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**ENVIRONMENTAL ENRICHMENT AS A KEY ASPECT
OF HUMAN WELL-BEING DURING THE COVID-19 PANDEMIC**



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**ЗБАГАЧЕННЯ СЕРЕДОВИЩА ЯК КЛЮЧОВИЙ АСПЕКТ
ДОБРОБУТУ ЛЮДИНИ ПІД ЧАС ПАНДЕМІЇ COVID-19**

ABSTRACT

Environmental enrichment (EE) has long been established as an effective method of improving neuroplasticity and reducing behavioral problems in captive mammals. As the creation of an enriched environment includes the effects of social stimuli and novel objects, its translation to humans can be considered reasonable. In this article, the authors suggest that environmental enrichment should be considered as a promising strategy to combat the social isolation caused by the pandemic, providing a better opportunity for behavioral adaptation.

Purpose: The aim of this review is to explore the importance of environmental enrichment as a fundamental component of promoting human well-being in the midst of the COVID-19 pandemic. The aim of this paper was to demonstrate the relationship between psychological distress, cognitive impairment and neuropsychological status in patients suffering from COVID-19 and COVID-related isolation, and to describe the benefits of the environmental enrichment approach and propose it as a potential solution to improve brain performance.

Methodology: Extensive searches were conducted in academic databases including PubMed, PsycINFO, Web of Science and Google Scholar. Keywords including 'environmental enrichment', 'nature exposure', 'physical activity', 'social interaction', 'cognitive stimulation', 'well-being', 'mental health', 'COVID-19 pandemic' and related terms were used. The search was limited to articles published in English and focused on human populations. Studies eligible for inclusion included empirical research, review articles, meta-analyses and theoretical papers relevant to environmental enrichment and human well-being during the COVID-19 pandemic. Relevant articles were screened using titles and abstracts to determine eligibility for full text review. Data were extracted from selected articles, including study objectives, methods, key findings and implications for human well-being. Studies were synthesized thematically to identify common themes, trends and gaps in the literature. The review aims to provide a comprehensive and rigorous synthesis of the literature on the role of environmental enrichment in promoting human well-being during the COVID-19 pandemic.

Scientific novelty: The review presents a new perspective by synthesizing the existing literature on environmental enrichment in the unique context of the COVID-19 pandemic. It explores how environmental factors such as exposure to nature, physical activity and social interactions can serve as critical resources for maintaining and enhancing human well-being in times of crisis. By specifically addressing the impact of the COVID-19 pandemic on human well-being, the review offers a novel examination of the challenges posed by pandemic-related restrictions, isolation and uncertainty. It highlights how environmental enrichment strategies can serve as adaptive coping mechanisms to mitigate the negative psychological and emotional effects of the pandemic. One of the key scientific novelties of the review is its interdisciplinary approach to understanding human well-being. It synthesizes findings from psychology, public health and environmental science to provide a comprehensive analysis of the role of environmental enrichment in promoting holistic well-being during the pandemic.

Conclusions. The review highlights the importance of environmental enrichment, which includes exposure to nature, physical activity, social interactions and cognitive stimulation, in promoting human well-being during the pandemic. Environmental enrichment strategies offer valuable resources for mitigating the negative psychological, emotional and social effects of the COVID-19 pandemic. By providing opportunities for stress reduction, mood enhancement and social support, these interventions contribute to resilience and adaptive coping mechanisms in times of crisis. Exposure to nature is emerging as a particularly powerful form of environmental enrichment, with therapeutic benefits for mental health, emotional well-being and overall quality of life. Encouraging physical activity and facilitating social interactions, albeit within the constraints of public health guidelines, play a critical role in maintaining human well-being during the pandemic.

Key words: environmental enrichment, human well-being, physical activity, social interactions, cognitive stimulation, mental health

АНОТАЦІЯ

Збагачення навколишнього середовища (ЗС) – це ефективний метод покращення нейропластичності та зменшення поведінкових проблем у ссавців, що утримуються в неволі. Оскільки створення ЗС передбачає вплив соціальних стимулів і нових об'єктів, його екстраполяція на людей можна вважати розумним. У цій статті автори пропонують розглядати ЗС як перспективну стратегію боротьби з соціальною ізоляцією, викликаною пандемією, надаючи кращі можливості для поведінкової адаптації.

Мета: Мета цього огляду – дослідити важливість ЗС як фундаментального компонента сприяння добробуту людей після пандемії COVID-19. Мета цієї статті полягала в тому, щоб продемонструвати зв'язок між психологічним дистресом, когнітивними порушеннями та нейропсихологічним статусом у пацієнтів, які страждають на COVID-19 та пов'язану з COVID ізоляцією, а також описати переваги підходу до ЗС та запропонувати його як потенційне рішення для покращення роботи мозку.

Методологія: був проведений пошук в академічних базах даних, таких як PubMed, PsycINFO, Web of Science і Google Scholar. Використовувалися такі ключові слова, як «збагачення навколишнього середовища», «вплив природи», «фізична активність», «соціальна взаємодія», «когнітивна стимуляція», «благополуччя», «психічне здоров'я», «пандемія COVID-19» та пов'язані з ними терміни. Пошук був обмежений статтями, опублікованими англійською мовою та зосередженими переважно на людських популяціях. Дослідження, які підлягали включенню, включали емпіричні дослідження, оглядові статті, мета-аналізи та теоретичні статті, пов'язані зі ЗС та добробутом людей під час пандемії COVID-19. Відповідні статті перевірялися з використанням заголовків і анотацій, щоб визначити придатність для рецензування повного тексту. Дані були відібрані з вибраних статей, включаючи цілі дослідження, методи, ключові висновки та наслідки для добробуту людини. Дослідження були узагальнені тематично, щоб визначити спільні теми, тенденції та прогалини в літературі. Огляд має на меті забезпечити всебічний синтез літератури про роль ЗС в сприянні добробуту людей під час пандемії COVID-19.

Наукова новизна: огляд представляє нову перспективу шляхом синтезу існуючої літератури про ЗС в контексті пандемії COVID-19. Він представляє, як фактори навколишнього середовища, такі як вплив природи, фізична активність і соціальні взаємодії, можуть служити важливими ресурсами для підтримки та підвищення добробуту людини під час кризи. Конкретно розглядаючи вплив пандемії COVID-19 на добробут людей, огляд пропонує новий аналіз проблем, пов'язаних із пандемією обмеженнями, ізоляцією та невизначеністю. У ньому підкреслюється, як стратегії ЗС можуть служити адаптивними механізмами подолання та пом'якшення негативних психологічних і емоційних наслідків пандемії. В огляді використано міждисциплінарний підхід до розуміння благополуччя людини. Він синтезує результати психології, охорони здоров'я та наук про навколишнє середовище, щоб забезпечити всебічний аналіз ролі ЗС в сприянні цілісного благополуччя під час пандемії.

Висновки. Огляд підкреслює важливість ЗС, яке включає контакт з природою, фізичну активність, соціальні взаємодії та когнітивну стимуляцію, для сприяння добробуту людей під час пандемії. Стратегії ЗС пропонують цінні ресурси для пом'якшення негативних психологічних, емоційних і соціальних наслідків пандемії COVID-19. Надаючи можливості для зменшення стресу, покращення настрою та соціальної підтримки, ці втручання сприяють стійкості та адаптивним механізмам подолання кризових ситуацій. Вплив на природу стає особливо потужною формою ЗС з терапевтичними перевагами для психічного здоров'я, емоційного благополуччя та загальної якості життя. Заохочення до фізичної активності та сприяння соціальній взаємодії відіграють вирішальну роль у підтримці добробуту людей під час пандемії.

Ключові слова: збагачення навколишнього середовища, добробут людини, фізична активність, соціальні взаємодії, когнітивна стимуляція, психічне здоров'я

Introduction

On 11 March 2020, the World Health Organization (WHO) announced that the COVID-19 epidemic, caused by the SARS-CoV-2 virus first identified in December 2019 in the city of Wuhan, China, had reached pandemic levels. As a result, an extensive programme of containment measures has been put in place, which has had a significant impact on the daily lives of people of all social groups, ages, genders and nationalities. Recent studies have shown that the long-term lack of social interaction and the monotony of the environment caused by quarantine have led to behavioral changes of various kinds, including negative ones. A strong relationship between the duration of quarantine and stress, anxiety and depression has been reported in the literature (Hamaideh et al., 2022). Psychiatric symptoms, including symptoms of post-traumatic

stress disorder (PTSD), anxiety and depression, have been reported in patients with SARS-CoV-1 during the atypical pneumonia epidemic and at 1 month, 1 year, 30 months or more after illness (Cheng et al., 2004a,b; Chua et al., 2004; Wu et al., 2005; Lee et al., 2007). In addition, symptoms of PTSD, depression and anxiety have been described in healthcare workers during the epidemic, 2 months, 2 and 3 years after the atypical pneumonia epidemic, and in the general population during and after the epidemic (Hawryluck et al., 2004; Verma et al., 2004; Lin et al., 2007; Lancee et al., 2008).

In the post-COVID patients, PTSD is often accompanied by a sudden fear of death, shortness of breath, difficulty falling asleep, nightmares and flashbacks. The most common symptoms are characteristic depressing memories or ideas associated with shortness of breath and other unpleasant sensations of the acute period

(Aiyegbusi et al., 2021; Al-Aly et al., 2022). Conditions associated with the effects of COVID-19 or long COVID are characterized by severe cognitive changes, including a condition recently termed 'brain fog'. The resulting cognitive impairment facilitates the spread of the virus, as infected individuals exhibit reduced anti-infection behavior (Gouraud et al., 2021). It should be noted that cognitive complaints are associated with both

anxiety and depressive symptoms and are independent of objective neuropsychological status, reflecting the leading role of anxiety and depression in the cognitive impairment found. It is characteristic that an increase in the number of somatic symptoms of COVID-19 2 months after the acute phase of the disease is associated with depressive, anxiety and post-traumatic symptoms (Fig. 1) (Ismael et al., 2021).

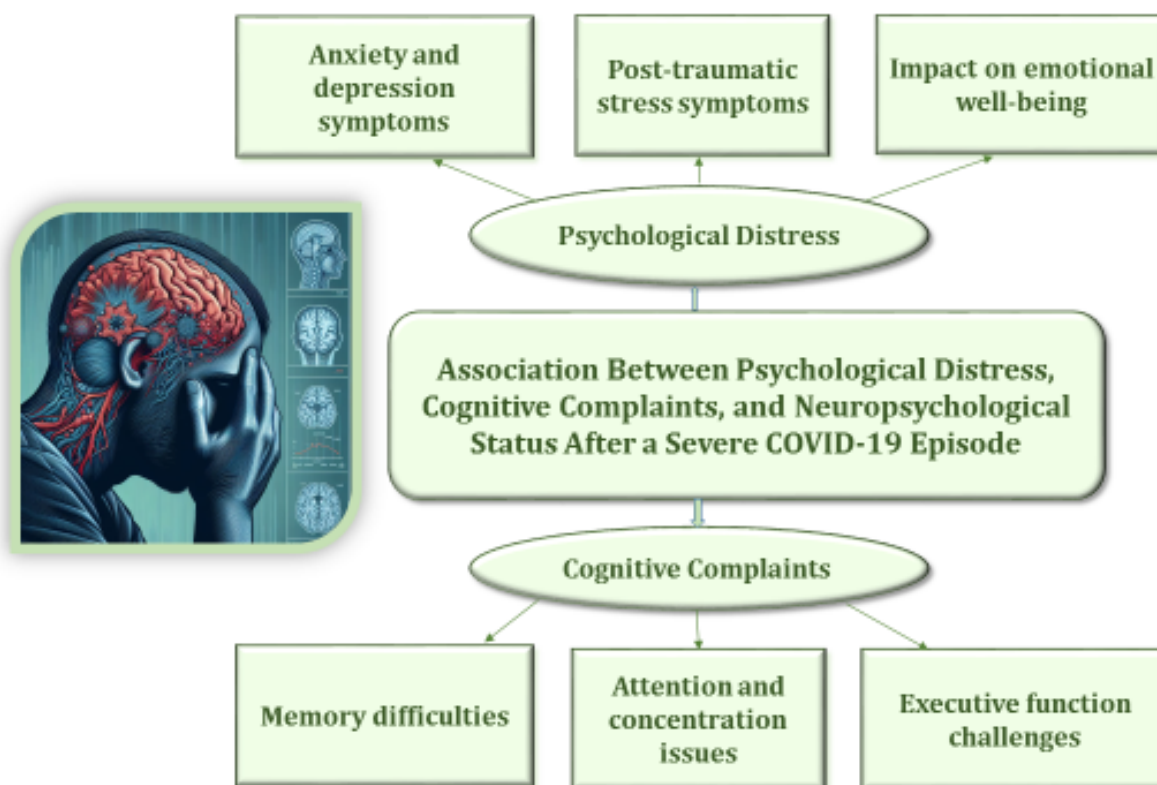


Fig. 1. Association between psychological distress, cognitive complaints and neuropsychological status after a severe COVID-19 episode

It is also known that people who have suffered from coronavirus infection experience cognitive deficits such as difficulties in facial emotion recognition, logical task performance and working memory decline (Hampshire et al., 2021). Cognitive dysfunction, including impairment of executive function and memory, as well as asthenia and a dysregulation syndrome with frontal symptoms in severe cases of the disease, may be caused by respiratory and/or circulatory hypoxemia. Hypoxic damage, microhemorrhage and inflammation of neurons have been identified in various areas of the brain, particularly in the brainstem. The brainstem contains many different nuclei and sections that regulate different physiological processes such as respiratory, cardiovascular, gastrointestinal and neurological. Neurons with a high metabolic demand for oxygen become dysfunctional, leading to cognitive impairment. Hypometabolism in the parahippocampal gyrus, thalamus and some white matter regions may be a secondary consequence of

hypoxic damage to these areas, leading to memory loss and cognitive dysfunction (Yan et al., 2021). The pathogenesis of mental disorders in the post-Covid period is multifactorial and multi-organ in nature, caused by systemic (regulatory, tissue and organ) pathological disturbances of the functioning of the whole organism. The basis of the observed tissue and organ disorders are metabolic disorders at the cellular and subcellular levels, caused in particular by damage to mitochondria, acceleration of lipid peroxidation and the development of oxidative stress. In addition, the side effects of pharmacotherapy for COVID-19 should be taken into account, in particular the use of corticosteroids, interferon, hydroxychloroquine and anti-interleukin monoclonal antibodies (Ceban et al., 2022; Premraj et al., 2022). It is therefore necessary to minimize the negative consequences of human adaptation to new social conditions and to create opportunities to stimulate the brain's cognitive abilities.

The aim of this review is to explore the importance of environmental enrichment as a fundamental component of promoting human well-being in the midst of the COVID-19 pandemic. This review will examine the multiple ways in which the COVID-19 pandemic has affected human well-being, including psychological, emotional and social aspects. The paper will explore the concept of environmental enrichment and its role in improving human health and well-being. It will discuss different forms of environmental enrichment, including exposure to nature, physical activity, social interactions and cognitive stimulation.

Materials and methods

Extensive searches were conducted in academic databases including PubMed, PsycINFO, Web of Science and Google Scholar. Keywords used included 'environmental enrichment', 'nature exposure', 'physical activity', 'social interaction', 'cognitive stimulation', 'well-being', 'mental health', 'COVID-19 pandemic' and related terms were used. The search was limited to articles published in English and focused on human populations. Studies eligible for inclusion included empirical research, review articles, meta-analyses and theoretical papers relevant to environmental enrichment and human well-being during the COVID-19 pandemic. Relevant articles were screened using titles and abstracts to determine eligibility for full-text review. Data were extracted from selected articles, including study objectives, methods, key findings and implications for human well-being. Studies were synthesized thematically to identify common

themes, trends and gaps in the literature. The review aims to provide a comprehensive and rigorous synthesis of the literature on the role of environmental enrichment in promoting human well-being during the COVID-19 pandemic.

Maximizing brain potential through environmental enrichment

It has long been known that animals' ability to develop adaptive behavior is linked to their survival. Every day they face tough challenges: avoiding predators, finding food, shelter and a mate. The daily routine creates a need for animals to learn alternative and diverse behavioral strategies, in which events must be studied, selected and somehow connected for future decision making. Inconsistencies in these processes caused by captivity (lack of intellectual stimulation, lack of social contact, reduced physical activity) have a profound effect on the physiological, cognitive and emotional state of the animals, affecting their survival (Fehlmann et al., 2020). For example, many captive orcas have been found to suffer from pneumonia, kidney and gastrointestinal disease, and various infections (Marino et al., 2020). Scientists also report numerous attempts by the animals to cope with captivity through stereotypical, aimless habits. For example, constant nodding of the head and constant wiggling or chewing of the rod of the cell have been observed in laboratory rhesus monkeys, which are not only abnormal behaviors but also directly correlate with brain abnormalities (Poirier and Bateson, 2017).

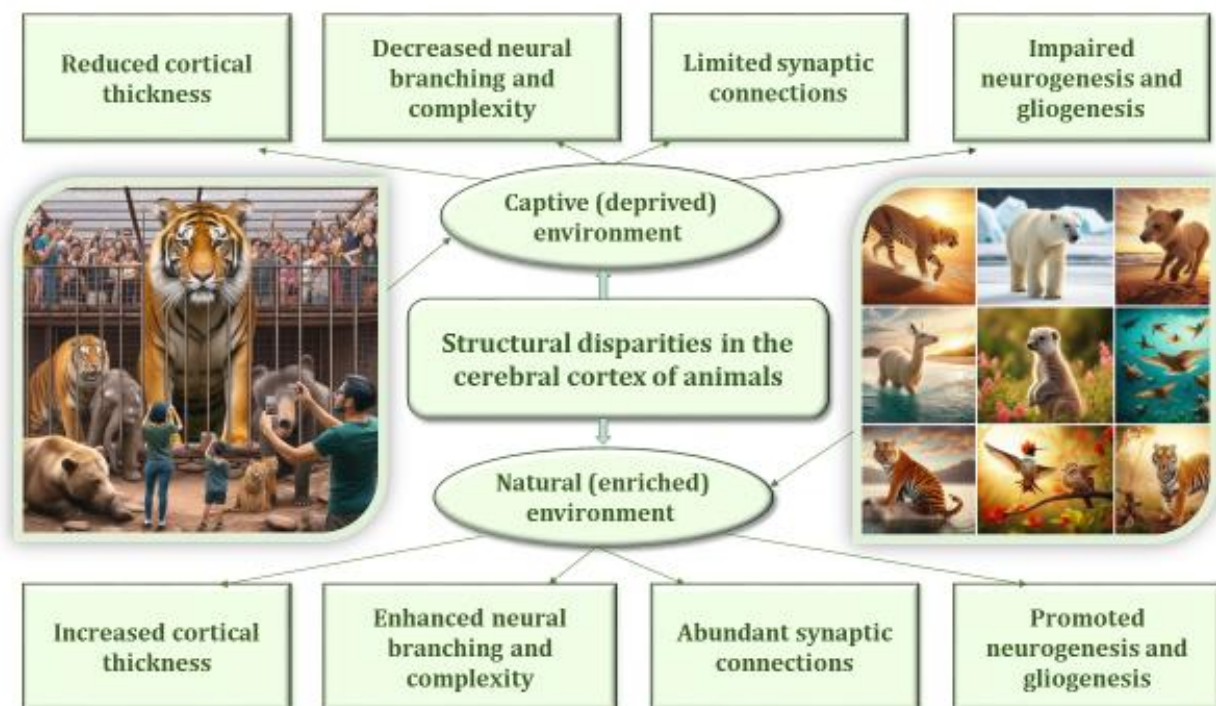


Fig. 2. Differences in the structure of the cerebral cortex in animals kept in deprived (captive) and enriched (natural) environments

For example, laboratory mice with various neurodegenerative diseases were placed in enriched conditions, i.e. conditions with sensory, cognitive and motor stimuli (rich and varied diet, cells). The mammalian brain is formed through the implementation of complex genetic and epigenetic programs. However, sensory, cognitive and motor stimulation through interaction with the environment from birth to old age also plays a key role in the formation of neural circuits necessary for normal brain function. In recent decades, genetic and pharmacological factors modulating brain function and dysfunction have been extensively studied, while environmental parameters have received much less attention (Mayeux, 2003). Without intellectual stimulation and social interaction, the cerebral cortex – the part of the brain responsible for higher cognitive activity, including memory, planning and decision-making – becomes thinner, the capillaries narrow and the brain does not receive enough blood to function normally. A thinner cerebral cortex, the part of the brain involved in voluntary movement and higher cognitive function, can lead to poor decision-making and memory. Neurons become smaller, as do dendrites, which disrupts communication within the brain. This means that captive animals are less effective at processing information. The chronic stress of living in captivity with no control over their environment leads to learned helplessness, a trauma response that affects the hippocampus, which handles memory functions, and the amygdala, which processes emotions. As a result, a captive animal's memory and emotions are irregular, and some animals have been shown to become emotionally unpredictable. Prolonged stress also disrupts the balance of serotonin and dopamine in an animal's brain, which can lead to repetitive and often harmful behaviors. The main change is that animals lose some of their natural behaviors, such as foraging, avoiding predators and rearing young, and replace them with stereotyped, destructive behaviors brought on by chronic stress and boredom. These new behaviors, such as gnawing on bars and running headlong into walls, are often self-destructive. They also show a marked difference between a captive animal and its wild relatives (Haslam, 2013; Tuite et al., 2022).

The lack of a sufficiently stimulating natural environment also has a significant impact on neuroplasticity – the ability of the nervous system to regenerate by increasing the number of neurons and restructuring neural networks, creating new synapses and altering synaptic transmission, which underpins adaptive behavior (McEwen et al., 2015; Been et al., 2022). In other words, repetitive actions, strong emotional influences or stimuli, including negative ones, can cause structural changes in neurons, affecting the appearance of so-called "dendritic trees" and neural bridges, which are

directly related to the number of synapses and brain performance. It is known that each of the 86 billion neurons in the brain is capable of forming about 10,000 synapses simultaneously. However, this potential depends solely on the number and intensity of stimuli to induce structural changes in neurons with subsequent behavioral changes (Davim et al., 2021). The formation of new synapses is extremely important because it allows animals to change behavioral strategies that are essential for survival.

One of the most prominent approaches to identifying key experience- and environment-related changes in brain structural and functional plasticity is the use of the so-called enriched (multi-stimulus) environment (EE) (Ward and Cohen, 2004). EE can be defined as an environment that contains a variety of social and non-social stimuli that influence different aspects of brain development and function. This definition implies that the importance of any one factor cannot be neutralized and that the combined effect of several factors of different types ensures the formation of a biological response that cannot be achieved by the action of any one factor alone (Rosenzweig and Bennett, 1969). The aim of EE is to maximize the brain's potential by organizing the space in which the organism exists so that it is more complex, interactive and rich in events similar to real life, thus offering a greater variety of possibilities to control this environment and reduce or prevent cases of abnormal behavior and cognitive impairment (Hannan, 2014; Cutuli et al., 2022) with mazes, running wheels, toys, increased social interactions), showed significant positive dynamics of brain activity, qualitative structural changes, i.e. slowing down the onset and progression of the motor disorder syndrome, the process of reducing the volume of the cerebral cortex, a deficiency in the expression of β -amyloid peptide (leading to the death of neurons), improved performance in problem-solving tasks, an increase in the number of dendritic branches, expression of the GluR1 protein, which plays an important role in the formation of the neural network underlying normal motor behavior (Nithianantharajah and Hannan, 2006).

Thus, laboratory mice with various neurodegenerative diseases placed in enriched conditions, i.e. conditions with sensory, cognitive and motor stimuli (rich and varied diet, cells equipped with mazes, running wheels, toys, increased social interactions), show significant positive dynamics of brain activity and qualitative structural changes, such as delayed onset and progression of motor disorder, deficiency of β -amyloid peptide expression.

EE may contribute to neuronal activation, signaling and plasticity in different areas of the brain. Increased sensory stimulation, including an increase in somatosensory and visual information,

activates the somatosensory (red) and visual (orange) cortices. Increased cognitive stimulation – for example, encoding information (the ability to turn information into a concept, an image stored in the brain that can then be retrieved from long-term memory) related to spatial mapping, object recognition, novelty and attention modulation – is

likely to activate the hippocampus (blue) and other cortical areas. In addition, increased motor activity, such as natural exploratory movements (including fine movements that are radically different from simply riding a bike), stimulates areas such as the motor cortex and cerebellum (green) (Fig. 3).

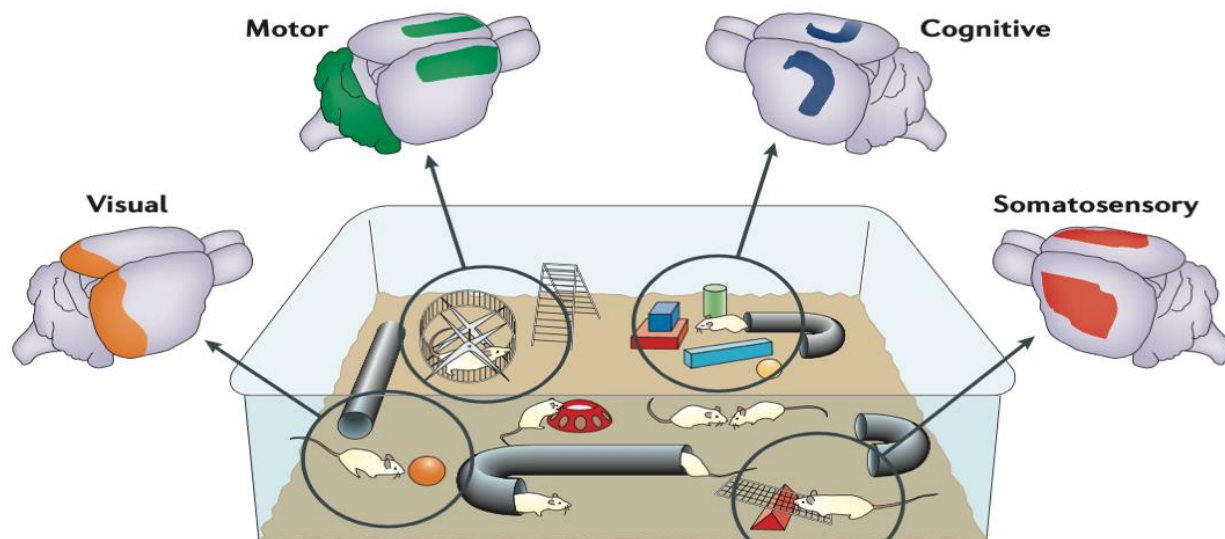


Fig. 3. Effects of EE and enhanced sensory, cognitive and motor stimuli on different brain regions (<https://sites.oxy.edu/>)

The key components of EE are physical activity, socialization and cognitive stimulation. Although the efficacy demonstrated in animals with EE is quite high, it remains largely a laboratory phenomenon with little use in clinical settings, for example in patients with severe brain damage (stroke) or mental retardation, because of difficulties in standardizing methods, introducing control groups, lack of data on which aspects are critical for improving brain plasticity, and the wide range of responses to therapy. It is not known how long an intervention should last or what the necessary 'dose' of enrichment is, as most laboratory studies use continuous enrichment periods – a condition that most clinicians consider inappropriate (Hummel and Cohen, 2005; McDonald et al, 2018; Ball et al, 2019).

Relationship between neurons and glia in an enriched environment

The relationship between neurogenesis and the intricate interplay between neurons and glial cells within an EE is a fascinating area of study in neuroscience. The dynamic process of neurogenesis, the generation of new neurons, interacts in a complex manner with the supporting role of glial cells, including astrocytes and oligodendrocytes (Nilsson and Pekny, 2007). This chapter aims to explore the multiple links between these elements within EE, looking at how environmental factors

affect the differentiation and integration of neurons, while also influencing the functions of glial cells. By examining these interactions, we aim to gain a deeper understanding of the complex mechanisms underlying brain plasticity in the context of EE. Neurogenesis in the developing or mature brain is one of the most attractive targets for the action of environmental factors that regulate neuroplasticity processes (Hummel and Cohen, 2005; Decimo et al., 2012). The debate on the effect of EE on the number of cells in the adult brain has a long history. In 1964, J. Altman and G. D. Das, who first described neurogenesis in the adult hippocampus (Altman and Das, 1964), investigated whether EE could affect the generation of neurons. However, they only found an increase in the processes of gliogenesis (Altman and Das, 1964). Subsequent studies showed that the increase in glial cell numbers was associated with oligodendrocytes and a slight increase in astrocytes in EE animals (Walsh and Cummins, 1975; Kempermann et al., 2002). EE, like exercise, helps to increase the number of new neurons in the dentate gyrus. However, the mechanisms by which new cells are generated may differ between the two conditions. EE mainly affects cell survival rather than cell proliferation. In contrast, isolated running activity stimulates both cell division and neuronal survival in mice (van Praag et al., 2000; Mohammed et al., 2002). Interestingly, EE without high motor activity only slightly stimulates hippocampal neurogenesis

(Clark et al., 2009; Mustroph et al., 2012), whereas the use of treadmills in socially and physically deprived mice promotes more intense cell proliferation in the dentate gyrus than in EE mice (Bednarczyk et al., 2009; Schaefer, 2013).

Early experiments showed that enrichment increased neurite branching and synapse formation in the cortex (Greenough et al., 1985), and animals kept in EE conditions showed a higher order of dendritic arborization than the control group (Greenough et al., 1985). Subsequent studies found that environmental enrichment decreased neuronal density but increased the synapse/neuron ratio, synaptic disc diameter and subsynaptic plate openings (Greenough et al., 1985). In the hippocampus, similar morphological changes were characteristic of granular neurons in the dentate gyrus and pyramidal cells in CA1 and CA3 areas. Recently, a large number of dendritic spines and an increased density of imperforate synapses were found in the CA1 region after enrichment (Rampon et al., 2000). EE was found to promote neurogenesis only in the dorsal hippocampus. These results suggest that environmental factors may differentially regulate neurogenesis in region-specific areas. This phenomenon is thought to underlie the heterogeneous functions of newborn neurons along the septotemporal axis of the hippocampus, which has functional implications (Rampon et al., 2000; Petrosini et al., 2009).

Studies of enrichment-induced plasticity have traditionally focused on changes in neurons, particularly their synaptic function. However, the effects of EE on glial cells are no less important. There is a growing body of data on the response of astroglia to EE. Given the important role of astrocytes in the regulation of neuronal activity through the implementation of the mechanism of neuron-astroglial metabolic coupling, ensuring neurogenesis and the mechanisms of so-called gliovascular control in active zones of the brain, the presence of such an influence is quite predictable. For example, EE promotes a significant increase in the number of astrocytes in the dentate gyrus, but not in the CA1, CA3 areas of the hippocampus or cortex (Rampon et al., 2000). It has long been known that astrocyte morphology changes in response to EE. The changes depend on the duration of EE exposure and the localisation of the astrocyte pool in the brain (Markham and Greenough, 2004; Tanti et al., 2012). Morphological plasticity of astrocytes in response to EE occurs on a similar time scale to changes in neurons. Other studies support a strong correlation between changes in astrocyte morphology and synapse formation, highlighting the synergy between neurons and astrocytes within and around a synapse (Ullian et al., 2001). In general, one of the

important targets of EE action is neuron-astroglial interactions, which ensure the efficiency of synaptic transmission, the adequacy of energy supply to neurons and the local adaptation of blood flow (Hummel and Cohen, 2005; Halassa et al., 2007).

Structural and functional changes in the brain after exposure to EE in experimental animals are impact on (Fig. 4).

Behavior

Exposure to an EE can improve learning and memory, prevent memory decline in adults, reduce anxiety and increase exploratory activity (Kempermann et al., 2002; Friske and Gammie, 2005; Bennett et al., 2006). However, later studies found that the activity of mice after 8 weeks of EE was comparable to that of humans under standard conditions. It has also been noted that changes in anxiety and seeking activity appear to be independent of neurogenesis in the hippocampus (Silva et al., 2011).

Exposure to an EE can lead to various behavioral changes, particularly in animals. Animals exposed to EE often show increased levels of exploration and curiosity. They may actively seek out new stimuli and environments in their surroundings. EE can enhance cognitive abilities, leading to improved learning and memory. This is often seen in tasks such as maze navigation or object recognition. EE with stimulating activities and social interactions can reduce stress and anxiety levels in animals. This can lead to calmer and more relaxed behavior. EE typically provides opportunities for physical activity, such as running wheels or climbing structures. As a result, animals may engage in more physical activity, leading to improved physical health and fitness. EE have also been associated with increased neurogenesis (the formation of new nerve cells) and increased brain plasticity. This may lead to improved brain function and adaptability. In addition, exposure to EE has been associated with a delay in age-related cognitive decline in animals. This suggests that continued exposure to stimulating environments may help maintain cognitive function into old age (Friske and Gammie, 2005; Bennett et al., 2006; Takuma et al., 2011; Kempermann, 2019).

Structural changes. Exposure to an EE can induce several structural changes in the brain, particularly in regions associated with learning, memory and sensory processing. One of the most notable structural changes is an increase in neurogenesis, which refers to the generation of new nerve cells. EE has been shown to promote neurogenesis in regions such as the hippocampus, a brain area critical for learning and memory (Almeida Barros et al., 2021).

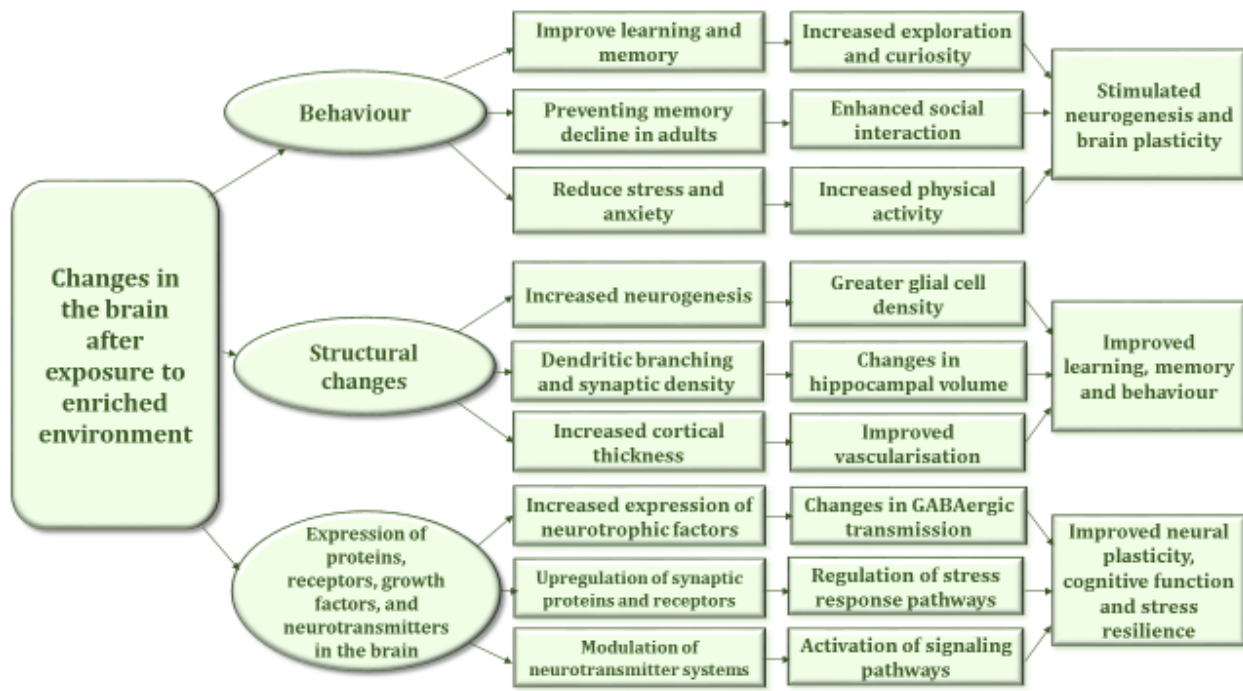


Fig. 4. Structural and functional changes in the brain after exposure to enriched environments

EE can lead to increased dendritic branching and synaptic density in neurons. Dendrites are the branching extensions of neurons that receive signals from other neurons, and synapses are the connections between neurons where information is transferred. Increased dendritic branching and synaptic density are associated with improved neural connectivity and information processing (Bindu et al., 2007). Exposure to EE has been associated with an increase in cortical thickness, particularly in regions involved in sensory processing and higher cognitive functions. This structural change may reflect increased neural connectivity and complexity in response to environmental stimuli (Alvarez et al., 2014). Glial cells, including astrocytes and oligodendrocytes, provide support and insulation for neurons in the brain. EE has been associated with an increase in glial cell density, which may contribute to maintaining neuronal health and function (Bhide and Bedi, 1984). EE has been shown to increase the volume of the hippocampus, a brain structure critical for learning and memory. This increase may be due to a combination of factors, including neurogenesis, dendritic growth and synaptic plasticity (Miguel et al., 2019). EE can promote the growth of blood vessels in the brain, a process known as vascularization. Improved vascularization can increase blood flow to brain regions, providing nutrients and oxygen essential for neuronal function and plasticity (Chen et al., 2023).

Exposure to an EE can reduce the intensity of spontaneous apoptosis, increase the intensity of

neurogenesis and the integration of new cells into functional circuits, increase brain weight, cortical and hippocampal thickness, dendritic branching, length and density, synaptic size and number, and the number of dendritic spines (van Praag et al., 2000; Johansson and Belichenko, 2002; Leggio et al., 2005). There is a marked increase in cell proliferation and cell survival in the early postnatal period, with a large increase in the number of neurons forming the granule cell layer (Rizzi et al., 2011). A reduced pro-inflammatory response to lipopolysaccharide injection into the hippocampus was also observed. There was also a significant reduction in the levels of the chemokines TNF and the inflammatory cytokine IL 1 β (Williamson et al., 2012). There was an increase in the strength of synaptic contacts and modulation of synaptic plasticity, such as long-term potentiation (LTP), an increase in the slope of the excitatory postsynaptic potential (EPSP) and an increase in the potential from the hippocampal region (Foster and Dumas, 2001; Artola et al., 2006).

Expression of proteins and receptors, growth factors, neurotransmitters. Exposure to an EE can lead to significant changes in the expression of proteins, receptors, growth factors and neurotransmitters in the brain. These changes play a critical role in neural plasticity, learning, memory and overall brain function. Neurotrophic factors such as brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF) and others are critical in promoting neuronal survival, growth and diffe-

rentiation. Exposure to EE often results in increased expression of neurotrophic factors, which in turn promotes neurogenesis, dendritic arborization and synaptic plasticity (Falkenberg et al., 1992). EE can increase the expression of proteins involved in synaptic function, including neurotransmitter receptors (e.g. glutamate receptors such as NMDA and AMPA receptors) and synaptic scaffolding proteins (e.g. PSD-95). This upregulation is associated with increased synaptic strength and efficacy (Cai et al., 2010; He et al., 2010). EE can affect the activity and expression of several neurotransmitter systems. For example, exposure to EE has been shown to increase the release of neurotransmitters such as dopamine, serotonin and acetylcholine, which are involved in the regulation of mood, motivation and cognitive function (Saadati et al., 2023). EE can also modulate the activity of gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the brain. Changes in GABAergic transmission can affect neuronal excitability and synaptic plasticity, contributing to adaptive responses to environmental stimuli (Sbrini et al., 2020). EE has been shown to modulate stress response pathways, including the hypothalamic-pituitary-adrenal (HPA) axis and the expression of stress-related proteins such as corticosterone and corticotropin-releasing hormone (CRH). These changes may help to mitigate the effects of stress and promote resilience (Ros-Simó and Valverde, 2012). Exposure to EE activates several intracellular signaling pathways involved in synaptic plasticity and neuronal survival, including the mitogen-activated protein kinase (MAPK), phosphoinositide 3-kinase (PI3K)/Akt and cyclic AMP (cAMP) pathways (Horwood et al., 2006). EE can affect gene expression patterns in the brain, resulting in the upregulation of genes associated with neuronal growth, synaptic function and cognitive processes. This regulation of gene expression underlies the

long-term adaptive changes induced by environmental enrichment (Li et al., 2007).

Exposure to an EE led to changes in the expression of genes involved in synaptic transmission and cellular plasticity. An increase in the expression of synaptic proteins (the presynaptic vesicle protein synaptophysin and the postsynaptic density protein 95, PSD-95) was observed. Increased expression of NMDA and AMPA receptors, which are involved in glutamatergic signaling, was also observed. Increased expression of mRNA encoding EGR-1 (or NGF-1A, Zif268) (which regulates angiogenesis) was also observed. An increase in the activity of the transcriptional regulator of endothelial cell activation - Kruppel-like factor (KLF2) - was observed (Rampon et al., 2000; Pascual-Leone et al., 2005; Lambert et al., 2005). An increase in the levels of the main neurotrophic factors (brain-derived neurotrophic factor, BDNF, and nerve growth factor, NGF, glial neurotrophic factor, GDNF) has been observed (Gobbo and O'Mara, 2004). There is an increased secretion of acetylcholine and selective enhancement of serotonin 1A receptor gene expression (Rosenzweig and Bennett, 1969).

Factors that optimize brain function and prevent cognitive decline

Obviously, modern medicine will have to solve several problems before EE therapy can be introduced into clinical practice, but the benefits of this approach are undeniable and its use in everyday life is reasonable. As EE is a complex of inanimate and social stimuli, it is suggested that the approach must be comprehensive and manifest itself in standards of diet, physical activity and social interactions. A number of lifestyle factors and habits can help optimize brain function and reduce the risk of cognitive decline (Fig. 5).

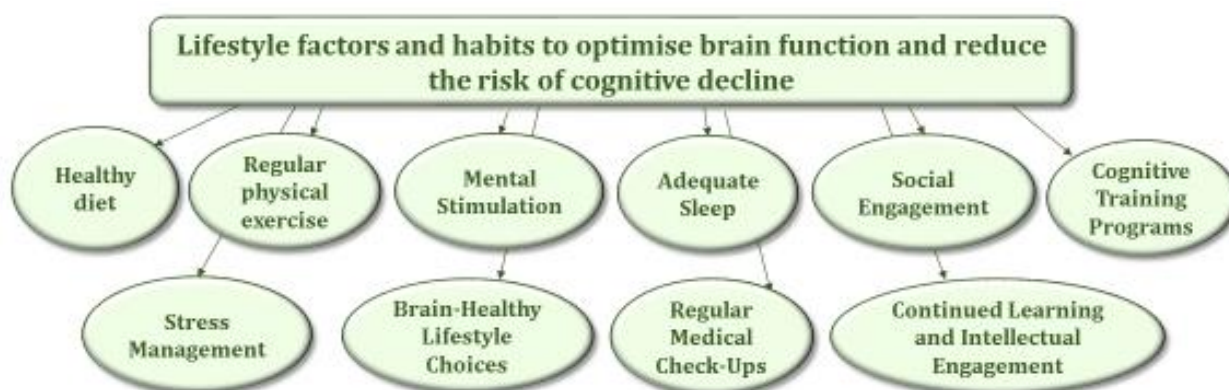


Fig. 5. Factors that optimize brain function and prevent cognitive decline

Adequate nutrition is necessary to optimize brain function and prevent cognitive decline. The brain needs a steady supply of amino acids to synthesize neurotransmitters, especially serotonin and catecholamines, which can correlate with reduced learning ability when levels are low (Fernstrom and Fernstrom, 2007; Martínez García et al., 2018). Adequate nutrition is necessary to optimize brain function and prevent cognitive decline. It is also recommended to consume products with an adequate ratio of omega-6:3 fatty acids (the Mediterranean diet, which includes fruits, vegetables, whole grains, beans, nuts and seeds, olive oil, fish, poultry and dairy products), as they are associated with improved memory and a lower risk of cognitive decline (Bourre, 2004a; Martínez García et al., 2018). Vitamins B1, B6, B12, B9 (folic acid), D, choline, iron and iodine are neuroprotective and have a positive effect on mental performance (Bourre, 2004b, 2006; González and Visentin, 2016; Derbyshire and Obeid, 2020). Antioxidants (vitamins C, E, A, zinc, selenium, lutein and zeaxanthin) play a very important role in protecting against oxidative stress, which is associated with mental decline (González and Visentin, 2016; Demmig-Adams et al., 2020). It is also important to avoid foods rich in saturated fats and refined sugars and to favor fruit and vegetables (Martínez García et al., 2018).

Another EE factor is regular exercise, which stimulates the development of bone and muscle tissue necessary for weight gain (Russo, 2009; Ferraro et al., 2014). Regular exercise improves cardiorespiratory activity, which effectively increases physical performance by improving and accelerating the circulation of oxygen, hormones and nutrients essential for brain metabolism and cognitive development (Nystoriak and Bhatnagar, 2018; Pinckard et al., 2019). Regular aerobic exercise, such as brisk walking, jogging, swimming or cycling, can improve blood flow to the brain, promote neuroplasticity and reduce the risk of cognitive decline. Regular physical activity has an impressive array of health benefits. As well as helping the brain, it can reduce the risk of conditions such as cardiovascular disease (Tian and Meng, 2019), type 2 diabetes (Asano et al., 2014), hypertension (Hegde and Solomon, 2015), colorectal cancer (Oruç and Kaplan, 2019) and breast cancer (García-Chico et al., 2023). Exercise may also have a protective effect against cognitive decline and dementia (Law et al., 2020). People who carry the APOE4 gene variant (which is associated with susceptibility to Alzheimer's disease) may particularly benefit from exercise (Colovati et al., 2020). Recent studies show that regular exercise of at least 30 minutes a day significantly reduces the risk of cardiovascular disease and boosts immunity (Hötting et al., 2016).

Keeping the brain active through mentally stimulating activities such as reading, puzzles,

games, learning new skills or hobbies can help maintain cognitive function and build cognitive reserve, which may protect against cognitive decline (Gómez-Soria et al., 2023). Participating in structured cognitive training programs that target specific cognitive functions (e.g. memory, attention, executive function) can help improve cognitive abilities and delay age-related cognitive decline (Sung et al., 2023). Prioritizing good sleep hygiene and ensuring adequate sleep duration (7-9 hours per night for most adults) is also crucial for cognitive function, memory consolidation and overall brain health. Poor sleep quality and sleep deprivation have been linked to cognitive impairment (Worley, 2018). Brain health and cognitive function can be adversely affected by chronic stress. Practicing stress-reduction techniques such as mindfulness meditation, deep breathing exercises, yoga, or spending time in nature can help mitigate the effects of stress on the brain (Qi et al., 2020). Maintaining social connections and participating in social activities can provide cognitive stimulation, emotional support and a sense of belonging, all of which contribute to brain health and resilience (Miceli et al., 2018). Avoiding smoking, limiting alcohol consumption and managing chronic health conditions such as hypertension, diabetes and obesity are important for maintaining brain health and reducing the risk of cognitive decline (Livingston et al., 2020). Regular monitoring of overall health, including blood pressure, cholesterol, blood sugar and other risk factors for cardiovascular disease, can help identify and manage conditions that may affect brain health (Rippe, 2018). Lifelong learning and intellectual engagement can promote cognitive vitality and help maintain cognitive function as we age, such as taking courses, attending lectures or engaging in intellectually stimulating conversations (Flexman, 2021).

The social isolation caused by the pandemic could affect the structure and function of the brain. One of the areas most affected by chronic stress is the hippocampus (the area of the brain responsible for emotions, memory and learning). Studies have shown that stressors such as job loss or isolation alone lead to increased secretion of glucocorticoids, followed by brain cell damage, synaptic disruption and ultimately a reduction in hippocampal volume and the onset of a depressive state (Snyder et al., 2011). Chronic stress can also alter the prefrontal cortex (the center of executive control in the brain) and the amygdala (the center of fear and anxiety). Long-term exposure to excess glucocorticoids can disrupt connections both within the prefrontal cortex and between it and the amygdala. As a result, the prefrontal cortex loses its ability to control the amygdala, leaving the center of fear and anxiety out of control (McEwen et al., 2016). This pattern of brain activity (overactive amygdala and insufficient connection to the prefrontal cortex) is typical of

people with post-traumatic stress disorder (PTSD), another condition that escalated dramatically during the pandemic (Leistner and Menke, 2020; Thakur et al., 2022). In this case, social enrichment, the active expansion of the network of social interactions, normalizes the destabilized psychological state and qualitatively changes the brain – increasing the volume and number of connections in the prefrontal cortex, amygdala and other areas (Schmälzle et al., 2017).

Conclusions

Maximizing brain potential through environmental enrichment is a multifaceted approach that emphasizes the role of the environment in shaping neural architecture and cognitive function. Environmental enrichment refers to the manipulation of the environment to provide sensory, cognitive and social stimulation that promotes neural growth and cognitive function. The concept of environmental enrichment originated from research in laboratory animals, which showed that enriched environments led to structural and functional changes in the brain. These changes include increased dendritic arborization, synaptogenesis, neurogenesis and enhanced synaptic plasticity. The basic idea is that exposure to diverse stimuli and challenges causes the brain to constantly adapt and rewire itself, resulting in improved cognitive abilities and resilience to neurological disorders. Environmental enrichment holds promise as a non-pharmacological intervention for several neurological and psychiatric conditions. In clinical settings, structured enrichment programs tailored to specific populations, such as those with autism spectrum disorders, attention deficit hyperactivity disorder (ADHD) or traumatic brain injury, can complement traditional therapies and improve outcomes. By harnessing the inherent plasticity of the brain, environmental enrichment offers new avenues for rehabilitation and recovery.

Behavioral changes induced by EE are often attributed to the complex interplay between

environmental stimuli, neural activity and genetic factors. Enriched environments provide opportunities for sensory, cognitive and social stimulation that can have profound effects on behavior and brain function. Structural changes in the brain exposed to EE reflect the brain's remarkable ability to adapt to environmental experiences, a phenomenon known as neuroplasticity. EE provides a variety of sensory, cognitive and social stimuli that promote neural growth, connectivity and function, ultimately leading to structural changes that support improved learning, memory and behavior. Overall, exposure to EE induces a complex cascade of molecular and cellular changes in the brain that ultimately lead to improved neural plasticity, cognitive function and resilience to stress. These molecular changes provide the neurobiological basis for the beneficial effects of EE on brain health and function.

Some key factors that can optimize brain function and help prevent cognitive decline are exercise, a Mediterranean diet, protection against chronic inflammation, moderate alcohol consumption, prioritizing quality sleep, staying mentally active and socializing. By incorporating many factors into daily life, such as a healthy diet, regular physical activity, mental stimulation, adequate sleep, stress management, social engagement, brain-healthy lifestyle choices, cognitive training programs, regular medical check-ups, continued learning and intellectual engagement, individuals can optimize brain function, promote cognitive health and reduce the risk of cognitive decline as they age.

In conclusion, EE, which has been shown to be effective in producing positive behavioral and cognitive changes in animals, although not yet available for widespread clinical use, holds great promise for ensuring the well-being of human populations in environments with low cognitive, motor and sensory stimulation, such as after the COVID-19 pandemic.

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