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Neuroecological links of the exposome and One Health

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Abstract

This NeuroView assesses the interplay between exposome, One Health, and brain capital in health and disease. Physical and social exposomes affect brain health, and green brain skills are required for environmental health strategies. We addressed current gaps and strategies needed in research, policy, and technology, offering a roadmap for stakeholders.

eTOC blurb

This work explores how exposome, One Health, and brain capital intersect, calling for transdisciplinary strategies. It focuses on how environments influence brain health and stresses green skills, proposing a roadmap for advancing research, policy, and tech solutions for health resilience.

Keywords

Exposome; neuroscience; One Health; United Nations; brain capital; neurology; mental health

Introduction

The escalating environmental and social challenges underscore the imperative need to understand their impacts on brain health and sustainability ¹. This NeuroView examines the interplay between environmental factors of the exposome, ecological approaches to health (or One Health), and the new concept of brain capital, highlighting their joint importance in shaping the future of research and public health. Exposome ² refers to all the environmental exposures individuals encounter throughout their lifetime, offering a

comprehensive framework for understanding the external factors that influence brain health and disease. Meanwhile, the One Health approach, recognizes the inseparable connections between human, animal, and environmental health³. The One Health approach provides a multidisciplinary strategy to tackle complex issues such as zoonotic diseases (transmitted between animals and humans), food safety, antimicrobial resistance, environmental contamination, and the health impacts of climate change¹. The brain capital⁴ is a new economic asset that prioritizes, integrates, and optimizes human skills (e.g., resilience, creativity, wisdom), including green skills. It encompasses the social, emotional, and the diversity of cognitive brain resources of individuals and communities. Brain Capital is fundamental to understanding the human contribution to the economy and how economic factors, in turn, shape our lives. Green skills are a set of knowledge, abilities, values, and attitudes needed to live in, develop, and support a sustainable and resource-efficient society⁵. Creativity, ecological intelligence, and digital literacy are green skills that constitute critical mindsets for the transition to a low-carbon, resource-efficient economy. Such a shift requires systemic changes involving individuals, institutions, and societies.

Here we first outline how environmental and social determinants within the exposome affect brain health. We address how integrating One Health strategies can mitigate these impacts and explore the role of brain capital in fostering resilience, green skills, and advancing public health initiatives. Then, we tackle the current gaps in research, public policy, and technological development by envisioning future short- and long-term strategies. We underscore the urgency of adopting holistic and transdisciplinary approaches in neuroscience to safeguard brain health in the face of environmental and social challenges.

The exposome and its relevance to One Health

Both the physical environment and the societal structures impact brain and environmental health. The exposome² extends beyond the genetic predispositions to encompass every external exposure an individual encounters throughout their life, including pollutants, dietary factors, lifestyle choices, and socioeconomic circumstances⁶.

Physical exposome and brain health

Physical exposome includes environmental factors such as air and water pollution, and exposure to plastics, heavy metals, and other toxic substances². These factors have been shown to profoundly affect overall health, specifically the brain, influencing the development, progression, and risk of diseases⁷.

Pollutants like fine particulate matter, nitrogen dioxide, and volatile organic compounds found in air pollution have been linked to neurodevelopmental delays and increased risk for autism and attention deficit disorders in children and adolescents, and to cognitive decline and an increased risk of Alzheimer's disease, Parkinson disease, amyotrophic lateral sclerosis, and related disorders in late adulthood. Heavy metals such as lead, mercury, and arsenic, even at low levels of exposure, can disrupt brain development in children, leading to attentional deficits, reduced cognitive reserve, and behavioral problems. Plastics, particularly those that release bisphenol A and phthalates, have been implicated in neurodevelopmental disorders⁸. Recent studies have highlighted the alarming ability of micro- and nano-plastics

to cross the blood-brain barrier in animal models, a protective shield designed to keep harmful substances away from the brain ⁵. Once these plastics infiltrate the brain, they can induce behavioral changes, trigger inflammation, and activate pathways that may lead to neurodegenerative diseases. Altogether, this evidence points to a potential hazard to human health and the need to focus research efforts to study these associations further.

The social exposome and brain health

The social exposome encompasses aggregate- and individual-level factors related to disparity and inequality ^{2,9}. Research has shown that stress-related pathologies, including depression and anxiety, are more prevalent in populations facing aggregate levels of social and economic disparities. Measures such as the Gini coefficient or the Human Development Index (HDI) provide a broader context for understanding how societal structures can influence health outcomes, including those related to the brain burden ^{5,7}. These structural inequalities, reflected in disparities in income, education, and access to healthcare, further contribute to a broader range of health disparities at multiple levels. Individuals from disadvantaged backgrounds also experience chronic stress, poor nutrition, and limited access to healthcare, all of which can impair brain health. Social determinants of health (SDH), socioeconomic status (SES), education, access to healthcare, and exposure to stressors like discrimination and violence are also individual-level factors that impact brain health ^{7,9}, influencing the development of psychiatric and neurological diseases and also the resilience and capacity of the brain to cope with stress and injury.

Integrating external (physical and social) and internal exposomes

Brain diseases result from complex interactions between the external exposome and internal vulnerability factors ^{1,6}. The internal exposome also includes biological factors (i.e., microbiome) that play a significant role as both an internal and external influence on brain health. Environmental toxins can exacerbate the effects of social stressors ^{2,8}, while socioeconomic factors can influence an individual's exposure to environmental hazards. These inequalities, in turn, can negatively impact the environment in the long term, creating a vicious circle that threatens all health ^{2,5}. The exposome also affects brain health via epigenetic modifications, i.e., alterations in chromatin organization that do not change the genetic makeup but play an essential role in the modulation of gene expression. Epigenetic regulation of gene expression (EpiRegulome), mainly via DNA methylation (DNAm) and microRNAs (miRNA), is influenced by the environment and predisposed by biological constraints. These create a feedback loop of maladaptive stress response, such that exposure to further stress causes additional and more severe cellular abnormalities, eventually leading to brain system dysfunction and the manifestation of disease symptoms such as abnormal behavioral and emotional regulation ⁶.

The exposome may have specific early effects on development. Due to their rapid brain development, immature immune systems, and social dependence on caregivers, children, especially those from marginalized communities, are especially vulnerable to physical and social exposomes. Early exposure to extreme weather events and pollution has been linked to increased incidence of anxiety, depression, PTSD, educational shortcomings, diminished

self-regulation, and psychiatric disorders in later life. Even if the exposure happens at a very early stage, the neurodevelopmental impact of these exposures can be lifelong, resulting in a lifetime of suffering for both children and their families.

Given the high complexity and interrelationship, approaches that tackle one or other aspects in isolation fall short. Transdisciplinary approaches are needed to address brain health's physical, environmental, and social factors, paving the way for long-term and multi-level interventions ^{6,7}. Researchers and policymakers can develop more effective strategies for preventing and treating brain diseases with synergetic and syndemic approaches integrating environmental, whole-body health, and brain levels ^{1,6}.

Brain capital: from science to practice

The brain capital underscores the critical importance of cognitive-emotional resources and mental wealth in driving economic and societal progress ⁴. Moreover, green skills, part of the brain capital, are essential to developing long-term strategies for improving environmental health ⁵. Sustainability and technology benefit mental health while fostering eco-friendly lifestyles for physical and mental wellbeing. Such skills in the workforce help cut waste, emissions, and toxic substance use, protecting health and the environment. Ecosystem skills boost biodiversity and water quality, contributing to climate resilience and essential health services like disease control. These skills are critical in One Health, for example by reducing pollution and zoonotic diseases.

Neuroscience insights into public policy and practice emphasize the need to invest in brain health across the lifespan. Global leaders and stakeholders are beginning to recognize and act upon the interconnections between brain health, environmental exposures, and societal wellbeing through initiatives and projects launched at international forums such as the United Nations General Assembly (UNGA) and the World Economic Forum. One of the significant developments is the anticipation of the Global Plastics Treaty, which addresses the scourge of plastic pollution ⁸. These international public-private partnerships can tackle environmental challenges that directly and indirectly impact brain health ^{3,8}. By reducing exposure to harmful pollutants found in plastics, which are part of the physical exposome, the treaty has the potential to mitigate neurotoxic risks and, thereby, promote global brain health. Green skills promoted by brain capital can influence the behavioral changes required to develop sustainable and prosocial behaviors. Such transdisciplinary interaction follows the principles of One Health ³, which advocates for a holistic approach to protecting the health of people, animals, and the environment. Neither environmental nor social influences can be observed in isolation; instead, they form part of a complex set of factors jointly affecting brain health.

The linkage between brain capital, the exposome, and One Health is even more foundational in the context of global challenges. Together, these concepts create a powerful narrative for advancing brain health initiatives, underlining the necessity of interdisciplinary strategies that span from science to practice. By leveraging the momentum from international forums and harnessing the potential of agreements like the Global Plastics Treaty ⁸, there is a clear

pathway toward reducing environmental risks, enhancing brain capital, and promoting a healthier, more sustainable future for all.

Advocating for change

A new framework for the ecology of minds and environment requires a more integrative view with mutual influence and dependence ¹. A healthy, sustainable environment fosters optimal brain health and, by extension, societal wellbeing and resilience ⁵. More integrated approaches are required to address the impact of environmental and social factors on the brain and recognize the brain's potential to influence ecological outcomes through behavior, innovation, and policy. For this, a more significant synergy is required between the perspectives and expertise of a diverse array of stakeholders ¹. Neurologists, psychiatrists, neuroscientists, psychologists, and patient groups offer invaluable insights into the nuances of brain health and disease ⁷. Simultaneously, environmentalists and ecologists bring to the table a deep understanding of ecological dynamics and the threats posed by pollutants, such as plastics, to both the environment and human health. By uniting these diverse perspectives, a comprehensive and multifaceted approach to policymaking can emerge, effectively addressing the complex links between the brain, health, and the environment ⁴.

This collaborative taskforce necessitates a robust call to action for the neuroscience community to support global initiatives actively. Such support emphasizes the critical importance of reducing environmental risks to brain health and commitment to broader One Health initiatives ³. The health and scientific community can drive significant change, influencing policies that mitigate the adverse effects of the exposome and championing a holistic approach to health and environmental stewardship. This collective action is essential for building a sustainable future where brain health is recognized as a core component of global health and wellbeing, highlighting the indispensable role of an environmentally conscious and proactive brain health community in shaping the policies of tomorrow.

Addressing the current gaps by envisioning future strategies

The complex interplay of the exposome, brain health, and the ecological context calls for tackling research, public, and practice gaps ⁵. Bridging these gaps requires short (0–5 years) and long (5–15 years) efforts across disciplines, leveraging new technologies and interdisciplinary approaches to deepen our understanding and enhance our capacity for effective intervention (Box 1).

A primary research gap lies in the need for longitudinal studies that can more definitively map the causal relationships between specific exposome components (e.g., microplastics and smaller nanoplastics, which because of their size, are more likely to cross biological barriers) and brain health outcomes ⁶. Such studies would benefit from integrating advanced biomonitoring technologies capable of tracking individual exposures with unprecedented precision and granularity ¹⁰. Many communities suffering from sociodemographic disparities are also at risk for increased environmental stressors from global climate change. New research needs to engage these communities mainly regarding inclusivity and ecological justice. Additionally, there is a crucial need for research

that transcends traditional disciplinary boundaries⁷, combining insights from neurology, epidemiology, environmental science, and social sciences to holistically understand the impacts of the exposome on brain health^{2,6}. Projects like the Healthy Brain Network, which aims to create a comprehensive database of brain development in children by combining genetic, cognitive, and environmental data, exemplify the power of interdisciplinary research⁷. Similarly, the ENIGMA-Environment (ENIGMA-ENV) groups aims to elucidate how environmental exposures impact brain and behavior, as well as the biological underpinnings of environmental risks for various disorders.

On the public and practice fronts, a significant gap exists in translating research findings into actionable policies and interventions that can mitigate the adverse effects of the exposome on brain health. This gap underscores the need for tighter collaboration between researchers, policymakers, and practitioners to ensure that scientific insights translate into effective public health strategies and regulatory actions. Moreover, there is a pressing need for public education initiatives to raise awareness about the importance of exposome and brain health, empowering communities to advocate for change and adopt healthier lifestyles.

The potential for new technologies to revolutionize our approach to understanding and addressing the exposome and brain health is immense. For instance, satellite and remote sensing data can identify the exposome for retrospective exposures from multiple years earlier¹¹. Wearable sensors and smartphone applications can provide real-time data on individual exposures and health outcomes, facilitating more personalized health monitoring and interventions¹⁰. Extensive cohort data are required for research, spanning different age groups from pre-conception onwards and varying environmental and social exposures. Data integration, dimension reduction, and stratification into subgroups will pose a significant challenge, given the diversity of data sources. Artificial intelligence offers powerful tools for analyzing the vast datasets generated by such technologies, uncovering patterns, and making optimal predictions and inferences that can guide public health strategies and individual behaviors. Further development of biostatistical models will be required to detect associations with psychopathology and develop biomarkers.

Transdisciplinary approaches are equally vital, as they allow for the integration of diverse perspectives and expertise in tackling the complex challenges at the intersection of environmental exposures and brain health. One promising example is the collaboration between environmental scientists and neuroscientists to study the impacts of air pollution on neurodevelopment and cognitive aging. Similarly, partnerships between technologists, health professionals, and urban planners can lead to designing “smart” cities that minimize harmful exposures and promote brain health through green spaces, pollution control, and community resources.

Conclusions

Understanding and mitigating the impact of the exposome on brain health is challenging and fraught with complexities⁶. Yet, new technologies and transdisciplinary collaborations offer unprecedented opportunities to advance more integrative knowledge and develop effective interventions. By prioritizing research that bridges existing gaps, embracing innovative

technologies, and fostering transdisciplinary partnerships, we can pave the way for a future where the relationships between our environment, our brains, and our health are effectively managed to promote wellbeing and resilience in the face of changing global landscapes.

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Box 1.**Paths for future synergetics of environment and brain health****Research****Short-term actions (0–5 years):**

- Advanced biomonitoring technologies and decentralized capacity building for real-time tracking of exposome factors.
- Large-scale longitudinal studies to understand the immediate effects of exposome components on brain health in animals and humans.
- Global biobanks to store environmental-related biological samples for exposome research.

Long-term actions (5–15 years)

- Causative relationships between exposome components and brain health and disease.
- Translate findings into predictive models for brain health outcomes.
- Personalized intervention strategies based on exposome data.

Public Policy**Short-term actions (0–5 years)**

- Identify components of exposome research that allow actionable public health strategies and regulatory policies.
- Educational programs to increase public awareness of the exposome and brain health.
- International exposome-related policy development.
- Transdisciplinary-based training for neuroscientists.

Long-term actions (5–15 years)

- Enact global policies and agreements, such as the Global Plastics Treaty, to reduce harmful exposures.
- Integrate exposome considerations into urban implementations and building regulations and consider tailored approaches encompassing the more extensive diversity and inequalities across different nations.
- Monitor and evaluate the effectiveness of these new policies.

Technology**Short-term actions (0–5 years)**

- Integrate wearable sensors and other IoT devices for personal health monitoring related to the exposome.
- Employ AI for data analysis and pattern recognition in exposome research.

- Use AI to predict the most vulnerable communities and create appropriate mitigation and prevention strategies
- Guarantee an adequate regulatory framework tailored to different nations and regions.

Long-term actions (5–15 years)

- Achieve widespread use of AI for comprehensive and ongoing data analysis, including predictive analytics for brain health.
- Develop and implement smart city technologies that reduce harmful environmental exposures.

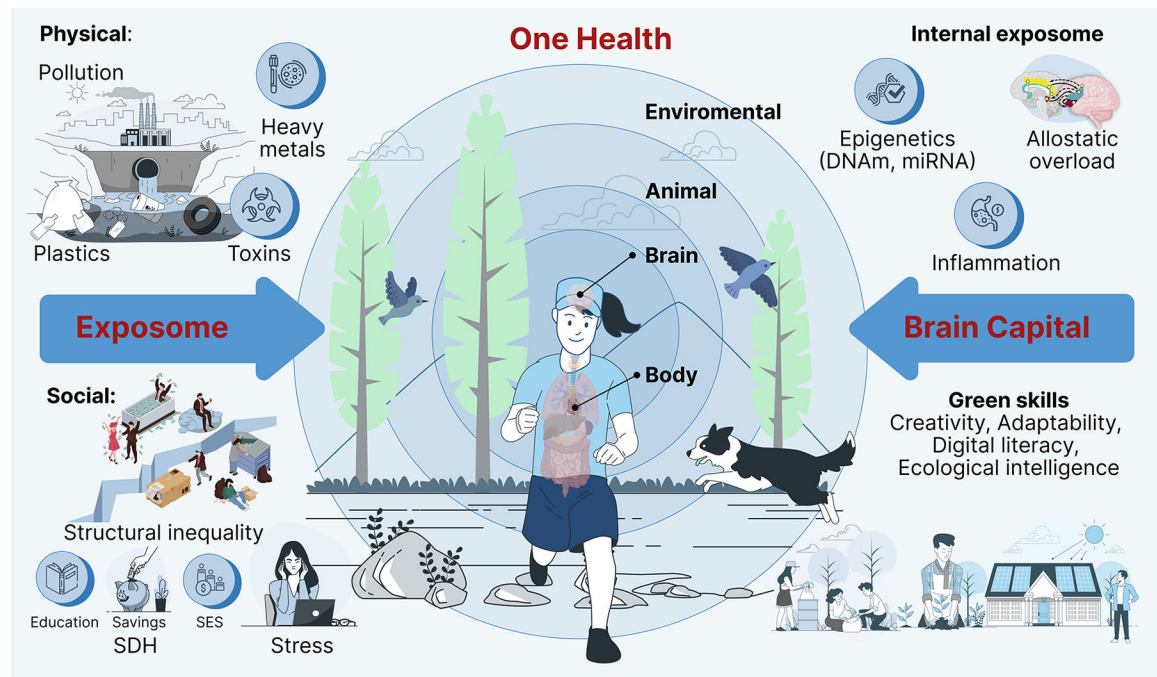


Figure 1. Brain-environmental interactions and One Health.

The figure illustrates a framework connecting the exposome, One Health, and brain capital. The left panel displays the exposome, encompassing both physical and social dimensions. The exposome impacts the One Health approach (center panel), highlighting the links between brain, body, animal, and environmental Health. The brain capital (right panel) emphasizes the bipartite components of the internal exposome and green skills for envisioning critical actions to improve One Health. SES: socioeconomic status; SDH: social determinants of health; DNAm: DNA methylation; miRNAs: microRNAs