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RESEARCH ARTICLE

Early prevention of cognitive impairment in the community population: The Beijing Aging Brain Rejuvenation Initiative

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Abstract

Facing considerable challenges associated with aging and dementia, China urgently needs an evidence-based health-care system for prevention and management of dementia. The Beijing Aging Brain Rejuvenation Initiative (BABRI) is a community-based cohort study initiated in 2008 that focuses on asymptomatic stages of dementia, aims to develop community-based prevention strategies for cognitive impairment, and provides a platform for scientific research and clinical trials. Thus far, BABRI has recruited 10,255 participants (aged 50 and over, 60.3% female), 2021 of whom have been followed up at least once at a 2- or 3-year interval. This article presents aims and study design of BABRI; summarizes preliminary behavioral and neuroimaging findings on mild cognitive impairment (MCI) and results of clinical trials on MCI; and

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discusses issues concerning early prevention in community, MCI diagnosis methods, and applications of database of aging and dementia. BABRI is proposed to build a systematic framework on brain health in old age.

KEYWORDS
Alzheimer's disease, brain aging, Chinese elderly, cognitive aging, cognitive impairment, cognitive training, cohort study, community-based, dementia, early prevention, longitudinal study

1 | BACKGROUND

China is rapidly becoming an aging society. By the end of 2018, 249.5 million (17.8%) of China's population of 1.4 billion were aged 60 years or older,[1] and the percentage is projected to be 33.3% by 2050. Of course, the march toward an aging society is not even across the nation. Beijing, as the nation's capital, is ahead of the national trend, with 25.4% of its population aged 60 or above in 2018.[2] As a consequence of its aging population, China has witnessed significant increases in dementia in recent decades, and age-standardized dementia prevalence has increased by 5.6% in China from 1990 to 2016, while global prevalence increased by 1.7% during the same period.[3] Dementia is now the eighth leading cause of death in China,[4] and it poses considerable challenges to the patients, their families, and more broadly the country's social and economic development. Therefore, there is an urgent need for the early prevention and effective management of the disease.

The key to early prevention is to identify precursors of dementia. Recent research has shown that the disease pathology underlying Alzheimer's disease (AD), the most common form of dementia, can be detected as early as 20 years prior to the onset of noticeable clinical symptoms.[5] Abnormal amyloid biomarkers and biomarkers of neurodegeneration (e.g., tau pathology, hippocampal atrophy) have been found in patients with mild cognitive impairment (MCI) and even cognitively normal middle-aged individuals with higher risk of dementia.[5] However, because of poor awareness and inadequate knowledge of the disease, early detection of dementia and cognitive impairment has been greatly hindered. According to one meta-analysis, the pooled rate of undetected dementia worldwide was 61.7%, and the number was even higher in lower income countries (93.2% in Asia vs. 62.9% in North America and 53.7% in Europe),[6] leaving a great number of patients undetected in communities and without timely intervention. This fact has also been highlighted with evidence that outpatients are at more advanced stages of the disease than patients from communities, as remarkably elevated risk of conversion from normal cognition to MCI[7] and progression from MCI to dementia[8] have been revealed in clinic-based cohorts compared to community-based cohorts. Because accumulating evidence has shown the potential to delay or prevent dementia via interventions on modifiable risk factors,[9] more work is needed to advance the research on health disparities that are related to dementia, specifically, to promote early detection of the disease in communities and to obtain more details on what (cognitive training or medical treatment), how (clinical-based or community-dwelling), and when (at early stages with symptoms or without symptoms) the early prevention would take effect.

These problems are of greater urgency and importance in China. Compared to other countries, in which national plans on dementia have been published (e.g., United States, England, and Australia) and cohort studies (e.g., the Alzheimer's Disease Neuroimaging Initiative [ADNI][10]) or intervention clinical trials (e.g., the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability [FINGER][11]) have been ongoing for decades, there is a huge gap in the amount of research concerning aging and dementia in China. Moreover, as there are great differences between China's population and the populations of other countries, such as physical conditions, living habits, and cognitive patterns, among other modifiable risk factors of dementia,[9] along with the substantial differences of dementia diagnosis and treatment in urban and rural regions,[12] a database on the Chinese population is also necessary for the development of regional-specific prevention strategies on dementia for Chinese elderly individuals. With national plans on aging and dementia being under consideration and scheduled to be introduced in the forthcoming years, the following specific issues need to be considered: (1) largest number of dementia patients with high undetected rate, poor awareness, and inadequate knowledge of dementia; (2) lack of long-term follow-up data on aging and dementia; (3) sex differences, with a higher ratio of women in the elderly population and greater risk of dementia in female individuals; (4) regional and urban–rural disparities of aging and disease management due to different economic development levels; and (5) lack of community-based early prevention and intervention strategies for dementia.

When considering these nation-specific issues, community-based large-scale longitudinal studies on the Chinese aging population are crucial for the development of effective prevention and management of dementia, as well as for the development of region-specific evidence-based health-care systems. To address these issues, a community-based preventative project called the Beijing Aging Brain Rejuvenation Initiative (BABRI) was initiated in 2008. To the best of our knowledge, BABRI is the first community-based cohort study on the prevention of dementia in China, and the project is designed to serve as the foundation for the early detection and prevention of dementia in communities and to help facilitate the development of the Chinese National Plan on aging and dementia.

2 | BEIJING AGING BRAIN REJUVENATION INITIATIVE

Established at Beijing Normal University in 2008, BABRI has conducted cohort studies based on the registry of a large community population in the greater metropolitan area of Beijing. With an ultimate goal of 10,000 participants in the cohorts by 2028, BABRI collects comprehensive information on aging, tracks changes in cognitive function and brain structure and function over years, and designs preventative clinical trials targeting both elderly individuals with normal cognition and patients with cognitive impairment.

This community-based longitudinal project is generally proposed to build a multidimensional database, and by integrating basic disease research with clinical trials, to fulfill the following four specific goals: (1) to identify markers of different stages of cognitive impairment and dementia/AD, (2) to understand basic principles of cognitive aging and their underlying brain mechanisms, (3) to formulate and validate the tools and norms for cognitive screening of Chinese elderly individuals in community settings, and (4) to develop prevention strategies and potential alternative interventions on cognitive impairment and dementia at early stages.

2.1 | Study design

By cooperating with local hospitals, health authorities, and community service centers, participants included in BABRI have been primarily recruited from communities in Beijing since 2008 and from communities in other regions of China (e.g., Shanghai, Guangdong, Inner Mongolia, Qinghai, and Hubei provinces) since 2017, when BABRI was expanded into a multisite project known as the BABRI-National Consortium (BABRI-NC) project.

For Beijing, as displayed in Figure S1 in supporting information, there were significant differences in the level of population aging across its 16 districts, thus the recruitment of participants was mainly conducted in the 8 central districts (which were officially reorganized into 6 districts in July 2010), which ranked in the top 3 in the number or percentage of residents aged 60 and over. By applying a multistage cluster sampling design,[13] in the first stage, according to the city planning in Beijing Urban Master Plan (2004–2020), the 6 districts were divided into two categories: the Capital Core Functional Area and the Urban Functional Extension Area (see Table S1 in supporting information). After selecting either of the two categories, in the second stage, one district was chosen and four communities in the district were randomly chosen with the probability of selection proportionate to size. In the third stage, a sample of elderly residents was selected by using a simple random sampling method, and if the selected person was unavailable to be interviewed (either by telephone or face-to-face), or if they refused to participate, it was recorded as a non-response. It should be mentioned that after the selection of communities, a series of public lectures and formal/informal talks on brain health, dementia, and prevention strategies for brain disease were organized for all of the residents for 1 to 2 months, to facilitate both personal interviews and intervention programs.

RESEARCH CONTEXT

1. **Systematic review**: A literature search was conducted via PubMed using the terms "cognitive aging," "community," "cohort study," "China," and "Alzheimer's disease." There are few community-based cohort studies focusing on cognitive impairment and its early prevention conducted in China.
2. **Interpretation**: It is of great urgency and importance to advance a research framework in the field of aging and dementia among China's rapidly aging population, and to develop community-based prevention strategies for the management and control of dementia. We initiated a community-based cohort study (Beijing Aging Brain Rejuvenation Initiative [BABRI]) to facilitate the abovementioned issues, and now presented the study design and progress during the last 12 years.
3. **Future directions**: BABRI is proposed to provide a population-based model of the asymptomatic phase of the disease, and to facilitate the development of multilevel preventative strategies on cognitive impairment and dementia by establishing trial-ready cohorts. With in-depth investigations on the discrepancies between normal aging and dementia development and a much more concrete understanding of the independent and interrelated age-related changes in cognition and the brain, BABRI is expected to build a systematic framework on brain health, concerning one systematic brain derived from the aging brain and the diseased brain, and to develop prevention strategies and early alternative interventions for cognitive impairment and dementia.

All of the participants who were registered in BABRI would be revisited every 2 or 3 years within the total duration of the 20 years of the project (see Figure 1). The participants who met the inclusion criteria were informed about the aims and general design of the project and underwent comprehensive examinations. Furthermore, the BABRI cohorts also served as subject pools for clinical intervention programs (which would be implemented by hospitals or medical institutions cooperating with the BABRI research group) that focused on alternative treatments and modifiable factors (e.g., traditional Chinese medicine [TCM], lifestyle interventions, and cognitive training).

2.2 | Participant inclusion and exclusion criteria

All of the participants who were registered in BABRI should be native Chinese speakers with normal or rectified vision, hearing, and speech

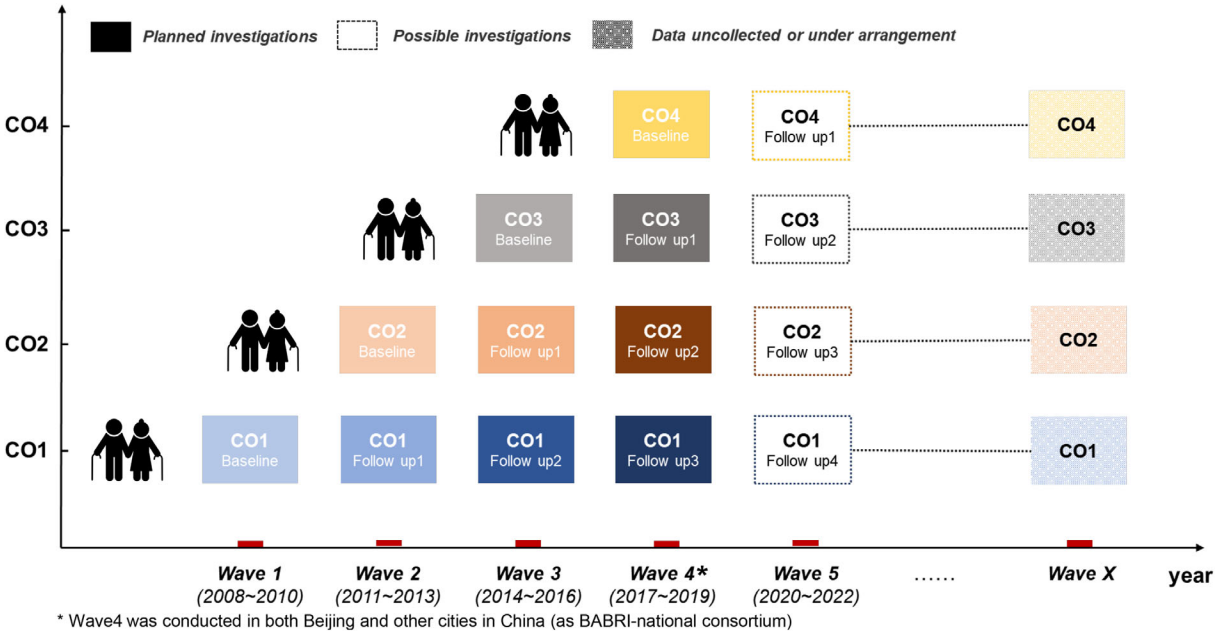

FIGURE 1 Study design of the Beijing Aging Brain Rejuvenation Initiative (BABRI)

functions. They should be aged 50 years or above at the time of baseline enrollment, and capable of living independently. Elderly residents were prescreened via brief telephone or face-to-face interviews concerning demographic and medical information, and they were screened out of the study according to one of the following conditions: (1) clinical diagnoses of neurodegenerative diseases (e.g., AD and Parkinson's disease), nervous system diseases (e.g., severe cerebrovascular diseases, brain tumors, and brain trauma), or psychiatric disorders (e.g., severe major depression disease, bipolar disorder, and schizophrenia) and (2) histories of substance or alcohol abuse/dependence. To be included in further analyses, participants should have 6 or more years of formal education, which is required for the cognitive assessments.

The BABRI project was approved by the Ethics Committee of the State Key Laboratory of Cognitive Neuroscience and Learning and the Institutional Review Board of the Imaging Center for Brain Research at Beijing Normal University, and the following intervention programs were approved by the ethics committees of the primary institutions for the implementation of the trials. Written informed consent was obtained from each participant at the time of baseline recruitment and a separate written informed consent was or would be obtained for subsequent enrollment in the clinical intervention programs.

2.3 | Measurements and data acquisition

All of the participants were interviewed and examined in detail at baseline and at each follow-up visit. Demographic information was first briefly collected via telephone or face-to-face interviews, followed by one-on-one assessments of health status, lifestyles, and cognitive function. Further acquisitions of blood samples, multimodal magnetic resonance imaging (MRI), and positron emission tomography (PET) brain scans were conducted within 3 to 6 months.

Generally, measurements included in BABRI can be grouped into the following eight categories (see Figure 2, Table 1): (1) demographic characteristics, including age, sex, years of formal education, and socioeconomic status; (2) medical records, including personal and family histories, as well as treatments of a series of diseases or disorders, such as hypertension, hyperlipidemia, diabetes mellitus, cerebrovascular diseases, and psychiatric disorders; (3) cognitive profiles, including general cognitive ability (derived from the Chinese version of the Mini-Mental State Examination [MMSE]), cognitive function across five domains (memory, executive function, attention, visuospatial ability, and language, measured via a battery of neuropsychological tests[14]), subjective cognitive decline (self-reported and/or by informants), and daily function (measured via activities of daily living [ADL] and instrumental ADL [IADL] questionnaires[15]); (4) lifestyles and habits, including leisure time activity (frequencies on a range of common activities among Chinese elderly individuals), dietary intake (assessed via Eating Habits Inventory[16]), and sleep quality (assessed via the Pittsburgh Sleep Quality Index[17]); (5) emotional status, including aloneness (evaluated via UCLA Loneliness Scale[18]) and depression (evaluated via Geriatric Depression Scale[19]); (6) biochemical markers, including blood lipids (low and high density lipoprotein, cholesterol and triglyceride measurements) and glucose metabolism (fasting blood-glucose, and glycated hemoglobin levels); (7) genotypes, including risk and protective genes related to dementia and aging (e.g., apolipoprotein E [*APOE*] and brain-derived neurotrophic factor [*BDNF*]); and (9) neuroimaging features, including structural indices (derived from T1-weighted, T2-weighted, and diffusion tensor MRI scans), functional indices (derived from resting-state and task functional MRI scans, and PET scans), and biomarker status (derived from PET scans).

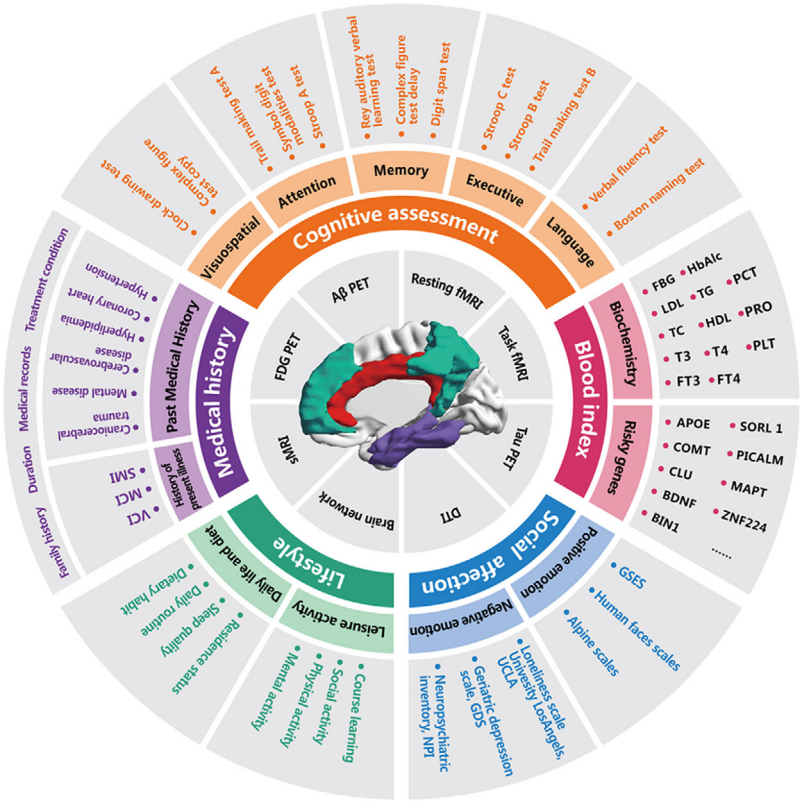

FIGURE 2 Categories and indices of the measurements of the Beijing Aging Brain Rejuvenation Initiative (BABRI) database. Figure adopted from Chen et al.[49]

TABLE 1 Categories and indices of the measurements of the BABRI database

Index categories	Evaluation methods	Indices/examinations
Demographic characteristics	Self-report and/or by informant	Age, sex, years of formal education, and socioeconomic status
Medical records (treatment, family history)	Self-report and/or by informant	Hypertension, hyperlipidemia, diabetes mellitus, coronary heart disease, atrial fibrillation, cerebrovascular diseases, and psychiatric disorders, etc.
Cognitive profiles		
Memory	One-to-one assessment	Rey Auditory Verbal Learning Test, Complex Figure Test, Digit Span Test
Attention		Clock Drawing Test, Complex Figure Test
Language		Stroop Test, Trail-Making Test
Visuospatial ability		Symbol Digit Modalities Test, Trail-Making Test
Executive function		Verbal Fluency Test, Boston Naming Test
Daily Function		Activities of Daily Living, Instrumental Activities of Daily Living
Lifestyle and habits	Self-report and/or by informant	Dietary intake, sleep quality, leisure activity
Emotional status	One-on-one assessment	UCLA Loneliness Scale, Geriatric Depression Scale, etc.
Genotypes	Blood genotyping	*APOE*, *BDNF*, *COMT*, *PICALM*, *SORL1*, etc.
Biochemical markers	Fast blood examination	FBG, HbAlc, HDL, LDL, TG, TC
Neuroimaging features	MRI scans	T1-weighted MRI, T2-weighted MRI, diffusion MRI
		resting-state functional MRI, task functional MRI
	PET scans	Amyloid beta PET, fluorodeoxyglucose PET, etc.

Abbreviations: *APOE*, apolipoprotein E; BABRI, Beijing Aging Brain Rejuvenation Initiative; *BDNF*, brain-derived neurotrophic factor; *COMT*, catechol-O-methyltransferase; FBG, fasting blood glucose; HbAlc, glycosylated hemoglobin HbAlc; HDL, high density lipoprotein; LDL, Low density lipoprotein; MRI, magnetic resonance imaging; PET, positron emission tomography; *PICALM*, phosphatidylinositol binding clathrin assembly protein; *SORL1*, sortilin related receptor 1; TC, total cholesterol; TG, triglyceride.

TABLE 2 Characteristics of the Beijing Aging Brain Rejuvenation Initiative (BABRI) cohorts

	BABRI entire cohorts	Beijing cohorts	National consortium cohorts
Participants, *N*	10,255	6976	3279
Wave 1 (2008 ~ 2010)	1211	1211	—
Wave 2 (2011 ~ 2013)	258	258	—
Wave 3 (2014 ~ 2016)	1755	1755	—
Wave 4 (2017 ~ 2019)	7031	3752	3279
Baseline age, mean (IQR), y	66.21 (61, 72)	66.57 (61, 72)	65.55 (60, 71)
[50, 60], %	25.13%	24.91%	25.59%
(60, 70], %	46.08%	45.24%	47.88%
(70, ~), %	28.79%	29.85%	26.53%
= < 65, %	49.78%	48.45%	52.61%
Formal education, mean (IQR), y	10.45 (9, 12)	11.01 (9, 13)	9.38 (6, 12)
> = 12, %	40.37%	46.38%	27.88%
Females, %	60.31%	64.85%	50.66%
MCI prevalence,[a] %	25.99%	20.88%	36.79%
APOE ε4 carrier,[b] %	–	16.90%	–
MCI ε4 carrier,[b] %	–	22.81%	–
Diabetes mellitus, %	21.23%	24.58%	14.09%
Hypertension, %	47.91%	52.48%	38.18%
Hyperlipidemia, %	32.76%	40.21%	16.93%

Abbreviations: *APOE*, apolipoprotein E; IQR, interquartile range; MCI, mild cognitive impairment.
[a]Diagnosis at baseline recruitment.
[b]Data were from participants enrolled in the Wave 1 cohorts.

The BABRI cohorts will also apply state-of-the-art measures whenever available, with additional approvals from the ethics committees and the institutional review boards.

2.4 | Diagnosis criteria

During the follow-ups, diagnoses of dementia/AD were performed via clinical review panel meetings according to the standard criteria (DSM-V[20] or NINCDS-ADRDA[21]). At baseline recruitment and the follow-ups, diagnoses of MCI and its subtypes were based on the Petersen's criteria:[8] (1) presence of subjective cognitive complaints (self-reported and/or by informants); (2) normal general cognition (a score higher than 23 on the MMSE); (3) intact daily function (a score of 0 in the ADL and the IADL); and (4) objective cognitive impairment (a score less than 1.5 standard deviations [SDs] below the age- and education-adjusted norms of the Chinese elderly population).

3 | CURRENT PROGRESS OF THE BABRI PROJECT

3.1 | Participant enrollment

The first-round recruitment (*N* = 1211) of the BABRI project lasted from September 2008 to December 2010, and the follow-ups of the initial cohort were conducted in 2011, 2014, and 2017. More participants (*N* = 258) were enrolled from the same communities at the first revisit of the project, and further extensions of the BABRI cohorts were initiated in 2014 and 2017 by including more communities in the urban districts of Beijing (*N* = 1755 and 3752, respectively). In addition, as the BABRI-NC project started in 2017, participants from other regions in China were recruited (*N* = 3279). Therefore, by July 2019, there were 10,255 subjects in the BABRI cohorts, and among participants in Beijing, 2021 participants (62.7% of the participants who were enrolled before 2016) had been followed up at least once, whereas 762 participants (51.9% of the participants who were recruited before 2013) had been revisited twice and more (see Tables 2 and 3).

3.2 | Cohort characteristics

The BABRI cohorts were evenly distributed across late adulthood and 49.8% of the participants were younger than 65 years. The ratio of female participants (60.3%) was relatively high in the cohorts, and the cohorts were relatively well educated, as 40.4% of the participants reported to have 12 or more years of formal education, compared to 23.8% of the general elderly population in China.[22] As expected, most of the participants in the cohorts were cognitively normal, and the overall prevalence of MCI was 26.0%, with a relatively low progression rate of normal cognition to MCI (11.9% at their follow-ups). In terms

TABLE 3 Profiles of the Beijing Aging Brain Rejuvenation Initiative (BABRI) cohorts with available longitudinal data

	Followed up once	Followed up twice and more
Participants, N	1259	762
Baseline age, mean (IQR), y	66.14 (60, 71)	64.78 (59, 70)
Formal education, mean (IQR), y	11.09 (9, 13)	10.60 (9, 13)
Females, %	63.46%	59.22%
Diabetes mellitus, %	25.50%	25.46%
Hypertension, %	47.18%	51.05%
Hyperlipidemia, %	38.76%	35.56%
MCI prevalence*, %	18.11%	17.32%
MCI incidence, %	11.93%	17.14%
Follow-up interval, mean (IQR), y	2.60 (2.24, 2.84)	6.52 (4.63, 8.04)

Abbreviations: IQR, interquartile range; MCI, mild cognitive impairment.
*Diagnosis at baseline recruitment.

of chronic diseases, the highest prevalence was found for hypertension (47.9%), and 21.2% and 32.8% of the participants reported a current history of diabetes mellitus and hyperlipidemia, respectively.

3.3 | Preliminary research on MCI

Based on cross-sectional data from the BABRI cohorts (participants who were mainly enrolled in Wave 1), various studies have been conducted. By characterizing the age-related trajectories of multiple cognitive domains, studies have identified potential modifiable lifestyle factors (e.g., leisure activity, eating habits, and diabetes) as being related to cognitive impairment.[14,23] Furthermore, neuroimaging analyses on MCI have also found that the reorganization of the default mode network may serve as markers of disease progression,[24–26] and the structural and functional integrity of the network serves an important role in mediating the relationships between risk genes (e.g., the *APOE* ε4 allele) and cognitive function.[27–29] Moreover, explorative analyses on vascular-related conditions that are closely related to cognitive impairment have also revealed distinct patterns of structural and functional dysfunction in diabetes mellitus[30–32] and hypertension.[33,34]

3.4 | Clinical trials on cognitive impairment

Two preventative clinical trials targeting MCI patients and cognitively normal elderly participants have been initiated, with one trial being initiated in late 2012 focusing on the therapeutic effects of TCM (registered number: ChiCTR-TRC-12003073) and the other trial being initiated in 2020 to explore the benefits of cognitive training (registered number: ChiCTR-1900028065). By combining neuropsychological tests with functional MRI indices, it has been found that TCM may target either brain regions or networks, modify their activation or connectivity, and finally maintain and improve cognitive function in MCI patients.[35,36]

4 | DISCUSSION

Interventions at early stages have been increasingly emphasized in the field of dementia in the past few years, partially due to disappointing results in clinical trials wherein none of the tested drugs were able to halt or slow down the disease progression in mild–moderate stages of AD.[37–39] According to annual updates on the state of AD drug development,[39] the enrollment of earlier populations has recently been one new feature, as nearly half of the ongoing phase 3 trials (20 out of 42 trials) enrolled patients with MCI/prodromal AD and cognitively normal individuals with signs of high risks (e.g., the existence of amyloid pathology). In addition to drugs, primary prevention strategies targeting modifiable risk factors, such as cardiovascular risk factors and lifestyle habits, have become a realistic and relevant therapeutic strategy for disease prevention.[38] Furthermore, the efforts in disease modification have also revealed the lack of knowledge of the potential benefits of risk factor reductions on disease incidence, and the urgent need to identify and characterize asymptomatic individuals. As has been previously mentioned, due to poor awareness and inadequate knowledge, the ratio of undetected dementia is more than 60% and even higher in less developed regions.[6] In other words, most individuals with cognitive impairment cannot receive effective guidance or treatments until the onset of clinical symptoms. Therefore, BABRI has been initiated in the settings of local communities rather than in memory clinics or hospitals, and it has been expected that through active and systematic brain health suggestions, participants with possible cognitive impairment or dementia in the BABRI cohorts can be identified as early as possible and can receive appropriate and timely interventions.

Examinations used in the diagnosis of cognitive impairment have been broadly discussed over decades. Since the publication of the National Institute on Aging-Alzheimer's Association (NIA-AA) workgroup recommendations,[40–42] biomarkers of amyloid beta (Aβ) accumulation, tau/phosphorylated tau deposition, and neurodegeneration (atrophy based on structural MRI scans or hypometabolism based on fluorodeoxyglucose PET scans) have been addressed in formulating the diagnosis criteria for clinical, symptomatic, and asymptomatic phases of dementia. However, as the use of the biomarkers is argued to be limited in clinical applications,[43,44] and for the purpose of monitoring the emergence of clinical symptoms and evaluating the effects of early prevention, more research is needed to identify new primary endpoints that incorporate physical and psychological measures with AD biomarkers.[42] This notion has been adopted in a range of observational cohort studies (e.g., ADNI) and intervention clinical trials (e.g., FINGER). However, as it typically takes hours (usually 1 to 3 hours) for elderly participants to finish the neuropsychological batteries or neurobehavioral tests, in addition to the probable mental and physical fatigue, the complex procedure of cognitive evaluations also seems to be less practical as part of routine examinations in the community

population. To this end, there have been attempts to optimize the evaluation procedures by selecting easy-to-use but sensitive tests,[45,46] and to formulate scores such as the Preclinical Alzheimer Cognitive Composite (PACC) scores[47] and the Alzheimer's Disease Composite Score (ADCOMS)[48] for cognitive assessments. Based on existing data from all of the cohorts, BABRI has also introduced an index, the BABRI-score, as an indicator of cognitive impairment via computerized examinations of memory, orientation ability, and subjective cognitive complaints. Currently, the index has been adopted by the Beijing Municipal Health Commission and has been applied in dementia screening for 200,000 elderly residents across 16 districts in Beijing over the last 2 years.

The abovementioned discussions distinguish BABRI from other cohort studies for cognitive aging and dementia. The study setting of communities, the longitudinal design, and the participants being as young as 50 years old, maximize the probability of providing a population-based model of disease development and proposing multilevel preventative strategies for cognitive impairment and dementia. Generally, BABRI was designed according to the well-known Framingham Heart Study (FHS), but it should be noted that BABRI also serves as a foundation for prevention trials, similar to the Global Alzheimer's Platform (GAP, https://globalalzplatform.org/), the European Prevention of Alzheimer's Dementia (EPAD, http://ep-ad.org/), and the Alzheimer's Prevention Registry (APR, https://endalznow.org/) derived from the Alzheimer's Prevention Initiative (API). Participants in those trial-ready cohorts could be easily enrolled at any time of the follow-ups once they meet the additional inclusion criteria, with comprehensive cognitive and neuroimaging data and complete profiles of lifestyle factors and health conditions. With this goal, BABRI has also arranged for prevention clinical trials targeting cognitively normal individuals and MCI patients over the last few years, and it has been expected that lessons can be learned to develop sensitive methods for detecting early cognitive declines and new strategies for dementia prevention.

BABRI is currently at its 12-year benchmark, which is more than half way through the 20-year blueprint of the initiative. As the study cohorts have already been larger than the goal of 10,000 participants, follow-ups in the next decade will be crucial to the early management and control of cognitive impairment and dementia. Combined with routine investigations on cross-sectional data, statistical analyses of longitudinal data via mixed-effects approaches could better clarify the discrepancies between normal aging and dementia development and provide a much more concrete understanding of the independent and interrelated age-related changes in cognition and the brain. In the long term, BABRI is expected to build a systematic framework on brain health, concerning one systematic brain derived from the aging brain and the diseased brain, and to develop prevention strategies and early alternative interventions for cognitive impairment and dementia.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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