India's Elderly

India's Elderly:

Issues and Perspectives

Edited by

Uma Charan Pati, Monalisa Mohapatra
and Subhankari Pati

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FOREWORD

ODISHA STATE HIGHER EDUCATION COUNCIL (OSHEC)
PUSTAK BHAWAN (2ND FLOOR), A-11, SUKA VIHAR,
BHUBANESWAR-751022

Asoka. K. Das,

Vice Chairman, Odisha State Higher Education Council (OSHEC)
Former Vice Chancellor, Utkal University, Distinguished Scientist, BARC and Senior Professor, Homi Bhabha National Institute

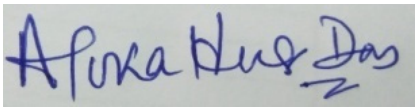
I am extremely delighted to pen a message for this book, *India's Elderly: Issues and Perspectives*, being prepared, published and released by the Odisha Center for Geriatric and Gerontology of GM University, Amruta Vihar, Sambalpur. This unique center at the historic GM University was conceptualized as a part of Project OHEPEE of the Department of Higher Education, Government of Odisha, which aims at establishing Research Centers of Excellence at major state public universities for carrying out cutting-edge research on societally relevant topics of contemporary nature.

The center's uniqueness lies in its thematic significance. As the new millennium progresses, the Indian elderly population is gradually becoming a truly sizable group (20% by 2050) with a growth rate that is likely to reach to 134% in the 60+ age group and 279% in the 80+ age group. However, the challenges being faced by the elderly are simultaneously becoming formidable, alongside the rapid urbanization as well as globalization across India, increase in life expectancy, and consequent erosion of the typical Indian value system of caring for elders of the family. Consequently, this significant elderly population has become highly vulnerable, being besieged by challenges of gender inequities, the rural–urban divide, economic and socio-cultural deprivation, access to health care in the face of chronic morbidities, functional deficiencies with respect to activities in daily life, psychological depression, sleep disorders, and lack of technology handling competencies, among other factors. There is a need to find solutions to this

growing sociocultural problem through a multidisciplinary platform where scientists, academicians, administrators, policy makers, social reformers and civic society can collaborate to develop pathways to provide the elderly with a life of dignity, good health and fulfilment. This is the task taken up by the center.

I must congratulate the researchers associated with "Odisha Center for Geriatrics and Gerontology" at the GM University for their attempt at effectively collating the results of their research – primary data from a survey carried out by them and analysis of timely articles on this very important topic. I hope, that their efforts result in helping our senior citizens to lead a better life.

Bande Utkal Janani



Asoka Kumar Das

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Bringing out an edited volume is a daunting task and it becomes more challenging when the subject of concern is a field of study that is still in an evolutionary stage. The Center of Excellence of Odisha Center for Geriatrics and Gerontology is a unique center in the state of Odisha and the Gangadhar Meher University is blessed to have it. We are thankful to the Department of Higher Education, the Government of Odisha and the Odisha State Higher Education Council (OSHEC) for allowing us to research the emerging challenges of an ever-growing old age population under the flagship program of OHEPEE. We are thankful to Prof. Ashoka Kumar Das, Vice Chairman, OSHEC for helping us at every stage of the publication of this volume.

The very idea of the Center of Excellence was conceptualized by our beloved former Vice Chancellor Prof. Atanu Kumar Pati, presently an Executive Member of the OSHEC, who deserves appreciation of the highest order. His contribution to this publication is also beyond comparison. Our honorable Vice Chancellor Prof. N. Nagaraju has been the backbone of the center and he is behind this book's taking shape too. We are grateful to him for his constant guidance and support. Smt. Jugaleswari Dash, former Registrar and Sri Jagannath Rout, Comptroller of Finance did come forward whenever required and their support can't be lost sight of.

The present form of this book is the result of the hard work and persistent efforts put in by the Coordinator of the CoE Dr. Monalisa Mohapatra. She played a major role right from the beginning of the whole process. All the Co-PIs along with the Coordinator deserve to be appreciated for everything they have done for this volume to see the light of day. We acknowledge the whole-hearted cooperation rendered by the members of the editorial team: Dr. Uma Charan Pati, Dr. Monalisa Moahapatra and Dr. Shubhankari Pati throughout the arduous journey.

We are grateful to all the authors and contributors without whose timely support this volume would not have come to fruition. Writing articles on multiple dimensions of the burning and emerging issues of geriatrics and gerontology is not that easy an affair and hence we have words of praise for all the contributors. We must not forget the contribution made by Cambridge Scholars Publishing in bringing this

volume to the public domain, which carries the prospects of opening new vistas for research on issues faced by our elderly.

Editorial Team:

Dr. Uma Charan Pati
Dr. Monalisa Mohapatra
Dr. Shubankari Pati

CHAPTER 1

AGING AND COGNITION

BABITA PANDE[1], ATANU KUMAR PATI[2,5] AND ARTI PARGANIHA[3,4,*]

[1]DEPARTMENT OF PHYSIOLOGY, ALL INDIA INSTITUTE OF MEDICAL SCIENCES, RAIPUR, 492099, INDIA

[2]ODISHA STATE HIGHER EDUCATION COUNCIL, GOVERNMENT OF ODISHA, BHUBANESHWAR - 751002, INDIA

[3]SCHOOL OF STUDIES IN LIFE SCIENCE, PT. RAVISHANKAR SHUKLA UNIVERSITY, RAIPUR - 492 010, INDIA

[4]CENTER FOR TRANSLATIONAL CHRONOBIOLOGY, PANDIT RAVISHANKAR SHUKLA UNIVERSITY, RAIPUR - 492010, INDIA

[5]KALINGA INSTITUTE OF SOCIAL SCIENCES, BHUBANESWAR - 751024, INDIA

Abstract

Cognition is an attribute related to mental processes, such as memory and attention, which are required for the successful execution of day-to-day activities. Cognitive impairment with advancing age has been linked with alterations in brain structure and neural networks in different cognitive domains. There is an array of methods to study this, including questionnaires, neuropsychological batteries, electrophysiological and brain imaging techniques, and genetic and biochemical markers for cognitive assessment. Deterioration of cognitive abilities with aging depends upon the type of cognitive abilities, viz., crystallized or fluid. Various factors like sleep and circadian rhythm, neuronal changes, genetic factors, physical and mental health issues, social determinants, gender, and lifestyle factors determine the extent of age-associated cognitive impairment. The age-related cognitive repercussions can be conserved or compensated through boosting neuronal activity, specifically increasing prefrontal activation. These goals can be achieved by managing sleep

health, aligning circadian sleep-wake rhythm, cognitive interventions, and cognitive training/cognitive rehabilitation. Lifestyle intervention concerning physical health, behaviour, social interventions, and management of relevant clinical comorbidities can augment cognitive abilities. Spreading awareness regarding cognitive decline and its management through policies and programs at the government level is essential.

Keywords: Cognition, aging, cognitive assessment, cognitive reserve, cognitive intervention

Introduction

The word "cognition" originates from the Latin word "*cognōscere*" (which means "to know, to learn about"). Cognition is one of the inherent attributes of almost all living organisms (Pande, 2013). Cognitionytxdsz YH/ is defined as the "mental actions or processes involved in acquiring, maintaining, and understanding knowledge through thought, experience, and the senses" or "the process by which knowledge and understanding are developed in the mind" (Dumper et al., 2019; https://opentext.wsu.edu/psych105/chapter/7-2-what-is-cognition/).

Aging is the process of alteration and transformation accompanied by deterioration from subtle molecules to gross morphology, anatomy to physiology, and brain to behaviour. Development in technology and medical amenities has increased longevity such that life expectancy will increase to 72 years by 2050 as per the World Health Organization (WHO, 2017; Dartora et al., 2021). With increasing life expectancy, age-related problems – specifically the cognitive aspects which are essential for successful survival in society – will become a menace for the individual as well as for society generally. Nonetheless, to ensure a better quality of life and healthy mental and physical status, there is a need to understand the impact of normal aging on cognition, and the ways to diagnose cognitive aging as well as the interventions or management of such cognitive impairment.

Normal aging, or mild cognitive impairment vs. dementia

The most common problem observed in the functioning of mental faculties in the course of aging is memory complaints. However, if such a condition worsens, it leads to mild cognitive impairment (MCI) that eventually increases the risk of dementia with characteristics of memory loss (Anstey & Low, 2004). Due to the increase in average life expectancy, the prevalence of MCI among community dwellers is on the rise and this phenomenon

could be attributed to increased life expectancy. It has been documented that the incidence of MCI is a little above 15% (Bai et al., 2022). The instances of cognitive disabilities in elders are higher in developing countries with a lack of treatment facilities where cognitive problems faced by elders are mostly ignored (Jadenur et al., 2022).

I. Theories of cognitive aging

We can discuss age-dependent changes in the cognitive abilities of elderly people with regard to two types of abilities: namely, crystallized and fluid abilities (Fig. 1-1; Table 1-1; Anstey & Low, 2004; Murman, 2015).

(1) Crystallized abilities: Crystallized abilities are the cognitive abilities that encompass the gathered information or knowledge during a lifetime. They are the outcome of cognitive processing and involve long-term memory (Anstey & Low, 2004; Murman, 2015). These abilities include retaining historical information, vocabulary or world knowledge, reading, and language comprehension. They are strengthened with age through experience, exposure, education, knowledge, and intellectual pursuits and are less affected by age-related diseases. These abilities consistently enhance with age till 60 years of age and then remain constant with further increases in age and decline in the 90s (Christensen, 2001).

(2) Fluid abilities: Fluid abilities are cognitive abilities that entail complex, instant, and new information processing that requires manipulation and transformation and depends on short-term memory. For example, problem-solving, spatial manipulation, processing speed, and selectively attending any event/situation are fluid cognitive abilities. Studies showed that fluid abilities maximize in the mid-20s, then progressively deteriorate with an increased age around 60, and after that, the deterioration occurs more rapidly (Anstey & Low, 2004; Murman, 2015).

The other theories or concepts regarding aging and cognition are:

The scaffolding theory of aging and cognition (STAC): Cognitive behaviour in adulthood is maintained through "scaffolding", that is neuronal deterioration is compensated through additional neuronal activity to specifically increase prefrontal activation with aging as observed through functional imaging studies (Park & Reuter-Lorenz, 2009). This has been regarded as an adaptive measure of the brain as a compensatory support in response to the insults posed in structures and functions, like amyloid deposition, brain shrinkage, and white matter alteration, with advancing age (Rodrigue et al., 2009). This protective machinery limits cognitive aging

and can be achieved through engaging in a cognitive task or exercise, and other cognitive engagements.

Table 1-1 The cognitive domains and the associated crystallized and fluid cognitive abilities during normal aging

Cognitive domain	Crystallized abilities	Fluid abilities
Attention	Simple attention tasks	Complex attention tasks that rely on selective and divided attention
Memory	Nondeclarative memory, like procedural memory, temporal order memory, and recognition memory; declarative memory, like semantic memories and episodic memory	Delayed free recall; source memory; prospective memory; some episodic memory
Executive functions	Concept formation, abstraction, mental flexibility	Response inhibition, inductive reasoning, reasoning with unknown/new material, speeded motor associated executive functions
Visuospatial/ Construction abilities	Visuospatial abilities, like recognition of objects, shapes, gestures, and conventional signs	Visuoperceptual judgment, spatial orientation, and visual construction skills
Language	Vocabulary, verbal reasoning, and speech comprehension in normal conversation	Speech comprehension in a noisy environment, verbal fluency, retrieval, and loss of choice of words in spontaneous speech.

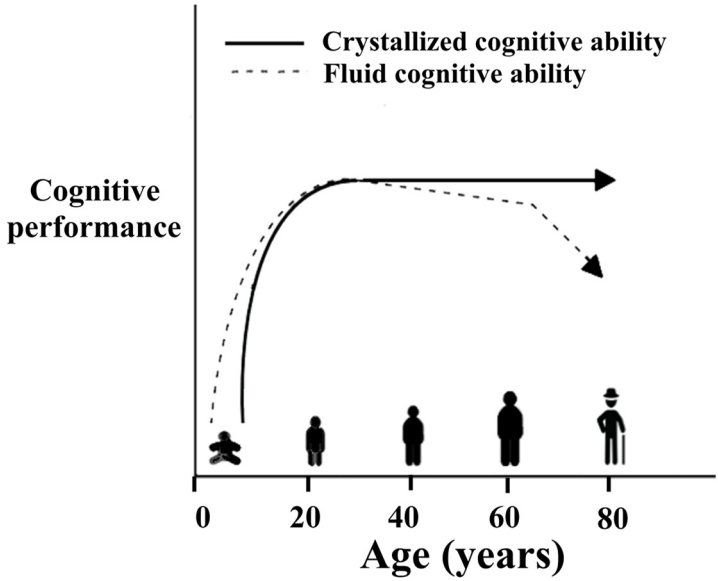

Fig. 1-1 Change in crystallized and fluid cognitive abilities with advancing age (based on Anstey & Low, 2004)

Cognitive reserve: The cognitive reserve hypothesis/model deals with the concept of curtailing age-related cognitive deterioration at the behavioural level as well as the efficient use of different brain networks to compensate for cognitive decline (Stern, 2002). According to the cognitive reserve hypothesis, certain individuals show better cognitive maintenance and endurance against pathological conditions or brain insults like amyloid protein deposition. Factors like education, physical activity, socialization, high socioeconomic position, and premorbid intelligence level act as neuroprotective factors that preserve cognitive skills from an early expression of deterioration. Brain volume, neurons, and synapse numbers are considered passive reserves while the active reserves are the plasticity and reorganization ability of the brain as a protective factor against neuropathologic changes (Stern, 2002; Gow et al., 2012; Harada et al., 2013). The STAC as discussed in the previous section is also one of the strategies to compensate for cognitive loss and is visible in certain active elders (Park & Reuter-Lorenz, 2009).

Superagers: Elders who exhibit cognitive skills like memory similar to or better than normal cognitively well-functioning individuals at least 20–30 years younger are known as superagers (Sun et al., 2016). Magnetic resonance imaging (MRI) studies have shown higher cortical thickness (including the anterior midcingulate cortex and temporal cortex, and the rostral medial prefrontal cortex) in these individuals compared to their 50- to 60-year-old cognitively normal counterparts (Rogalski et al., 2013). The anterior cingulate gyrus of superagers possesses more von Economo neurons and they also show a lower frequency of the ε4 allele of apolipoprotein E (APOE ε4 allele) than people with average cognitive functioning. The absence of age-related brain atrophy engaged in memory encoding, storage, retrieval, attention, and executive processes leads to better memory performance in superagers (Sun et al., 2016).

(I) Cognitive attributes of aging

1. *Attention*
2. *Memory*
3. *Executive cognitive functions*
4. *Visuospatial/construction abilities*
5. *Language*
6. *Processing speed and time perception*

Cognitive abilities are the subtle mental processes related to receiving external information through sense organs, processing it, and helping in appropriately and timely responding. Cognitive abilities have been divided into different cognitive domains (Murman, 2015; Fig. 1-2):

1. Attention: Attention is the state of awareness for some stimuli. Selective attention deals with the capacity to concentrate on a particular stimulus out of many inputs in the environment, ignoring the irrelevant and distractive information at that moment. Selective attention is observed when a person listens and replies to a nearby person while talking in crowded and noisy places like railway stations and markets. Divided attention is a type of multitasking. For example, while walking on the street, talking and looking around could be the reflection of the divided attention that helps to execute these functions at the same time. The ability to pay attention to any stimulus or task crumbles with aging; this is prominently noticeable, specifically while doing the complex tasks associated with selective and divided attention. Simple attention degrades slowly with advancing age, for example, performances on digit span that demand simple attention are less affected (Lezak et al., 2012; Harada et al., 2013; Murman 2015).

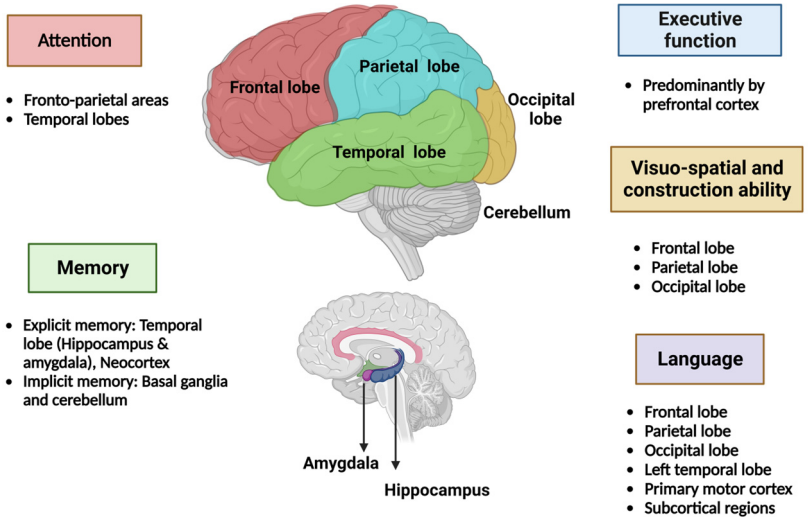

Fig. 1-2 Cognitive abilities and the associated brain areas. Created with BioRender.com

2. Memory: Memory is the cognitive attribute that helps to encode storage and retrieval of information collected through stimuli reaching the brain. Different types of memories vary across the lifespan in their manifestation. Broadly, memory is of two types, namely declarative and nondeclarative memory. Declarative or explicit memory is the consciously collected facts and information that include episodic memory or autobiographical memory (related to memories of personal past events) and semantic memory (memories collected as general knowledge). It has been observed that some of the episodic memories regress throughout life while the semantic memories worsen in later life (Rönnlund et al., 2005; Harada et al., 2013). Nondeclarative (implicit) memory is the subconsciously collected memory. For example, implicit memories rely on long-term memory, such as *procedural memory* (e.g. riding a bicycle, playing badminton), *temporal order memory* (remembering a sequence of events, memory related to past time or events/occasions like marriages, birthdays), *recognition memory* (retrieving information related to any familiar situation/stimulus with the help of cues, such as retrieving the name of a flower when the colour is presented) show less deterioration with age. These memories are the components of crystallized cognitive abilities (Harada et al., 2013; Murman 2015). Some of the memories associated with fluid behaviour rely on the working memory that declines with age, such as *delayed free recall* (which

is associated with new learning capability or unplanned and instantaneous retrieval of any information like recalling [without any cues] the names learnt a few minutes back); *source memory* (recalling the source of information, news or a story, be that a newspaper, television, or a person); and *prospective memory* (memory for intentions that facilitate performing any pre-planned actions in future – for example, remembering to take medications after dinner or replying to an email after the meeting).

Working memory, long-term memory, and short-term memory

Working memory (Miller et al., 1960), is the temporary storage of new information and processing of that information mentally while planning and executing any activity in hand, like solving a mathematical problem without paper and pen (Cowan, 2008). Reasoning, speech comprehension, and recalling things instantly are some of the cognitive tasks that rely on working memory, which declines with the aging process. Long-term memory can be retained for a longer duration (months, years, decades), like remembering the day of a wedding or a skill was learned decades ago. Both cross-sectional and longitudinal studies have shown a steady decline in cognitive functions underlying both working as well as long-term memories that commence in young adulthood and gradually increase with advancing age (Hultsch et al., 1998; Park et al., 2002) warding off the cohort effect (Park & Reuter-Lorenz, 2009). Short-term memories are the recent memories that are remembered from minutes to days (James, 1890). For example, short-term memory plays a role in remembering a phone number for a short period or dinner plans made a few days before.

The decline in working memory in elderly people is attributed to the incapability to extract relevant or irrelevant information while executing any work at that instant. This might involve attention problems and response suppression or task switching. Short as well as long-term memories differ in precision among older adults, while not in recalling (Rhodes et al., 2020). Working memory and long-term memory are both affected by perceptual and motor speed with aging (Park et al., 1996). Age-related working memory deterioration depends on factors like gender, education (Pliatsikas et al., 2019), and genetic repertoire (Rogalski et al., 2013). Long-term memory like episodic memory remains intact and slowly deteriorates with age (Pudas et al., 2013).

3. Executive cognitive functions: Executive cognitive functions are a higher level of cognitive skills required to organize and regulate other cognitive skills, such as planning, problem solving, sequencing, working

memory, abstract thinking, decision making, emotional regulation, self-monitoring, mental flexibility, and multitasking. An inverse association of age has been noticed with most of the executive functions which are complex, new, and time-bound. However, executive functions, such as concept formation, abstraction, and mental flexibility regress after 70 years. Long-term memory-based activities, such as explaining the meaning of proverbs, and reasoning about familiar material, however, remain intact throughout life. Response inhibition is the ability to suppress one's automatic response to distractions while attending to a stimulus: for example, in a classroom, some students paying attention to the lesson get distracted by noise and have poor response inhibition while some students who do not respond to the noise maintain their concentration on listening. This latter group has better response inhibition capability, something that also decreases with aging. The executive functions involving motor speed, inductive reasoning (verbal and mathematical reasoning), and reasoning with new materials also recess with increasing age (Harada et al., 2013).

4. Visuospatial/construction abilities: The cognitive functions related to the perception of space in two and three dimensions (i.e., visuospatial processing), the construct skills to construct complex figures, visuoperceptual judgment, and the ability to perceive spatial orientation deteriorate with increased age. While visual recognition of objects, shapes, and conventional signs remain as the visual construction of simple figures, recognizing known objects remains stable with advancing age.

5. Language: Language and speech show both crystallized and fluid characteristics. Language ability, specifically vocabulary, develops with age. In addition, verbal reasoning, speech comprehension in a normal context, and naming common objects remain preserved with age. However, verbal fluency, verbal retrieval, naming objects within restricted time, speech comprehension in a noisy environment, and word choice ability in spontaneous speech degrade with age (Harada et al., 2013). Lexical retrieval capability remains intact in the 50s and 60s while declining gradually in the 70s and 80s (Zec et al., 2005, Harada et al., 2013). This indicates age-related cognitive impairment associated with the age-related alteration in auditory and visual perception capacity.

6. Processing speed and time perception: Processing speed is simply how fast one executes cognitive functions and motor responses. The decline in processing speed commences during the 30s and continues with advancing age, resulting in a decline in many cognitive domains, like attention,

memory, and executive functions (Harada et al., 2013). Sensory capacity (visual and auditory acuity) and information processing speed deteriorate with progressing age. Therefore, different cognitive domains are affected and cognitive impairment reflects in the associated cognitive ability with aging. There is evidence that with increasing age the variability in temporal perception increases and its accuracy remains intact (Pande, 2013).

II. Age-related changes in brain structure and neuronal changes associated with cognitive impairment

It is well known that cognitive functions are the output of the functions of different brain regions. Developments in the neuroscience field and brain imaging have helped to trace the neurological changes in different brain regions that are concerned with different cognitive functions.

The attention-related cognitive functions are controlled by frontoparietal areas. Studies on animals and humans using neuro-imaging and electrophysiology techniques showed that temporal lobes are also engaged in multiple attention activities (Stemmann & Freiwald, 2019; Sani et al., 2021). The brain regions involved in explicit memories (episodic and semantic memories) are the hippocampus and amygdala in the temporal lobe, and the neocortex (part of the cerebral cortex forming the outside surface of the brain). Memories are stored temporarily in the hippocampus and are transferred to the neocortex. The implicit memories are processed by brain structures, like the basal ganglia and cerebellum, and the short-term working memory is processed primarily by the prefrontal cortex (https://qbi.uq.edu.au/brain-basics/memory/where-are-memories-stored). The executive functions are mostly processed in the prefrontal cortex. The complex cognitive skills that are executive skills, such as visuospatial and construction ability, decision making, planning, and problem solving, are predominantly processed by neurons of the frontal lobe. The parietal lobe is also involved in visual and spatial processing (Buening & Brown, 2018). Multiple brain areas of the cerebral cortex related to motor, visual, auditory, and other cognitive processing are involved in language and speech processing and its expression (Lumen learning; https://courses.lumenlearning.com/waymaker-psychology/chapter/reading-parts-of-the-brain/).

Broadly, cognitive changes have been associated with reduced brain volume, neuron size, neuronal death, and altered synaptic connections among neurons in grey and white matter during aging that progresses in certain patient groups, like those with Alzheimer's disease. Normal aging showed a neuronal loss in specific regions of the brain and accounted for

the 10% loss of that adult brain (Pannese, 2011; Murman, 2015). However, the loss of 40% or more of neocortical synapses than normal adults leads to dementia (Murman, 2015). A decrease in the number and length of dendrites and axons, loss of dendritic spines, and demyelination of axons are common phenomena associated with an aging brain. During normal aging from 20 years onward the density of neocortical synapses decreases (Terry & Katzman, 2001). The prefrontal cortex undergoes atrophy more prominently than other parts of the brain with aging. The medial temporal lobe parts which are involved in episodic memory, the hippocampus (HC) and the entorhinal cortex (EC), specifically the HC volume, markedly decrease in volume in healthy adults from 50 years and increases thereafter with alteration in hemodynamic integrity (Raz et al., 2004). Studies using radiotracer ligands and positron emission tomography (PET) scanners showed deposition of beta-amyloid (Aβ) protein in the cortex of 20–30% of normal adults making them susceptible to mild cognitive impairment and leading to Alzheimer's dementia (AD) through synaptic dysfunction. They also showed reduction in the volume of the hippocampus and impaired episodic memory in cognitively normal individuals (Pike et al., 2007; Harada et al., 2013). Longitudinal magnetic resonance imaging (MRI) scans of older people in the age range 59–85 years have a higher loss in brain tissues in frontal and parietal lobes than temporal and occipital lobes, even in a healthy sample. The grey matter (the part of the cerebral and cerebellar cortex and subcortical nuclei of which the majority contains cell bodies and dendrites) loss is more in orbital and inferior frontal, cingulate, insular, and inferior parietal regions, and minimally visible in mesial temporal regions (hippocampus and entorhinal cortex). The white matter (region of the brain with the myelinated axons connecting to the grey matter) volume structures are also reported to reduce with age in very healthy as well as older adults (Resnick et al., 2003). In addition, the reduction in the size of neurons as well as the reduction in the number of synaptic connectivity among neurons composing the grey matter has been linked to declining cognitive problems with aging. Dendritic arborization, dendritic length, and neuritic spines also show an inverse relation with age. Changes in receptors, synaptic transmission, and myelin dystrophy are linked to cognitive impairment with aging (Harada et al., 2013). The total prefrontal volume and white matter volume of older healthy individuals with a mean age of 90 years were observed as numbering less than healthy older individuals with a mean age of 70 years (Salat et al., 1999). The magnetic resonance diffusion tensor imaging of healthy people has shown that with aging the white matter integrity is reduced, something linked with progressive cognitive impairment (Dennis & Thompson, 2014). A positive connection has been

elucidated between higher general cognitive ability (GCA) and cortical volume or less cortical atrophy with aging in 20–88 year-old adults irrespective of years of education (Walhovd et al., 2022).

III. Cognitive assessment

1. *Inventories*
2. *Web-based/Computerized neuropsychological batteries*
3. *Electrophysiological method*
4. *Brain imaging techniques*
5. *Genetic and biochemical markers*
6. *Other technologies*

The diagnosis of cognitive impairment has been routinely carried out using neuropsychological tests or inventories since 1960, as well as post-mortem appraisal of structural changes in the brain. However, since 1985 emerging technologies like neuroimaging, biomarkers, genetics, longitudinal studies, and animal models have been popular to evaluate cognitive problems or status during normal aging (Dartora et al., 2021).

1. Inventories

Many inventories are used to assess cognitive functions and to screen the frequency of impaired cognition in both general and clinical populations. These questionnaires/inventories are also useful to observe age-related cognitive impairment. The individuals screened for cognitive impairment are then confirmed using advanced instruments and technology. The widely used neuropsychological tests with a certain set of questions which in a short time robustly determine cognitive statuses are:

1. **The mini-mental state exam (MMSE)**: This inventory is based on 11 questions that assess orientation (time and place), attention/short-term memory, language, visuospatial abilities, and the ability to understand (Folstein et al., 1975). Scores less than ≤23 out of 30 are taken as cognitive impairment.
2. **The Montreal cognitive assessment (MoCA):** This test is more precise than MMSE and useful for the early detection of many cognitive disorders, such as Parkinson's and Alzheimer's disease (Nasreddine et al., 2005). It also contains 11 items and is used to assess cognitive abilities, like visuospatial abilities, executive function, attention, concentration, memory, language, abstraction,

calculation, and orientation. A score of <26 out of a total score of 30 shows mild cognitive impairment.

Other tests used to evaluate cognitive abilities in elderly people are the Mini-Cog (Limpawattana & Manjavong, 2021), the Saint Louis University Mental Status Exam (SLUMS), the Blessed Orientation-Memory Concentration Test, Kokmen Short Test of Mental Status, Memory Impairment Screen, Ottawa 3DY, Brief Alzheimer's Screen, Caregiver Completed AD8, and many other dementia screening scales (Carpenter et al., 2011). Though inventories like MMSE and MoCA are better measures, they are only allowed to be administered by clinicians or health care professionals and not by a non-medical person, which is a limitation for their widespread use. The second limitation is literacy, as most of the questions can be solved by the literate group only.

2. Web based/computerized neuropsychological batteries

Computer based neuropsychological tests, such as digit span tests, n-back tests, pattern recognition tests for testing memory, Stroop tests, and trail making tests for assessment of executive tests are widely used (Oosterman et al., 2009).

3. Electrophysiological method

Electroencephalograms (EEGs) directly measure neural activity using electrodes at different regions of the brain that have been linked with cognitive status. An EEG is an effective, reliable, objective, and non-invasive method. The different brain waves captured by EEG have shown an association with cognitive abilities, such as memory, language, and executive functions (Yue et al., 2021). Aging leads to alteration in neural activity associated with alpha, beta, theta, and gamma waves that reflect deterioration in cognitive functions, like memory consolidation, attention and inhibitory control, and processing speed (Anderson & Taraschenko, 2018). The cognitive processes can also be obtained using event-related potentials (ERPs) through P300 (positive wave seen after 300 ms of stimulus) which is an endogenous ERP component and index of cognitive attributes, like attention, and working memory (Helfrich & Knight, 2019; Yue et al., 2021). Older adults (65–76 years) with higher education showed an increased P300 amplitude and shorter P300 latency compared to middle-aged adults (52–64 years), specifically the female group (Pergher et al., 2019).

4. Brain imaging techniques

MRI and PET have the potential to identify cognitive decline through monitoring structural changes, like the volume of the hippocampus, glucose hypometabolism in the temporoparietal region, amyloid-β (Aβ) in the neocortical region, and tau protein aggregation in the medial temporal area of the brain (Dartora et al., 2021). MRI techniques, such as structural and functional MRI (fMRI), and PET are helpful in the early diagnosis of mild cognitive impairment, Alzheimer's disease, and the underlying neural mechanism along with the brain regions associated with cognitive dysfunctions, such as the hippocampus, entorhinal cortex, and grey matter in the medial temporal lobe (Yue et al., 2021; Yin et al., 2013). The diffusion tensor imaging technique is used to detect white matter damage while PET tracer compounds are used to detect amyloid plaques in the living brain of Alzheimer's patients (Yin et al., 2013). Nevertheless, neuroimaging techniques have limitations in determining the changed brain volumes among normal aging, cognitive impairment, and dementia patients (Petrella et al., 2003; Anand et al., 2020).

5. Genetic and biochemical markers

The different degrees of cognitive decline in the aged population reflect the genetic basis behind the cognitive impairment. *The carriers of the apolipoprotein (APOE ε4) allele and the* single-nucleotide polymorphisms (SNPs) *(APOE rs405509 and APOE rs440446) perform poorly on many cognitive functions, such as* episodic memory, executive functioning, overall global cognitive ability, and perceptual speed. The performance worsens with aging. The APOE contributes to neurodegeneration in the later stage of life as it is engaged in synaptic plasticity modulation, glutamate receptor function, and cholesterol redistribution (Liu et al., 2021). The SNPs in the *ADAMTS9* (ADAM Metallopeptidase with Thrombospondin Type 1 Motif 9), *BDNF* (Brain-Derived Neurotrophic Factor), *CASS4* (Cas Scaffold Protein Family Member 4), *COMT* (catechol-O-methyltransferase), *CR1* (Complement receptor type 1)*, DNMT3A* (DNA Methyltransferase 3 Alpha), *DTNBP1* (dystrobrevin binding protein 1), *REST* (RE1-silencing transcription factor), *SRR* (Serine Racemase), *TOMM40* (Translocase of Outer Mitochondrial Membrane 40), altered expression of circadian clock genes, and Alzheimer's diseases have been linked to age-related cognitive deterioration (Lin et al., 2017). These authors suggested that the interaction of *APOE* with *BDNF*, *CR1*, and *COMT* genes products or lifestyle factors, like smoking, alcohol consumption, lack of social support, and lower physical activity worsen cognitive impairment during normal aging.

The lower level of amyloid beta (Aβ) in plasma also reflects cognitive impairment. Aβ is the product of proteolytic cleavage of the amyloid precursor protein. The concentration of Aβ1-42 in cerebrospinal fluid (CSF) is used as a biomarker for MCI or AD, as the concentration is higher in AD than in MCI. Different levels of total tau protein (T-tau) are also used as markers for the diagnosis of cognitive impairment in normal aging and AD (Hampel & Blennow, 2004). Recently, interleukin-2 has been suggested as a promising biomarker for the diagnosis of Amnestic MCI than Aβ and tau protein (Liang et al., 2021).

6. Other technologies

Emerging technologies, like eye tracking systems, can detect cognitive impairment of deductive reasoning, working memory, attention, and memory recall in patients with mild cognitive impairment (Oyama et al., 2019). The video conference approach also effectively assists in the early diagnosis and treatment of cognitive deterioration, specifically among patients from remote areas (Castanho et al., 2016).

IV. Factors associated with age-related changes in cognition

Several risk factors, such as gender, lifestyle, education, physical activity, health condition, psycho-social well-being, and sensory problems (hearing and visual impairment), collectively determine cognitive functioning with aging (see Fig. 1-3).

1. *Sleep and circadian rhythm*
2. *Neuronal changes*
3. *Genetic and biochemical factors*
4. *Physical and mental health issues*
5. *Social determinants*
6. *Gender, racial, and ethnic differences*
7. *Lifestyle*

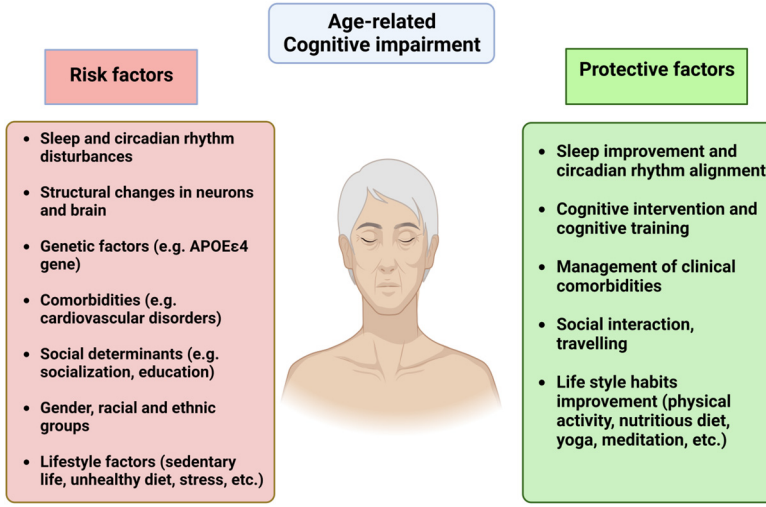

Fig. 1-3 The risk factors and the protective factors associated with age-related cognitive impairment. Created with BioRender.com

1. Sleep and circadian rhythm

Reports showed conflicting results on the impact of sleep on cognition during normal aging (Dzierzewski et al., 2018). Many aspects of sleep, such as slow wave sleep or rapid eye movement sleep reduce along with an increased rate of sleep disturbances with aging. Sleep problems/disorders like sleep disorder breathing have been associated with decreased cognitive abilities, attention vigilance, attention, reaction time, and executive functions, among other effects. Older adults sleeping longer (≥ 7 hours) or shorter (≤ 5 hours) performed poorly on cognitive tasks (Dzierzewski et al., 2018; Alves et al., 2021). An inverted U-shaped relationship has also been discerned between sleep duration and cognitive functions concerning speed, flexibility, and global cognitive function (van Oostrom et al., 2018).

With aging the rest-activity rhythm is disrupted, in terms of decreased amplitude, change in acrophase of activity, loss of phase resetting to zeitgeber, and altered sleep and wake times (Rogers-Soeder et al., 2018). Dampened circadian rhythm, lower circadian amplitude, and delayed circadian phase in older women are predictors of developing MCI or dementia (Tranah et al., 2011; Yi et al., 2021). Older males show decreased amplitude and weak rhythm, and advanced acrophase is linked to cognitive decline (Rogers-Soeder et al., 2018). A partial relationship between age-

related cognitive impairment and the correlations of rest-activity rhythm fragmentation has also been observed (Oosterman et al., 2009). Cognitive performance can also depend on the circadian phase or chronotype of an individual and the time of the day (Venkat et al., 2020; Salehinejad et al., 2021). Several studies have shown that morning/evening types exhibit superior cognitive performance in the morning/evening time and worse cognitive functions at other times, that is evening time for a morning chronotype and morning time for an evening chronotype. The elevated electrophysiological components during cognitive ability related to attention, working memory and motor learning capacity are greater during the circadian preferred time than non-preferred time (Salehinejad et al., 2021). It has been stated that increased cortical excitability including prominent cortical facilitation and decreased cortical inhibition, and long-term potentiation or depression-like plasticity is modulated by chronotype.

2. Neuronal changes

Mild cognitive impairment and dementia have been ascribed to hippocampal atrophy (Fotuhi et al., 2012). Drugs targeted for β-and γ-secretase inhibitors or amyloid (Aβ) vaccination could be the effective treatment for neurodegeneration caused by Aβ plaques leading to AD (Hampel & Blennow, 2004). As described in the above section (age-related brain structure and neuronal changes), the volume of the brain and alterations in grey matter and white matter are linked to impaired cognition.

3. Genetic and biochemical factors

One's memory maintaining capacity has been positively associated with education and physical activity level during a lifetime, specifically in socially interactive females. Socially and physically active females with longer education and carriers of the Met allele of the catechol-O-methyltransferase gene have greater memory maintaining capacity (Josefsson et al., 2012). The APOE-ε4 allele has been linked to the age-related decline in cognitive functions. It has been purported that the carriers of APOEε4 genes also showed an elevated rate of hippocampus shrinkage and beta-amyloid (Aβ) protein deposition compared to non-carriers (Raz et al., 2004; Rodrigue et al., 2009). A single APOEε4 allele carrier is also linked to temporal and frontal brain atrophy in normal functioning adults (Wishart et al., 2006). The Aβ protein deposition is inversely associated with episodic memory performance in 22–32 % of normal individuals (Rodrigue et al., 2009).

4. Physical and mental health issues

Blood pressure, hearing and visual impairment, and abdominal obesity are the risk factors for cognitive decline in females, besides dementia. Dementia and hearing impairment are also risk factors in elderly males (Lyu & Kim, 2016; Wang et al., 2020). Elderly males and females diagnosed with MCI and arterial hypertension are susceptible to increased mortality (Yaneva-Sirakova & Traykov, 2022). More constraints in Instrumental Activities of Daily Living (IADL) have been observed as one of the predictors of cognitive impairment besides high blood pressure, hearing impairment, and abdominal obesity as risk factors for cognitive decline in females, and Activities of Daily Living (ADL) as a risk factor in males. In addition, depression also emerged as a predictor for cognitive deterioration in both genders (Lyu & Kim, 2016). Chinese females aged >75 years from rural areas also showed a higher prevalence of cognitive aging than males attributed to factors like visual impairment and illiteracy in females and hearing impairment and social isolation in males (Wang et al., 2020).

5. Social determinants

Social determinants, like education, occupation, and socioeconomic status, are linked with cognitive functions. An array of literature has alleged that education is one of the predominant predictors of age-related cognitive decline irrespective of gender (Josefsson et al., 2012). Women with higher premorbid intelligence quotient (IQ) showed better cognitive performance than women with low IQ, and higher IQ acts as a protective factor against AD (Subramaniapillai et al., 2021). Individuals with more education showed greater cognitive reserve and are considered more capable of preventing cognitive deterioration (Laws et al., 2016; Nooyens et al., 2022). Poor socio-economic status in the aged (> 80 years) also leads to greater cognitive decline than seen in counterpart males (Miyawaki & Liu, 2019). Longer education in female elders (Habib et al., 2007), fewer comorbid medical conditions, and general healthy behaviour ensure better cognitive function (Barnes et al., 2007). These factors are the protective agents against neurodegeneration; they increase the cognitive reserve and thus the cognitive ability.

6. Gender, racial, and ethnic differences

Findings from longitudinal studies, like the Longitudinal Aging Study Amsterdam (LASA) and Doetinchem Cohort Study (DCS) showed enhanced memory, processing speed, flexibility, and global cognitive functions in