besides honouring these exceptional leaders, the spotlight of this Wave of *CBR Currents* is on CBR-TLSA, one of our flagship projects involving a comprehensive longitudinal study of brain aging in an urban cohort. An overview of the study's goals and expected outcomes, snapshots of various assessments that form integral parts of the study are presented. We also touch upon some interesting observations and preliminary research findings that are emerging from the project's diverse strands. As always, we offer a walk-through of events that have kept CBR vibrant with activity and excitement. We kickstart 'Diverse Discourses', a section we believe will be an opportunity for CBR's young voices to interface with our readers. We hope you enjoy flipping through this edition and would greatly appreciate your feedback.

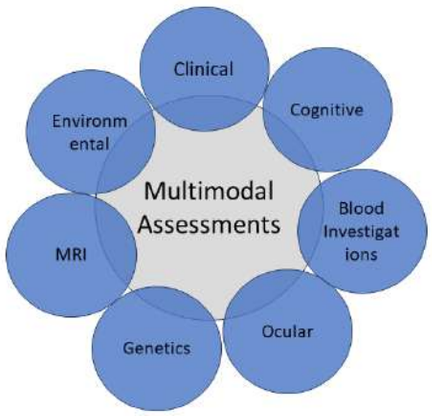
CBR-TLSA: A Flagship Project to Understand Aging and Dementia in Urban India

TATA TRUSTS

CBR-TLSA (Tata Longitudinal Study of Aging), initiated in 2015 with generous support from the Tata Trusts, is a unique long-term endeavour aimed at studying brain aging in a cohort in Bengaluru. The project's objective is to recruit and periodically monitor 1,000 cognitively healthy individuals aged 45 and above, with the goal of identifying risk factors and protective elements influencing dementia development and progression. Participants, drawn from the community, are subjected to multi-modal assessments to examine factors influencing cognitive changes associated with normal aging, Alzheimer's disease, and other brain disorders. Detailed assessments, including clinical, neurocognitive, biochemical, genetic, audiological, ophthalmological, and multi-modal neuroimaging measures, are conducted at baseline and during follow-up visits. Such an ambitious and elaborate exercise is possible only through the concerted effort of an interdisciplinary team of clinicians, psychologists, nurses, molecular neuroscientists, geneticists, biostatisticians, and others.

Given the scarcity of large-scale dementia research in India, the CBR-TLSA project aims to pave the way for further investigation in this area. Ultimately, the insights gained from this research will facilitate the design of optimal interventions aimed at delaying the onset or slowing down the progression of dementia. Implementation of these interventions at the community level through large-scale public health strategies holds the potential to minimize the global burden of dementia and maximize societal benefits.

CBR-TLSA runs synchronously in parallel with a rural counterpart. Funded by the Pratiksha Trust, CBR-SANSCOG (SrinivaspuraAging Neuro Senescence and Cognition) study is one of the largest, longitudinal studies in the world conducted on a rural aging population (projected n = 10,000 individuals).



Clinical Assessments

Initial observations indicate a higher prevalence of diabetes mellitus, hypertension, and obesity (BMI >30) in the urban cohort compared to the rural cohort. Conversely, depression appears to be more prevalent in the rural cohort.

Moreover, a comparison between urban and rural cohorts reveals a higher prevalence of cognitive impairment in rural populations, particularly affecting individuals aged 55 to 74. These initial findings are based on baseline data from both cohorts; ongoing recruitment and longitudinal data collection will allow for periodic review and analyses.

Cognitive Assessments

Cognitive assessments are crucial for understanding neurodegenerative conditions, offering valuable insights into changes in thinking and memory. As part of CBR-TLSA, an investigation examined participants' performance in the executive functioning cognitive domain (one of the initial domains affected by dementia) revealing notable differences between urban and rural participants. The study observed that urban participants exhibited superior performance compared to their rural counterparts. The diminished cognitive functioning among rural aging individuals could be attributed to occupations with lower cognitive demands and potentially lower cognitive reserve.

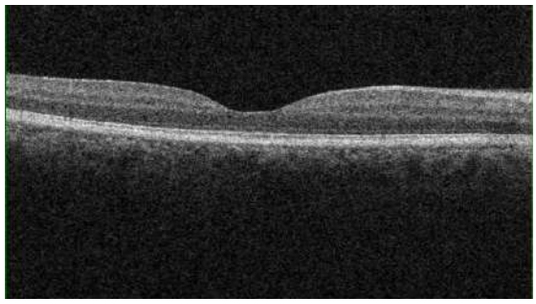
Another study by the CBR-TLSA team delved into how cognitive control is influenced by the number of languages known to individuals among the aging population in both urban and rural settings

in India. Cognitive control was measured using the Stroop test, visuospatial span, categorical, and letter fluency tests. Within the urban cohort, multilingual participants performed better than monolinguals in the categorical fluency task, whereas in the rural cohort, multilingual participants excelled across all tasks. Age and education influenced various visuo-cognitive components, while gender had specific impacts on visual attention and visuo-construction tasks. Additionally, education has emerged as a protective factor against Subjective Cognitive Decline (SCD), with a lower prevalence in urban cohorts compared to rural ones.

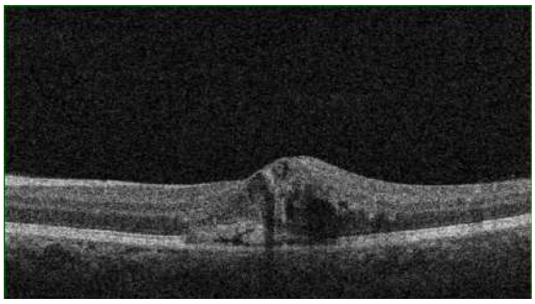
Special Assessments

The study participants are tested for visual acuity and refractive error (eye power) prior to assessments using Optical Coherence Tomography (OCT) and the fundus camera (to take photos of the retina). These basic assessments help explain the status of ocular health based on vision and the status of the retina.

OCT aids in the early detection of dementia by revealing retinal changes before cognitive symptoms manifest. It enables longitudinal monitoring of disease progression by correlating retinal thinning and vasculature changes with cognitive decline, particularly in Alzheimer's disease. Retinal changes detected by OCT serve as potential biomarkers, enhancing diagnostic accuracy, prognosis, and treatment monitoring. Insights from OCT research shed light on the pathophysiology of dementia, offering novel diagnostic avenues.



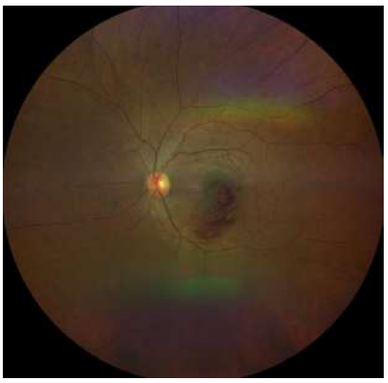
OCT scan showing normal retina



OCT scan showing (abnormal) diabetic macular edema

Fundus imaging (of the retina) is a valuable tool for assessing the retina's health, including its attachment status, the condition of blood vessels, the status of the optic disc, and media clarity (to explain the presence of cataracts, vitreous opacity, or any hemorrhages, etc.). More importantly, it detects conditions such as diabetic retinopathy and hypertensive retinopathy that are common in the elderly population. Observations in the CBR-TLSA cohort suggest that participants with mild cognitive impairment exhibit reduced retinal blood supply and blood flow compared to cognitively healthy participants.

Right eye – normal fundus



Left eye - fundus image showing retinal hemorrhage(blood leak)

Evaluation of Hearing

Hearing loss may not always imply complete inability to hear; other forms of hearing impairment include trouble finding the right words or signs to express oneself, difficulty processing what one has heard, especially in distracting environments, and challenges in interpreting speech in noisy surroundings. Even mild hearing issues can lead to poor communication, which may directly or indirectly impact cognition due to social isolation and/or depression.

In September 2023, CBR launched a cutting-edge audiological facility for comprehensive hearing evaluations. Whether or not you currently have hearing loss, regular hearing checks are necessary to monitor any changes in hearing ability and ensure appropriate treatment.
Our recent study has indicated that prevalence of hearing loss in CBR-TLSA participants was 41%. Further, it has been noted that individuals with hearing loss are 65% more likely to experience cognitive impairment compared to those without hearing loss. We believe that addressing hearing loss promptly will significantly improve communication, support better mental health, and ultimately improve quality of life.
"Blindness separates people from things; deafness separates people from people"
-Helen Keller.

Gait Analysis

There is a fascinating link between gait patterns and cognition in neurodegenerative diseases. Gait, defined as the way we walk, is a complex motor activity that involves coordinated effort between various brain regions. Even when cognitive tests are normal, gait abnormalities are detectable in very early stage of dementia. Moreover, changes in gait can also affect overall physical activity levels, limiting opportunities for social engagement and cognitive stimulation, which are also crucial for maintaining cognitive health. The recognition of the link between gait and balance and cognition presents an exciting opportunity for early detection and intervention in neurodegenerative diseases. Gait and balance analysis, combined with cognitive assessments, can potentially serve as a non-invasive and cost-effective tool for identifying individuals at risk of developing cognitive impairment.

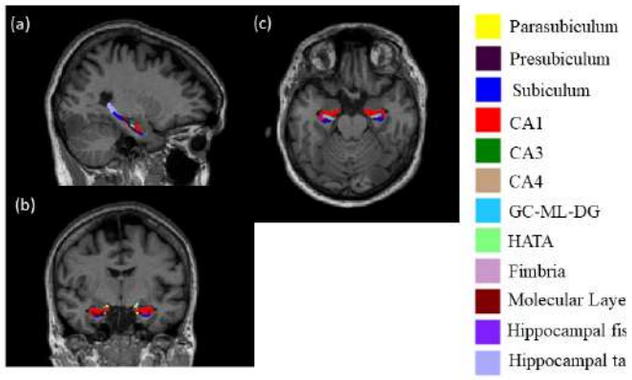
As part of CBR-TLSA, we have initiated gait and balance assessments to study the intriguing relationship between gait and cognition, exploring how changes in one can influence the other. Furthermore, we also assess postural stability/balance of individuals to identify individuals at high risk for recurrent falls. These evaluations are performed in the Cognitive-Motor Control Laboratory at CBR. For details, please see the section titled **'Infrastructure @ CBR'** in this edition.

Brain Imaging

Mild cognitive impairment (MCI) is a condition associated with an increased risk of developing dementia, particularly Alzheimer's disease (AD). Early and accurate identification of MCI is essential for timely intervention and effective

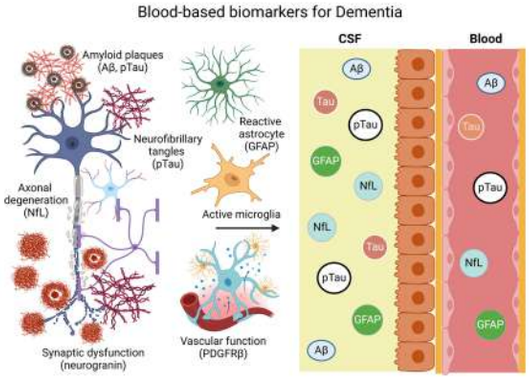
disease management. The hippocampus, a subcortical brain structure, crucial for memory formation and consolidation, is implicated in both MCI and AD. However, relying solely on overall hippocampal volume for differentiation between MCI and healthy individuals lacks precision.

The CBR-TLSA sought to explore alterations in the volumes of specific hippocampal subfields in MCI participants compared to healthy controls. The results revealed altered volumes in numerous left hippocampal subfields (parasubiculum, subiculum, presubiculum, CA1, CA3, CA4, GC-ML-DG, HATA, molecular layer, hippocampal tail) and a few right hippocampal subfields (subiculum, presubiculum, CA1, CA3, GC-ML-DG, molecular layer, hippocampal tail) among individuals with MCI. Moreover, a few subfields in the left hippocampus showed significant positive correlations with ACE memory scores in MCI participants.
The findings suggest that changes in hippocampal subfield volumes could hold potential for the early detection and monitoring of cognitive decline in MCI. Recognizing these nuanced alterations in hippocampal subfields could enhance diagnostic accuracy, paving the way for targeted interventions and a better understanding of the neurobiological underpinnings of cognitive impairment in MCI. This research contributes valuable insights to the ongoing efforts in neuroimaging and clinical management strategies for individuals at risk of cognitive decline.

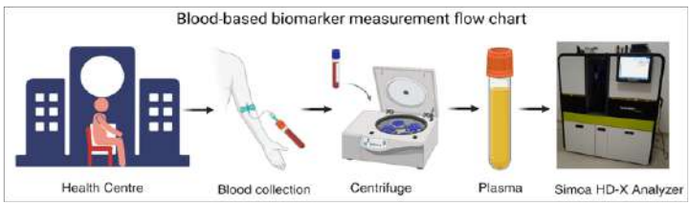


Blood-based Biomarkers of Dementia

The current notion is that the neuropathological pathways of dementia may manifest several years (approximately 20-30 years) before clinical symptoms appear, yet the underpinnings of these pathways in dementia remain to be investigated. Current challenges surrounding dementia revolve around timely diagnosis through blood-based biomarker assessment, treatment strategies, and disease management.



To elucidate blood-based biomarkers, we are currently conducting evaluations for all the study participants of CBR-TLSA. This involves measuring the levels of Aβ40, Aβ42, pTau-181, pTau-217, Tau, NfL, GFAP, and Aβ42/Aβ40 ratio in whole blood plasma using Single-MoleculeArray (Simoa) technology and HD-X analyzer (Quanterix, USA). This cutting-edge technology offers 1000x ultra-sensitive plasma biomarker detection, high specificity, full automation, high-throughput support, and the ability to multiplex up to 6 analytes in a single sample.

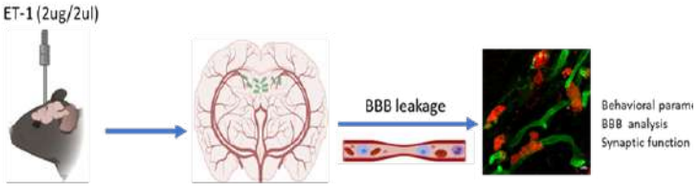


A comprehensive view of the blood-based biomarkers would enhance research and diagnostic capabilities. Moreover, this method can be implemented cost-effectively at primary healthcare centres and diagnostic facilities across India.

Studying Vascular Dementia in Mouse Models

Cerebrovascular lesions, seen as white matter hyperintensities on MRI scans of elderly population, are primarily caused by micro-infarcts and micro-bleeds, contributing to the development of vascular dementia (VD). These small vessel insults stem from prolonged presence of vascular risk factors such as hypertension, diabetes, hypercholesterolemia, and hyperhomocysteinemia. The compromised integrity of the blood-brain barrier (BBB) leads to increased vascular permeability and reduced cerebral blood flow, which have been linked to cognitive decline even in Alzheimer's disease (AD) patients. Even though evidence from numerous longitudinal studies (including our research at CBR) indicates the significant role of vascular risk factors, the underlying molecular drivers triggering neurodegeneration are not well investigated. Our current study aims to study pathological changes in BBB and their impact on synaptic function and neurons. Further, we are also interested in investigating whether presence of APP mutation contributes to structural changes in BBB, exacerbating AD pathogenesis. To induce small vessel insults, we utilized endothelin-1 (ET-1), a 21-amino acid vasoconstrictor peptide, administered bilaterally into the lateral ventricles of C57 mice brains. A single vascular insult resulted in a prominent transient deficit in associative and spatial memory, attributed to the loss of activity-dependent translation at synapses, suggesting potential molecular mechanisms (Diwakar L et al., *Scientific Reports*, 2021).

At present, we are performing recurrent vascular insults to establish a chronic vascular dementia model. Multiple doses of ET-1 are being administered through guide cannulas into the intracerebroventricular space. Following the dosing regimen, mice will be subjected to behavioral assessments and other analyses to evaluate the effects of chronic vascular insults on cognitive function and neuropathological changes.



Given that the transient model demonstrated reversal within 30 days of ET-1 administration, we anticipate identifying the factors associated with repair mechanisms. Hence, there is an opportunity to investigate both risk and protective factors of vascular dysfunction in aging.

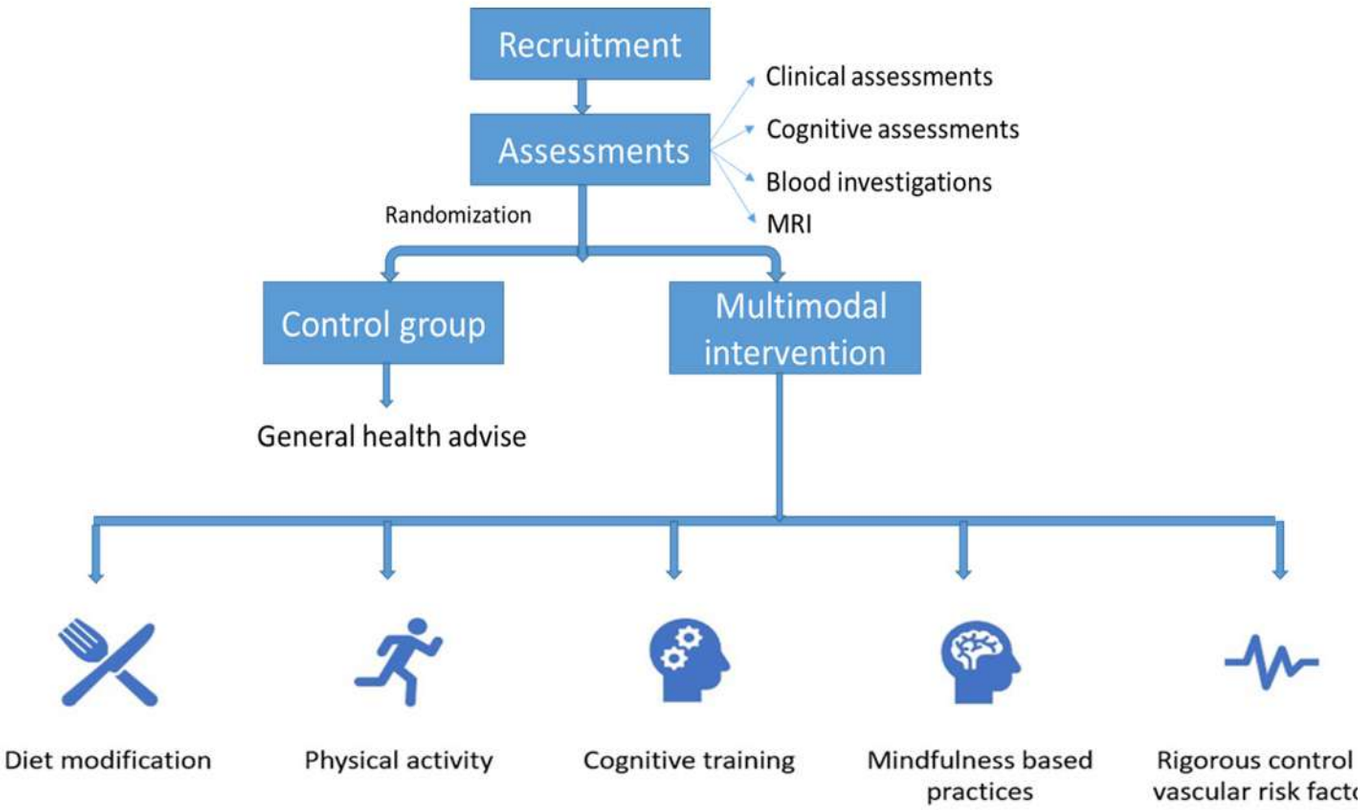
Intervention Study

As the aging population is set to increase, the burden of dementia is expected to rise proportionally, necessitating proactive management strategies. Drawing inspiration from the successful Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGERS), the CBR-TLSA has initiated a comprehensive intervention study aimed at preventing dementia, with a primary focus on lifestyle factors.

The study aims to develop a tailored

intervention for the aging Indian population, considering cultural, socio-economic, and geographical diversity. The study emphasizes the need for a culturally adapted, multimodal intervention to mitigate the risk factors associated with dementia. The primary objectives include assessing the effects of multimodal interventions on cognition, physical health, and psychological well-being, while also evaluating feasibility, cost-effectiveness, and adherence. The study's long-term goal is to establish a preventive protocol for reducing dementia risk among the elderly in India, with a specific focus on lifestyle modifications and vascular risk factor management.

The pilot phase entails a duration of one year and a sample size of 120 participants, comprising both healthy and MCI subjects. The meticulously planned intervention includes dietary modifications, physical activity, mindfulness practices, cognitive training, and vascular risk factor control. The success of the study could pave the way for a broader public health strategy to address the escalating dementia challenge



Diverse Discourses

Through this new section of *CBR Currents,* we hope to introduce our readers to the voices of CBR's doctoral students, postdoctoral fellows, and other young researchers. Watch this space for their explainers, ideas, and perspectives on a wide range of exciting research topics.

Predementia: Early Detection Makes Your Life Better

Ms Dwaiti Roy

According to the World Health Organization, 2.1 billion people will be of age 60 or older by 2050 and one-third of them will be living in lower- and middle-income countries like India. Moreover, an alarming rise in the cases of dementia in older people is estimated, from 55 million in 2019 to 139 million in 2050. Dementia brings about changes in memory and other cognitive functions, mood, and behaviours, leading to the inability to perform daily activities and an increased dependence on others.

Art by Mr G Rajesh

But can dementia only be diagnosed when the person cannot function independently? The answer is an emphatic "no". The course of dementia starts insidiously a few years or even decades earlier than when it starts to show symptoms. This phase before dementia symptoms occur is called PREDEMENTIA where the pathology has not fully invaded the brain. There are a few conditions that come under the spectrum of predementia: **Subjective Cognitive Impairment (SCI)**, Mild Cognitive Impairment (MCI) or Mild Behavioural Impairment (MBI). Subjective Cognitive Impairment (SCI) is the earliest stage of predementia where the person experiences decline in cognitive functions that are not diagnosable by traditional neuropsychological tests. **Mild Cognitive Impairment (MCI)** refers to the condition where the individual experiences changes in cognitive functions like memory or language that are diagnosable in neuropsychological tests but the daily independent activities are intact. On the other hand, Mild Behavioural Impairment (MBI) is the condition where the person develops psychiatric and behavioural symptoms rather than typical cognitive symptoms.

To date, research has not identified any drug that can prevent the development of dementia. Instead, we can focus on delaying its onset. In fact, if detected early, during the predementia stage, we can plan interventions to delay the disease's progression. This, in turn, can reduce the burden of dementia and improve quality of life.

Ms. Roy is a PhD student in the lab of Prof. Thomas Gregor Issac. She studies patterns related to gait and autonomic functions in the context of cognitive decline in older adults.

Navigating Parkinson's: A Journey of Understanding, Progress, and Hope

Ms Manasvi Chopra

Parkinson's Disease is the second most common brain-aging disorder, impacting millions on a global scale. At its essence, this disorder disrupts the intricate coordination of movements within the human body. Named after Dr. James Parkinson, who meticulously documented its characteristics in 1817, Parkinson's disease primarily results from the gradual deterioration of dopamine-producing nerve cells—a neurotransmitter critical for facilitating smooth and controlled motions. The symptoms of Parkinson's are diverse, ranging from tremors, often the initial noticeable sign, to stiffness, slowed movements, and impaired balance. These collectively transform daily activities into a choreography that demands conscious effort and adaptability.

Tracing the historical progression of Parkinson's unveils a scientific journey of retracing steps through time.
Dr. Parkinson's foundational work acted as a catalyst, bringing this complex condition into the limelight. Researchers have been like detectives, figuring out more about Parkinson's as time goes on.

In managing Parkinson's, therapeutic interventions play a pivotal role in restoring balance to life's journey. Medications, such as Levodopa, serve as frontliners by adjusting dopamine levels and mitigating erratic movements. Physical therapy, like following a set of organized lessons, empowers individuals to regain flexibility, enhance muscle control, and refine movements. Deep Brain Stimulation represents a sophisticated intervention; this procedure involves implanting electrodes into specific brain regions, emitting controlled electrical impulses to alleviate symptoms and enable a smoother execution of movements.
The ongoing research landscape against Parkinson's mirrors a continual exploration. Scientists explore gene therapies, cutting-edge medications, and holistic approaches, contributing distinct elements to the evolving understanding and management of this complex neurological condition.

In conclusion, although Parkinson's Disease is a tough challenge, the teamwork of medical advancements, ongoing research, and the strong spirit of those affected give us hope. We aim to understand this neurological puzzle better and help people live their lives freely despite Parkinson's. As we make progress, celebrating achievements and looking ahead to a future with better results is crucial in our fight against Parkinson's disease.

Ms. Chopra is a PhD student in Dr. Latha Diwakar's lab. For her thesis, she works on neurotransmitters and other molecules that play prominent roles in the trajectory of Parkinson's disease progression.

Events @ CBR

As always, CBR has been bustling with activity and contagious excitement over the past few months. This section presents highlights of some of the most notable events since the last Wave of *CBR Currents*.

Promoting Alzheimer's Awareness

To commemorate World Alzheimer's Month, CBR organised an Awareness Meet on 27 September 2023. This session, attended by over 100 enthusiastic participants, included a brief Yoga session and an interaction with CBR-TLSA volunteers wherein updates on the longitudinal study were presented and feedback was sought. Col (Dr) MP Cariappa, Technical Advisor – Tata Education Trusts, gave insights on healthy aging, and Ms. Daphne Vallado, Program Officer – Tata Education Trusts, offered words of felicitation. The event was further marked by the release of the first edition of the CBR-TLSA monthly newsletter and the inauguration (by Dr. Uma Nambiar, Advisor and Consultant – Bagchi-Parthasarathy Hospital, IISc campus) of an audiology facility that will enable detailed speech and audiological assessments as part of CBR's flagship cohort studies.

World Mental Health Day

On the occasion of World Mental Health Day (10 October), CBR facilitated a seminar on workplace wellness and sleep hygiene by Dr. Satish Ramaiah, an eminent psychiatrist and Medical Director at Maarga Mindcare Hospital, Bengaluru. It was followed by a well-received quiz (on neuroscience and brain health) put together by the CBR-TLSA team.

Launch of CBR-TLSA Intervention Trial

As part of Phase II of CBR-TLSA, a multimodal intervention trial for the prevention of dementia was conceptualized. This drew inspiration from the initial findings of CBR-TLSA Phase I and the initial revelations from the CBR-SANSCOG cohort as well as from the landmark Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER). The intervention will involve physical exercises, Yoga, cognitive retraining, dietary changes, control of cardiovascular risk factors, and positive mental health practices like mindfulness activities. Subsequent to planning, resource procurement, and approval, the trial was rolled out on 15 November 2023 when the CBR-TLSA team interacted with the study participants, handed over participation kits, and laid out guidelines related to their involvement in the study. Prof. Narahari felicitated the participants and thanked them for their enthusiastic contributions.

Felicitation for Prof. H. P. Khincha

On 23 November 2023, CBR organised a felicitation ceremony to honour Prof. H. P. Khincha and express gratitude for his phenomenal contributions as the Chair of the CBR Building Construction Committee (2017-22) and an esteemed Member of the CBR Governing Board (2016-23). Dr. Kris Gopalakrishnan joined the meeting virtually and thanked Prof. Khincha for his indomitable support in various capacities over the years.

Sharwaree Gokhale Memorial Lecture

Prof. George Davey Smith, Director of the Integrative Epidemiology Unit at the University of Bristol, delivered the 5th Sharwaree Gokhale Memorial Lecture on 5 December 2023 at the Faculty Hall, IISc. Prof. Smith pioneered the use of germline genetic variants for investigating modifiable causes of disease ('Mendelian randomization'), developed several extensions of the basic method, and contributed to its application in many settings.

Throughout his illustrious career spanning several decades, he has promoted increasing the accessibility of data and implemented this in studies he has led, including the Avon Longitudinal Study of Parents and their Children (ALSPAC). His lecture titled *'Triangulation of evidence in aetiological epidemiology: principles, prospects, limitations'* was well-received by the CBR fraternity and attendees from several other centres and departments of IISc.

Ms. Sharwaree Gokhale was the first woman Collector of Mumbai City and retired as Additional Chief Secretary (Environment) after 36 years of distinguished administrative service. In an admirable gesture of payback to society, she made a generous donation to CBR to promote neuroscience research. She passed away in January 2016; in her memory, CBR instituted a lecture series, of which Prof. Smith's was the fifth.

Expression of gratitude to Prof. Narahari

On 5 January 2024, CBR organised a thanksgiving event to celebrate the visionary and empathetic leadership of Prof. Narahari and to express gratitude for his inspiring contributions since June 2022. The Director, faculty, and staff members fondly recalled the warm support extended by Prof. Narahari and sought his continued guidance in CBR's endeavours. Prof. Narahari acknowledged the cooperation of all stakeholders of the CBR community and wished Prof. Hari astounding success in his long innings ahead as Director.

CBR Young Clinician Researchers Meeting

In order to attract bright clinician-researchers to potential faculty and postdoctoral research positions, CBR organised a Young Clinician

Researchers Meeting on 19 January 2024. This in-person meeting was attended by aspiring clinician-researchers and public health researchers from across the country, motivated to embark on a research journey at CBR. Prof. Hari and Prof. Narahari gave elaborate overviews of the initiatives and opportunities at CBR. Representative faculty members gave detailed presentations on the various research projects. Prof. Navakanta Bhat (Dean, Interdisciplinary Sciences Division, IISc) and Dr. Uma Nambiar offered a sneak peek into the IISc Medical School Foundation's vision for healthcare, training, research, and innovation and kindly interacted with the attendees. A guided tour of the facilities provided a firsthand look at CBR's infrastructure and research environment.

CBR representation at the India Science Fest

CBR was represented at the India Science Fest, a highly sought-after public engagement event organised by the Foundation for Advancing Science and Technology (FAST India) at the Indian Institute of Science Education and Research Pune (20-21 Jan 2024). In collaboration with the Tata Institute for Genetics and Society, India, the CBR team passionately curated an interactive booth and a hands-on workshop aimed at demystifying and spreading enthusiasm about genetics, genetic variations in humans, and the groundbreaking advancements in gene editing technologies.

Distinguished Visitors to CBR

CBR has had the opportunity to host many distinguished visitors and invitees over the past few months. Most of them are potential collaborators and had extensive interactions with the CBR faculty and staff; technical lectures were delivered by some of the guests.

The list includes:

- Prof. V John Mathews, College of Engineering, Oregon State University
- Prof. Shubha Tole, Department of Biological Sciences, Tata Institute of Fundamental Research, Mumbai
- A delegation from the University of Copenhagen led by Prof. Henrik Wegener (Rector) and Prof. David Dreyer Lassen (Prorector)
- Prof. Bhismadev Chakrabarti, School of Psychology and Clinical Language Sciences, University of Reading
- A delegation from the Washington University in St. Louis led by Prof. Vijay Ramani (Vice-provost for Graduate Programs and International Affairs) and Prof. Shantanu Chakrabartty (Vice-Dean for Research and Graduate Studies)
- Prof. Yogesh Shouche and team, SKAN Research Trust, Bengaluru
- Prof. Maneesh Sahani, Gatsby Computational Neuroscience Unit, University College London and Smt. Sudha Murty Chair Professor, IISc
- A delegation from Sri Sri Institute for Advanced Research, Bengaluru, led by its Executive Director Dr. Divya Kanchibhotla
- Prof. Sunil Sharma, Translational Genomics Research Institute (TGen) and City of Hope Comprehensive Cancer Center
- A delegation led by Prof. Geraint Rees, Vice Provost - Research, Innovation & Global Engagement, University College London
- Prof. George Davey Smith, University of Bristol
- Prof. Caroline Relton, London School of Hygiene and Tropical Medicine
- Prof. Sanjay Kinra, London School of Hygiene and Tropical Medicine
- Mr. Ajaneesh Kumar, Ambassador of India to the Republic of Estonia
- Prof. Arogyaswami Paulraj, Professor Emeritus, Department of Electrical Engineering, Stanford University
- A delegation led by Prof. Ushiki Tatsuo, President, Niigata University
- A delegation led by Prof. Darshan Shankar, Vice-Chancellor, The University of Trans-Disciplinary Health Sciences and Technology, Bengaluru
- Prof. Nigam Shah, Professor of Medicine and Associate Dean for Research, Stanford School of Medicine
- Prof. Pitchaiah Mandava, Head of Neurology, Baylor College of Medicine
- Mr. T. V. G. Krishnamurthy, Trustee, Ola Foundation
- A delegation of scientists from the Jawaharlal Nehru Centre for Advanced Scientific Research, Bengaluru, led by Prof. Ravi Manjithaya, Chair of the Neuroscience Unit
- A delegation of scientists from the University of Trans-Disciplinary Health Sciences and Technology (TDU), Bengaluru, led by Vice-Chancellor Prof. Darshan Shankar
- Ms. Heather Rice, Director of Research, Rotherham Doncaster & South Humber NHS Foundation Trust, UK
- Prof. George Brody, President and Director, IISc Foundation
- Prof. B. S. Manjunath, Distinguished Professor and Chair, Electrical & Computer Engineering, University of California Santa Barbara.

Infrastructure @ CBR

Generous core funding from the Pratiksha Trust and support from other agencies like the Tata Trusts, DBT, DST, SKAN Research Trust, DBT/Wellcome Trust India Alliance, and Fidelity Foundation have helped assemble CBR's sophisticated infrastructure for advanced research on the aging brain and aging-related brain disorders. Through this recurring section of *CBR Currents*, we intend to inform our readers about the facilities housed by the Centre.

Cognitive and Motor Control Laboratory

As the global population ages, understanding the intricacies of age-related changes in mobility becomes increasingly imperative for preserving quality of life. Gait and postural stability analyses, particularly in the context of aging brain, offer valuable insights into health, functional ability, and rehabilitative interventions across diverse disciplines including neurology, geriatrics, sports science, and biomechanics.

The Cognitive and Motor Control Lab at CBR has state-of-the-art infrastructure for studying the spatiotemporal and kinematic features of gait and postural stability. The lab is equipped with a GAITRite Platinum Instrumented Walkway for gait analysis, MatScan Evolution platform for postural analysis, Movella DOT sensors, and Camera-based systems for biomechanical analysis. The lab provides invaluable resources for researchers delving into the complexities of gait and postural stability patterns among the elderly and in neurological disorders such as Alzheimer's, Parkinson's, and higher-order gait disorders.

State-of-the art facilities

The **MatScanEvolution** is an innovative pressure mapping system designed to analyse and assess foot pressure distribution during various activities. It employs an array of pressure sensors embedded in a flexible and thin mat. This mat is highly versatile and captures real-time pressure data as individuals engage in activities such as walking, sitting, or standing. The system enables the visualization of pressure distribution, identifying areas of high or low pressure that may indicate irregularities in biomechanics or potential musculoskeletal issues. It has various applications such as postural analysis, ergonomic assessments, and clinical evaluations. The system provides quantitative data, allowing for objective analysis and the development of targeted interventions and personalized treatments.

The **GAITRite Platinum system** is a sophisticated tool for gait analysis, offering unparalleled insights into the intricacies of walking patterns. Developed by CIR Systems Inc., the GAITRite system utilizes an electronic walkway embedded with thousands of sensors to capture and analyse spatial and temporal parameters of an individual's gait. By detecting the force exerted by a foot during the stance and swing phases of gait, the instrument captures subtle details of foot pressure distribution and spatio-temporal parameters for real-time monitoring of gait and generates comprehensive reports. For in-depth analysis, experimental protocols and data collection can be configured and customized. Since the assessments require no patient instrumentation, this markerless gait device can capture multiple walk cycles, gait geometry, and the relative arrangement of each footfall as a function of time and space in a few minutes.

The **Movella DOT** sensorsare wearable Inertial Measurement Units (IMU) that contain accelerometers, gyroscopes, and magnetometers, allowing for the measurement of accelerations, angular velocities, and magnetic field strength, respectively. When strategically placed on specific body segments, IMUs provide real-time kinematic data, enabling researchers to analyze joint angles, posture, and movement patterns during gait. The Cognitive and Motor Control Lab also utilizes high-speed cameras to capture video of individuals while performing gait and posture experiments allowing analysis of dynamic changes. By applying computer vision algorithms to track dynamic changes in joint positions and body segments, 2-D and 3-D biomechanical analysis is performed for clinical and research applications such as assessment of body sway, bradykinesia/ slowness, tremor, ataxia, and freezing of gait.

Integrating the Movella DOT sensors and Camera systems with the GAITRite Platinum System and MatScan Evolution platforms enhances the lab's capabilities, offering a holistic approach to gait and posture analysis. By combining traditional methods

with modern approaches, natural and unrestricted movements can be studied with high fidelity.

Applications in Aging Brain Research

Aging and neurological disorders
Understanding the gait patterns of aging individuals and those with neurological disorders, such as Alzheimer's disease and Parkinson's disease, is paramount in early detection and comprehensive care. Integrating GAITRite Platinum System with IMUs and high-speed camera system offers an advanced approach to dissecting the subtle alterations associated with cognitive decline. With Alzheimer's disease, gait abnormalities often precede observable cognitive symptoms, making gait analysis a potential early diagnostic tool. Gait analysis is also performed to study freezing of gait and incident dementia/cognitive impairment in cognitive phenotypes of Parkinson's disease. This comprehensive analysis aids in tailoring interventions and therapeutic strategies for improved patient outcomes.

Fall Risk Assessment
Loss of postural stability/falls are a significant concern for the aging population, often leading to severe consequences. A major objective of the lab is to identify the higher risk of falls by studying the response to cognitive and motor perturbations. Integrating information from the MatScan platform, GAITRite system, and IMUs allows for a comprehensive understanding of the factors contributing to falls in aging individuals. The data gathered will be used to develop predictive models for fall risk assessment and designing targeted interventions and preventive measures to reduce the incidence of falls, thus enhancing the overall safety and well-being of the elderly population.

Cognitive-Motor Integration
The Cognitive and Motor Control Laboratory also directs its research efforts towards exploring the complex relationship between cognitive function and motor performance in the aging brain.The lab evaluates the impact and influence of cognitive tasks on gait and postural stability. This is performed using dual-task paradigms, providing insights into the cognitive-motor integration challenges faced by aging individuals.

Future Directions and Advancements

Virtual Reality Integration
By combining biomechanical analysis with virtual reality environments, ecologically valid scenarios can be created to study gait in real-world situations. This would provide a more immersive understanding of age-related changes in mobility to help design interventions that translate effectively to daily life.

Machine Learning for Predictive Modeling
Machine learning algorithms have the capacity to analyse vast datasets, identifying nuanced patterns that forecast forthcoming alterations in gait and posture among aging individuals. This predictive capability not only aids in early diagnosis of neurodegenerative conditions but also enables the development of intervention strategies aimed at modifying the course of neurodegeneration.

The Cognitive and Motor Control Laboratory serves as a robust platform for driving cutting-edge research on brain aging. The research pursued by the lab is rooted in a deep understanding of the intricacies of aging and neurodegeneration. Furthermore, it has the potential for significant translational impact in terms of facilitating the development of targeted interventions to improve the quality of life for the elderly population.

United by Mission: Where Diversity Drives Discovery

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