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COMPREHENSIVE ANALYSIS OF BRAIN AGING: DISEASE RISKS AND TREATMENT STRATEGIES

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Abstract
This review explores brain aging as a dynamic, progressive process influenced by social, emotional, environmental, and biological factors. Structural and functional changes—such as cortical thinning, synaptic dysfunction, hormone shifts, circadian disruption, and neuroinflammation—contribute to cognitive decline and increased risk of neurodegenerative diseases like Alzheimer's, Parkinson's, and ALS. Shared pathophysiological mechanisms include proteinopathies, mitochondrial failure, and oxidative stress, with mitochondrial dysfunction emerging as a key factor linking neurodegeneration and epilepsy in older adults. Lifelong neurocognitive health is shaped by sex-specific hormonal changes and developmental factors. Advances in biomarkers, AI, and neuroimaging offer promise for early diagnosis and personalized treatments. The review advocates for strategies emphasizing early intervention, circadian rhythm management, sex-specific research, integrated care, and investment in novel neuroprotective therapies to enhance cognitive longevity and quality of life.

INTRODUCTION

The human brain is a dynamic organ that changes throughout life in terms of form, function, and chemical makeup. Cognitive and behavioral outcomes are shaped by a multitude of biological, environmental, emotional, and social factors that affect the brain from early childhood through adolescence and old life. The study of the neuroscience of ageing is a multidisciplinary endeavor that includes the pathophysiology of neurodegenerative disorders, hormone regulation, circadian rhythms, brain morphology, and emotional regulation. Adolescence is thought to be a particularly sensitive developmental window during which the emotional and social environment can profoundly influence long-term neurocognitive health, despite the fact that persons differ greatly in their emotional resilience and regulation capacity (Casey et al., 2019). Numerous mental illnesses linked to emotional dysregulation, including anxiety and depression, manifest at this time, suggesting a possible developmental connection between early-life stress and later-life neuropathology or cognitive decline (Kaufmann et al., 2019). These behavioral and emotional weaknesses may persist throughout maturity and old age, indicating that early brain alterations set the stage for long-term cognitive and psychological development.

Changes in the structure and function of the brain become more noticeable as it ages. Research has shown that major morphological changes, including

cortical thinning, synaptic dysfunction, and reductions in total brain tissue volume, continue well into the age range of 25 to 55 and become particularly noticeable after age 60, defying previous beliefs that brain structure stabilizes in mid-adulthood (Scahill et al., 2003). These alterations frequently occur before or alongside cognitive symptoms, such as executive dysfunction, memory loss, and learning challenges, which are telltale signs of aging-related neurodegeneration (Marchetti et al., 2020). Additionally, more accurate "brain age" estimation is now possible thanks to sophisticated neuroimaging and artificial intelligence models, which may help in early diagnosis and intervention (Bashyam et al., 2020). Crucially, oxidative stress, neuroinflammation, and hormone dysregulation, especially those related to Ferroptosis and mitochondrial dysfunction—are active mechanisms that contribute to the ageing brain's loss of neural integrity and synaptic connections rather than being a passive process (Moos, 2023).

Circadian rhythms and sleep are also important factors in brain ageing. In addition to controlling sleep-wake cycles, the body's natural 24-hour biological clock also controls immunological responses, hormone production, and metabolism (Meyer et al., 2022). Age-related declines in circadian rhythm amplitude, phase synchronization, and sleep efficiency can make people more susceptible to neurodegenerative disorders and cognitive impairment (Leng et al., 2019). Sleep fragmentation and circadian disturbance can happen years before symptoms of illnesses like Alzheimer's disease (AD) manifest, making them early biomarkers and possible factors in the development of the disease. Daily activity-rest cycle fragmentation has been associated with early onset of AD neuropathology and rapid cognitive decline, highlighting the significance of chronobiologic health in brain ageing (Duncan et al., 2020).

Hormonal alterations, especially those involving sex steroids like testosterone and estrogen, have an equal impact. Because it affects synaptic plasticity, neuroprotection, and mitochondrial energy production, estradiol (E2), the strongest form of estrogen, is essential for brain function (Russell et al., 2019). A key player in the neuroendocrine system, the hypothalamus controls several physiological functions, such as metabolism, reproduction, and circadian rhythms. It is also increasingly thought to be a possible master regulator of systemic ageing (Kim et al., 2019). Variations in sex hormone levels may have a significant impact on how the brain ages, as evidenced by sex variations in neurodegenerative disorders, such as the earlier start and faster progression of diseases like AD in women. Although sex-specific illness patterns have been extensively documented, research is still ongoing to determine the exact processes by which hormones affect neurodegeneration. Significantly, the pervasive effects of sex hormones on inflammation,
neurotransmission, and brain development suggest that they may alter susceptibility to conditions like AD, PD, and FTD via intricate neurobiological networks (Vegeto et al., 2020).

The aging brain is particularly susceptible to a range of neurodegenerative disorders. Alzheimer's disease is the most common, characterized by amyloid-beta plaque deposition, tau protein tangles, and widespread neuroinflammation leading to progressive cognitive decline and synaptic loss (Smith et al., 2020). Parkinson's disease, which primarily affects motor control through dopaminergic neuron loss in the substantia nigra, also involves mitochondrial impairment and oxidative stress (Johnson et al., 2019). Huntington's disease, a genetic condition caused by CAG repeat expansion in the HTT gene, leads to toxic protein aggregation, neuronal death, and severe motor and cognitive deficits (Jones et al., 2024). Similarly, tau and TDP-43 Proteinopathies are the pathological hallmarks of frontotemporal dementia (FTD), which affects the frontal and temporal lobes and causes early-onset personality, behavioral, and language impairments (Greaves et al.,

2019). Upper and lower motor neurons are lost in amyotrophic lateral sclerosis (ALS), which frequently co-occurs with FTD. ALS is associated with genetic alterations that interfere with RNA processing and protein homeostasis (Smith et al., 2023). Despite having distinct clinical manifestations, these disorders are all characterized by similar underlying processes, including neuroinflammation, synaptic loss, and mitochondrial dysfunction.

The relationship between brain ageing and epilepsy is another overlooked but crucial factor. The prevalence of epilepsy in older individuals rises with age, reaching its peak in the eighth decade of life, and is frequently a result of neurodegenerative disorders, cerebrovascular injury, or traumatic brain damage (Babunovska and Vicente., 2024). Seizures can further damage neural circuits and worsen the course of disease, making neurodegenerative populations more susceptible. One important connection between epilepsy and aging-related neurodegeneration is mitochondrial failure, which is the basis for both seizure production and neuronal death (Madireddy, 2023). Furthermore, managing epilepsy in this population is made more difficult by the existence of comorbidities such respiratory dysfunction, mental health issues, and cardiovascular illness (Beghi and Hu., 2020). Breakthrough seizures provide extra hurdles in therapeutic care, especially for patients with underlying traumatic or genetic causes of epilepsy, even when they are well-managed on anti-seizure medication (Doerrfuss, 2024).

It is clear from these many but related mechanisms that brain ageing is much more than a passive loss of function. Developmental trajectories, emotional experiences, hormone signaling, structural remodeling, circadian regulation, and vulnerability to neurodegeneration and seizures all influence this dynamic, multifaceted process. Developing early interventions, individualized therapies, and preventative measures that support cognitive longevity and quality of life in ageing populations requires a thorough understanding of these interrelated characteristics.

1- Neuroscience of Brain Aging

1.1 Neuroscience of emotional and social aging

Although people differ greatly in their ability to control their emotions, adolescents are believed to be a sensitive developmental stage when this ability may be particularly susceptible to the effects of the social and emotional environment. The rapidly developing literature on the development of the emotional brain aims to explain dynamic changes in emotional behavior, especially during adolescence, when the incidence of many mental disorders involving emotion dysregulation peaks. (Casey et al., 2019). It is probable that common risk factors for mental and other brain illnesses will align with biological pathways that impact the development and maintenance of the brain's structure and function throughout life. (Kaufmann et al., 2019). Cognitive aging is related with multiple life-course and lifestyle factors, good aging likely begins in early life, while sustaining cognition or remediating impairments is a life-long process (Zanto et al., 2023).

1.2 Sleep and Circadian Rhythms in Aging

One of the most noticeable aspects of our life is the daily cycle of sleep and wakefulness, which is a reflection of the innate 24-hour rhythmicity that underlies practically every bodily function (Meyer et al., 2022). Age-related alterations in circadian rhythms include diminished amplitude or robustness, a shift in synchronization with the environment, and a decline in the body's ability to coordinate its cycles. These changes in the circadian rhythm are particularly noticeable in age-related neurodegenerative diseases like Alzheimer's disease (AD), where they frequently occur years before other symptoms appear. Circadian rhythm disruption may play a role in the development and progression of the neuropathological changes that occur in AD, as evidenced by the findings that fragmentation of daily rest-activity rhythms in older

subjects who are not demented is linked to earlier cognitive decline, an increased risk of incident AD, and preclinical AD neuropathology (Duncan et al., 2020). The kind and severity of neurodegenerative disease determine the manifestations of circadian rhythm disturbances, which in certain cases appear prior to the emergence of typical clinical signs of neurodegeneration (Leng et al., 2019).

1.3 Role of Hormones in Brain Aging

There are three commonly considered estrogens, the most physiological relevant of which is estradiol (E2). The next two estrogens may be generated from estradiol, specifically estrone (E1) and estradiol (E3) (Russell et al 2019). There the most of physiological activities that deteriorate with aging are largely governed by the hypothalamus, a brain area controlling development, metabolism, reproduction, circadian rhythm, and homeostasis. Furthermore, the hypothalamus is positioned to bridge the gap between the brain and the body, allowing environmental factors that impact ageing to be conveyed through the brain and influence the systematic ageing of peripheral organs. Therefore, it is thought that the hypothalamus is the main regulator of the body's ageing process (Kim et al., 2019). Human neurodegenerative diseases are featured by sex disparities in term of onset and progression of disease, but existing information rejects the precise definition of the sex-related factors intervening in these diseases. Sex-specific synthesis of sex steroids has been linked in epidemiological and clinical studies to the prevalence and incidence of disease risk; however, given the widespread effects of hormones on sexual differentiation and brain development or functions, their sex-specific role in neuro-degeneration is still unknown (Vegeto et al., 2020).

1.4 Morphological changes in brain throughout life

It is commonly known that throughout life, there are regular patterns of changes in brain anatomy associated to development and ageing. However, the extent of change varies greatly throughout various brain areas and life stages, leading to intricate non-linear age trajectories of localized brain alterations (Fjell and Anders, 2013). Brain changes continuously throughout the lifespan, and notably, these changes are also present in the age range of 25 to 55, which was previously thought to be largely stable in terms of brain structural morphology. Deep learning revealed conserved patterns of brain change throughout the lifespan, which enabled Deep Brain Net to achieve a fairly accurate estimation of brain age (Bashyam et al., 2020).Typically, the effects of advancing chronological age, including cognitive decline, become significantly apparent between the ages of 60–75 years as evidenced by the significant loss of total tissue volume, which coincides with the peak onset of age-associated neurodegenerative diseases (Scahill et al., 2003).Furthermore, most of these morphological changes are correlated with increased synaptic dysfunction, which leads to the gain-of-function of behavioral deficits observed in aging, such as cognitive decline, learning, memory, and sensory deficits (Marchetti et al., 2020). The cell death and disruption of brain architecture seen in neurodegenerative diseases can also lead to epilepsy, limited data exists on epilepsy burden among Alzheimer dementia (AD) and Parkinson disease.

2. Neurodegenerative and Neurological Disorders

2.1 Alzheimer's Disease (AD)

Alzheimer's disease (AD) is the most common neurological illness that affects people worldwide. The disease is characterized by dysfunctional hyper phosphorylated tau protein tangles and elevated amyloid-beta plaques. Synaptic abnormalities, neuronal death, and a decline in mental function are all consequences of the disease-causing alterations. According to recent studies, neuroinflammation is crucial for accelerating the course of AD. Because activated microglial cells emit pro-inflammatory cytokines that further harm neurons, the neurodegenerative cycle worsens (Smith et al., 2020).

Alzheimer's disease diagnosis has changed significantly as a result of biomarker studies. Tau PET imaging in conjunction with measures of amyloid-beta 42 and phosphorylated tau in cerebrospinal fluid made it possible to accurately diagnose brain disorders early on. Therapeutic advancements have yielded encouraging outcomes for several researchers. Reputable research demonstrated that aducanumab and lecanemab, two anti-amyloid medications, effectively lower amyloid plaques while slowing cognitive deterioration (Cummings et al., 2021). Research demonstrates that cognitive training programs and physical activity reduce the incidence of AD and improve patients' lifestyle outcomes (Livingston et al., 2020).

2.2 Epilepsy

An underlying brain problem lowers the intrinsic seizure threshold in epilepsies, a set of diverse neurological conditions that increase the likelihood of spontaneous recurrent seizures (Balestrini., 2021). An imbalance of excitatory neurotransmitters over inhibitory neurotransmitters, as well as an increased frequency and synchronization of neuronal firing, are the causes of epilepsy. Neuronal loss brought on by epileptic convulsions can encourage epileptogenesis and seizures themselves (Madireddy., 2023). Epilepsy is more common in childhood and adolescence, less common in adults between the ages of 20 and 50, and then progressively more common after the age of 50, peaking in the eighth decade of life (Babunovska., 2021). Among this population with epilepsy, neurodegenerative, cerebrovascular, neoplastic, and psychiatric co-morbidities frequently exacerbate the clinical picture (Manacheril., 2015). Numerous medical and mental comorbidities, including as respiratory and cardiovascular disorders, anxiety, and depression, are more common in people with epilepsy (Beghi, E. 2020). Epilepsy is more common in childhood and adolescence, less common in adults between the ages of 20 and 50, and then progressively more common after the age of 50, peaking in the eighth decade of life (Babunovska., 2021). Among this population with epilepsy, neurodegenerative, cerebrovascular, neoplastic, and psychiatric co-morbidities frequently exacerbate the clinical picture (Manacheril., 2015). Numerous medical and mental comorbidities, including as respiratory and cardiovascular disorders, anxiety, and depression, are more common in people with epilepsy (Hu, Z, 2024).

I.Mytochondrial Dysfunctioning

Between 35 and 60 percent of people with mitochondrial disorders experience seizures. In many types of epilepsies, including those that are not mitochondrial in origin, mitochondrial dysfunction is pathogenic. Neurological problems, such as seizures, are brought on by altered neuronal bioenergetics, metabolism, and decreased ATP synthesis brought on by damaged brain cell mitochondria. Ferroptosis, a route for cell death that is triggered by iron-dependent lipid peroxidation, is consistent with changes in mitochondrial bioenergetics, metabolism, and morphology that are observed in neurodegenerative disorders (NDDs) (Moos., 2023). It is also known that mitochondrial dysfunction contributes to neuronal excitability and apoptosis, both of which can result in neuronal death in epilepsy (Madireddy., 2023).

II. Breakthrough seizures

Breakthrough seizures refer to unprovoked seizures in patients with epilepsy using ant seizure medication (ASM) who have been seizure-free for at least 12 months. The high rate of break-through seizures in patients with epilepsies caused by traumatic brain injury is worrisome. Patients with post-ischemic stroke epilepsy as well as patients with genetic generalized epilepsy have a reduced risk of breakthrough seizures (Doerrfuss., 2024).

III.Risk factor of Eplipsy in neurodegenrative population

Patients with dementia and other degenerative conditions may experience both non-epileptic staring

or confusional episodes as well as seizures. Epilepsy is characterized by repeated spontaneous bursts of neuronal hyperactivity and high synchronization in the brain (Vicente., 2024). As the population ages, we should anticipate a greater burden of epilepsy among older adults. Adults are more likely to suffer from neuro-degenerative diseases. The burden of epilepsy in neuro-degenerative populations is acutely important not only because of the expected growth of this population segment, but also because epilepsy treatment is of great clinical importance to these patients (Blank., 2021).

2.3 Parkinson's Disease (PD)

The gradual dysfunction of movement The substantia nigari's dopaminergic neurons are destroyed in Parkinson's disease. The primary pathogenic sign of Parkinson's disease manifests as intracellular Lowy bodies composed of alpha-syncline protein. Impaired mitochondrial dynamics and elevated reactive oxygen species (ROS) generation both contribute to neuronal death (Johnson et al., 2019). Along with other genetic variants, the LRRK2 and PARKIN genes have been linked to both familial PD and patients that did not have a known family history. Because alpha-syncline seed amplification assays (SAA) are so accurate at detecting Parkinson's disease (PD), their use in CSF represents a major diagnostic advance. Deep brain stimulation (DBS) and CRISPR-Cas9 gene editing are two significant new medicines that the medical community has developed to help individuals with Parkinson's disease. It has been found that deep brain stimulation therapy is notably effective because it improves quality of life outcomes while also reducing motor symptoms (Williams et al., 2022).

2.4 Amyotrophic Lateral Sclerosis (ALS)

Amyotrophic lateral sclerosis (ALS), a terminal motor neuron disease, leads to the progressive degeneration of both upper and lower motor neurons. As the condition advances, respiratory failure becomes unavoidable due to muscle weakness and paralysis. Research has identified genetic mutations at the C9ORF72, SOD1, and TARDBP loci as key contributors to ALS progression (Miller et al., 2020). These mutations induce cellular abnormalities that disrupt RNA processing, protein homeostasis, and axonal transport pathways, ultimately resulting in motor neurons death (Smith et al., 2023). Recent medical innovations, specifically antisense oligonucleotides (ASOs), offer promising therapeutic approaches targeting the genetic basis of ALS.

Medical research has proven the effectiveness of SOD1 mutation-targeting ASOs in preclinical stage and clinical stage testing. Patient results improve when patients receive combined respiratory support and physical therapy care from multidisciplinary teams (Brown et al., 2021).

2.5 Huntington's Disease (HD)

Due to aberrant CAG repeat expansions in the DNA of the HTT gene, HD is an autosomal dominant genetic disorder. Individuals who carry this mutation produce faulty huntingtin proteins, which upset cellular balance and lead to the death of nerve cells (Thompson et al., 2021). Researchers have studied huntingtin mutant protein features leading to transcriptional regulation problems and mitochondrial dysfunction and synaptic disruption (Thompson et al., 2021). Scientists continue to investigate RNA interference (RNAi) as well as CRISPR-Cas9 approaches to treat the genetic basis of HD (Jones et al., 2024). Research findings from clinical trials of RNAi-based medicinal drug RG6042 reveal that the administration of this com-pound both reduces mutant huntingtin protein quantities and slows Huntington disease progression (Jones et al., 2024). Tetrabenazine, which has demonstrated therapeutic effects, can effectively cure the neurological symptoms of HD, including chorea (Thompson et al., 2021).

There is evidence that the mHTT RNA is harmful, and that the proliferation of somatic CAG repeats in susceptible cells affects the progression of the disease

at the DNA level (Tabrizi et al., 2020). The HD-ISS uses a genetic definition of Huntington's disease and Huntington progression to characterize individuals for research purposes starting at birth, starting at Stage 0 (i.e., those who have the genetic mutation for Huntington's disease but do not exhibit any obvious clinical change). It is followed by quantifiable signs of the underlying pathophysiology (Stage 1), a discernible clinical phenotype (Stage 2), and finally a decrease in function (Stage 3). Individuals can be accurately categorized into stages according to the thresholds of landmark evaluations that are distinctive to each stage (Tabrizi et al., 2022). Animal models of HD were created using neurotoxins prior to the genetic etiology of HD being discovered. However, when N-methyl-D-aspartate-receptor agonists, like quinolinic acid, are injected into the striatum,HD-like disease is produced, with medium spiny projection neurons being lost and cholinergic and reduced nicotinamide-adenine dinucleotide phosphate diaphorase neurons being spared. A number of mitochondrial poisons, such as 3-nitropropionic acid, can be injected peripherally into rodents or primates to mimic some of the striatal disease characteristics of HD and These neurotoxin experiments point to a number of pathways that may be involved in HD cell death, and other metabolic poisons cause preferential toxicity in different parts of the brain, frequently those affected in other glutamine repeat diseases (Rose et al., 2020). An increased CAG repeat length in the huntingtin gene in a patient with clinical features of the condition is typically used to confirm the diagnosis of Huntington's disease (HD), an inherited neurodegenerative disease marked by neuro-psychiatric symptoms, a movement disorder (most commonly choreiform), and progressive cognitive impairment. Although the diagnosis is typically simple, unusual presentations can occur, and it can be challenging to determine when a person has changed from being an asymptomatic carrier into the disease state (Stoker et al., 2022). Huntington's disease (HD) is a rare neurodegenerative disease of the central nervous system that is inherited genetically autosomal-dominantly. It is caused by the expansion of a CAG trinucleotide repeat in the HTT (huntingtin) gene, and alleles with 40 or more repeats are fully penetrant. The disease is characterized by a variety of somatic symptoms, motor, cognitive, and psychiatric disorders, and progressive worsening that leads to a bedridden state with cognitive decline. The disease dies approximately 20 years after symptoms first appear, and more than a century after it was first described. Despite this, there is still no cure for HD, though symptomatic treatments are thought to be effective in managing some of its problematic symptoms (Bachoud levi et al., 2019). While the mutant huntingtin protein has an elongated polyglutamine tract at the amino terminus that causes protein aggregation and the ensuing toxicity, the disorder is caused by an expansion of the trinucleotide CAG repeat in exon 1 of the Huntingtin gene (HTT); the number of CAG repeats increases from the normal range of 16–20 repeats to >35 repeats in patients (Squadrone et al., 2022). The pathophysiology of HD is brought on by a mutation in the huntingtin gene that produces mutant huntingtin (mHtt), an aberrant protein that is widely expressed and known to be toxic to a variety of cell types (Denis et al., 2019).

2.6 Frontotemporal Dementia (FTD)

Because it affects both the frontal and temporal areas of the brain, frontotemporal dementia (FTD) is an illness that exhibits variability. Despite frequently being regarded as a rare disease, FTD is a heterogeneous neurodegenerative disorder that manifests as distinct changes in behavior, language, and motor function. With an estimated lifetime risk of 1 in 742, FTD is likely the most common type of dementia experienced by individuals under 60 (Greaves et al., 2019). According to current research, tau Proteinopathies and TDP-43 are pathogenic hallmarks of FTD (Robinson et al., 2022). Better diagnosis accuracy and information regarding illness

progression are provided by modern neuroimaging technology, particularly MRI with PET in conjunction with Neurofilament light chain (NFL) biomarkers. Along with medications that regulate the action of the TDP-43 protein, medical researchers are actively investigating therapeutic medications that target tau proteins (Brown et al., 2023). Numerous studies demonstrate that behavioral management strategies in conjunction with speech therapy can effectively treat patients and improve their situations (Robinson et al., 2022). Around 20% of patients with prehensile dementia have been diagnosed with FTD, which is a group of clinical neurologic syndromes characterized by early-onset relative memory loss, progressive behavioral abnormalities, personality changes, and language disorders. Research on FTD has shown that neuromolecular pathology varies among the various subtypes of FTD syndromes, and clinically, the syndromes are divided into three categories: behavioral variant frontotemporal dementia (bvFTD), the behavioral type; primary progressive aphasia (PPA), the linguistic variant type; and FTD amyotrophic lateral sclerosis (FTD-ALS/atypical Parkinson's disease), the sportive manifestation type (Wang et al., 2022).

The underlying pathology of behavioral variant FTD can be diverse and may reflect the underlying genetic mutation in f-bv FTD. The clinical syndrome is characterized by progressive changes in social behavior, personality, and cognition as a result of degeneration of frontal and temporal cortical regions (Heuer et al., 2020). Growing evidence, such as cortical inflammation, microglial activation, astrogliosis, and differential expression of inflammation-related proteins in the peripheral, indicates that neuroinflammation plays a role in the development of FTD, as it does in other forms of dementia (Bright et al., 2019). For FTD, there are no particular therapeutic choices; instead, the goal of treatment is to inform the patient's care giver about the illness and symptomatic medication (Pupal et al., 2021). A first-degree relative with a significant neurodegenerative disease is present in 20% to 30% of FTD patients, and family members can have any of the MND-FTD illnesses within a single pedigree, including pure MND, pure FTD, and a combination of both (Devennet et al., 2019). Although the evidence is limited, there is some indication that antidepressants and second-generation antipsychotics may benefit individual patients. The majority of medications that have been used to treat dementia of the Alzheimer's disease type are ineffective in FTD, and cholinesterase inhibitors and memantine should be avoided (Magrath et al., 2022).

Recommendations

Promoting healthy brain aging requires early-life interventions targeting emotional regulation and stress management, as adolescence shapes long-term brain health. Maintaining sleep hygiene and circadian rhythm stability is vital, especially in older adults, to reduce neurodegenerative risk. Sex-specific differences in disease progression highlight the need for tailored therapies. Advances in biomarkers and AI-driven brain age prediction support personalized, proactive care. As epilepsy rises with age, especially in neurodegenerative conditions, comprehensive management considering comorbidities is crucial. Multidisciplinary care models are essential for optimal outcomes, alongside continued investment in neuroprotective and disease-modifying therapies like CRISPR and antisense oligonucleotides.

Conclusion

A complex web of biological, emotional, environmental, and social factors interacts to alter neurological and cognitive outcomes throughout life, according to the neuroscience of ageing. Dynamic changes in morphology, neurochemistry, and functionality are hallmarks of brain ageing, which is far from a passive or uniform process. These changes are caused by a variety of factors, including oxidative stress, mitochondrial malfunction, hormone

dysregulation, neuroinflammation, and circadian disruption.

It is significant to note that overlapping pathophysiological mechanisms, such as proteinopathies, synaptic loss, and inflammation, are shared by neurodegenerative diseases such as Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), frontotemporal dementia (FTD), and amyotrophic lateral sclerosis (ALS). With mitochondrial failure appearing as a common thread, the increasing prevalence of epilepsy in ageing populations further highlights the intricate relationship between neurodegeneration and neural circuit instability.

The course of brain ageing and disease vulnerability are also significantly influenced by sex-based hormonal differences, emotional and social influences during adolescence, and disrupted circadian rhythms. Therefore, it is necessary to see brain ageing as a continuous process that influences early development all the way through late adulthood, necessitating a comprehensive and longitudinal viewpoint.

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