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Perspective

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Global synergistic actions to improve brain health for human development

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Abstract

The global burden of neurological disorders is substantial and increasing, especially in low-resource settings. The current increased global interest in brain health and its impact on population wellbeing and economic growth, highlighted in the World Health Organization's new Intersectoral Global Action Plan on Epilepsy and other Neurological Disorders 2022–2031, presents an opportunity to rethink the delivery of neurological services. In this Perspective, we highlight the global burden of neurological disorders and propose pragmatic solutions to enhance neurological health, with an emphasis on building global synergies and fostering a 'neurological revolution' across four key pillars — surveillance, prevention, acute care and rehabilitation — termed the neurological quadrangle. Innovative strategies for achieving this transformation include the recognition and promotion of holistic, spiritual and planetary health. These strategies can be deployed through co-design and co-implementation to create equitable and inclusive access to services for the promotion, protection and recovery of neurological health in all human populations across the life course.

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Introduction

During the World Health Assembly in May 2022, the World Health Organization (WHO) introduced the new Intersectoral Global Action Plan (IGAP) on Epilepsy and other Neurological Disorders 2022–2031 (ref. 1). By setting out strategic objectives and targets, and outlining the means to verify the achievement of these targets, this plan provides an integrated approach to tackle the global burden of neurological conditions. The IGAP aims towards a world in which "brain health is valued, promoted, and protected across the life course; neurological disorders are prevented, diagnosed and treated, and premature mortality and morbidity are avoided; and people affected by neurological disorders and their carers attain the highest possible level of health, with equal rights, opportunities, respect and autonomy"[1]. This plan marks a new paradigm for neurological disorders and neurology, which could be revolutionary if combined with the innovative concepts of holistic, spiritual[2] and planetary[3] health. Co-design[1,4,5] and co-implementation of these solutions will be vital to achieve equitable and inclusive access to services for the promotion, protection and recovery of brain health in all human populations across the life course.

In this Perspective, we highlight the global burden of neurological disorders and describe the specific features of this burden in certain groups and populations. We also discuss definitions of brain health and introduce the concept of the neurological quadrangle, which encompasses surveillance, prevention, acute care and rehabilitation, as a framework to implement the WHO IGAP to improve brain health and wellbeing across the lifespan. The fundamental role of brain health in achieving the Sustainable Development Goals (SDGs) set out by the United Nations (UN) as a call to action to address poverty, inequality and climate change, among other issues, is also discussed, with a particular focus on the third SDG on health[1,6]. Perhaps most importantly, given the increasing prominence placed on the interconnectedness of all life forms and a holistic approach to health, including spiritual and social health — by the WHO IGAP and the COP26 Special Report on Climate Change and Health, among other movements[1,7–10] — we articulate an integrated holistic approach to brain health. We recommend synergistic action, which must not only leverage new scientific evidence and technological innovation but also build a broader coalition of stakeholders, including the six Ps: patients, healthcare service and product providers, policymakers, payers (funders of health care), implementation partners and the general population. This multisectoral approach will use a quadruple helix comprising academia, policy-makers, the private sector and the population.

The global burden of neurological disorders

The increasing burden

Neurological disorders, including all disorders of the brain, cranial nerves, spinal cord, peripheral nerves and neuromuscular systems, are highly prevalent: at least one in three people will have a neurological disorder at some point during their lifetime[11]. Between 1990 and 2016, neurological disorders were the leading cause of disability-adjusted life years (DALYs) and the second largest cause of deaths globally, accounting for nine million deaths per year[12]. Owing to their immense and growing burden relative to other diseases, neurological disorders should be prioritized at the local and global levels by all stakeholders, particularly health-care providers and policy-makers, to maximize benefits for directly affected individuals and to aid prevention in the wider population. In 2016, the top five neurological causes of DALYs globally were stroke (42.2%), headaches (migraine, 16.3%), dementias (10.4%), meningitis (7.9%) and epilepsy (4.9%)[12]. Of nine million global deaths in 2016, the three leading neurological causes among 15 neurological disorders that were assessed were stroke (67.4%), Alzheimer disease and other related dementias (20.3%) and meningitis (3.7%)[11,12]. Other common neurological disorders included in the assessment were Parkinson disease, encephalitis, spinal cord injuries, traumatic brain injuries, multiple sclerosis, CNS cancers, cervical and lumbar spondyloses, motor neuron disease, peripheral nerve and neuromuscular diseases and tetanus and other neuroinfectious diseases[11]. In addition, inherited neurometabolic diseases comprise more than 1,400 different genetic diseases and together pose a substantial burden, with a cumulative incidence ranging from 1 in 800 to 1 in 2,500 newborns[13].

Huge direct and indirect costs are incurred from neurological diseases. For example, stroke, as the leading neurological cause of death and disability, costs almost US $900 billion per annum globally[14], and dementia cost US $1.3 trillion in 2019 (ref. 15). Poor sleep and sleep–wake disorders, which affect over 20% of the general population[16], are associated with reduced functioning and wellbeing and are estimated to result in economic costs of nearly US $700 billion annually across five Organization for Economic Cooperation and Development countries (Canada, USA, UK, Germany and Japan)[17]. In addition, sleep disorders are associated with an increased risk of developing neurological and mental health problems such as stroke, neurodegenerative disorders and depression[18–22] and have been reported to aggravate the course of other neurological disorders, including epilepsy, migraine, neuroimmunological disorders and pain conditions[18]. This impact of sleep disorders on other neurological conditions could, therefore, result in further indirect costs.

Studies examining the comparative costs between neurological disorders and other diseases in Europe and the USA further highlight the economic burden of neurological disease[23]. The cost of neurological disorders in Europe was estimated at €798 billion in 2010, 63% of which were indirect costs[24]. This total was equivalent to the cost in Europe of heart disease, cancer and diabetes combined. Similarly, a US study reported an annual cost of US $789 billion from nine major neurological disorders in 2014 (ref. 25). Both studies concluded that, to prevent the financial burden becoming unmanageable, neurological disorders require investment and focus equivalent to that received by cancers and heart disease. In many countries, particularly low-income and middle-income countries (LMICs), a lack of universal health coverage further increases health-care and social-care costs. However, a lack of studies investigating the burden of neurological disorders in LMICs hinders the ability of governments to leverage change[23]. The growth of the ageing population will create an increasing demand for treatment, rehabilitation and support services for people with neurological disorders, resulting in an even larger financial burden. In addition, compared with other non-communicable diseases (NCDs) such as heart disease, cancers and diabetes, many neurological disorders have few established modifiable risk factors; more investment in neurological translational research is therefore necessary to unravel more risk factors and develop effective targeted prevention and treatment strategies[23].

The NCDs Countdown 2030 report stated that the risk of dying from neurological disorders from birth to 80 years of age increased in more than half of all countries from 2000 to 2016, making them the fastest-growing cause of death among NCDs[26]. Estimates suggest that at the current growth rate, only 23% of the burden from neurological disorders can be prevented by 2040, and within this time frame, DALYs attributable to neurological disorders are expected to increase by 50% (ref. 27). The implication of these estimates is that if efforts are not accelerated, neurological disorders will cause an even greater burden

than we currently face, especially in populations that are currently affected the most, as discussed subsequently[27].

Priority groups and populations

The burden of neurological disorders in certain groups and populations deserves dedicated attention to foster inclusiveness and equity and to maximize the global impact of interventions. Women represent the majority of caregivers for patients with a number of neurological disorders[28–30], which can cause substantial financial and emotional burden. The burden of paediatric neurological disorders also demands attention because of the potential deleterious effects on the developing brain. Survival with these disorders is improving as a result of better general care and the increasing availability of disease-modifying treatments; however, the burden on the child, parents and caregivers, and society in general, in terms of DALYs and costs, remains extremely high[31]. For example, children who survive brain tumours often need lifelong socioeconomic support as they can have a considerably reduced earning capacity in adulthood and higher somatic health-care costs than healthy, age-matched comparison individuals[32]. Elderly individuals also have a high burden of neurological disorders; in particular, stroke and neurodegenerative diseases. Furthermore, elderly individuals are at an increased risk of having comorbidities of two or more neurological diseases, such as stroke–epilepsy–dementia, Parkinson disease–dementia or stroke–dementia, as well as other NCDs such as spondylosis, osteoarthritis and benign prostatic hyperplasia.

The burden of many neurological disorders is much heavier in LMICs than in high-income countries (HICs)[33]. For example, 80% of the burden of stroke is borne by LMICs, with age-standardized stroke-related mortality and DALYs being almost four times higher than those in HICs in 2019 (ref. 34). Stroke frequently affects individuals in LMICs during their working years, and for those who survive, many are unable to return to work or have reduced capacity for work[34]. The high burden of stroke in LMICs is attributable to reduced access to stroke prevention, acute treatment and rehabilitation services[35]. Epilepsy also disproportionately affects people living in LMICs, accounting for around 80% of cases worldwide, largely owing to preventable causes, including perinatal injury, infection and brain trauma[12,36]. In addition, LMICs have a substantial burden of dementia; for example, in 2015, an estimated 2.13 million cases of dementia occurred in sub-Saharan Africa, resulting in an estimated cost totalling US $6.2 billion[37]. Although the incidence and prevalence of some neurological disorders such as stroke have been declining in HICs over the past few decades, cases have been persistently rising in most LMICs[38]. The demographic transition owing to increasing age of the general population is expected to further exacerbate the burden of neurological disorders that are more common in elderly individuals, especially in LMICs. Similarly, related economic and epidemiological transitions are likely to worsen the burden of neurological disorders more severely in LMICs than in HICs[39].

Despite the high burden of neurological disorders in LMICs, the global dearth of neurologists is more pronounced in these countries, with only three adult neurologists per ten million people, in contrast to 475 adult neurologists per ten million people in HICs[40]. African countries are particularly affected: in sub-Saharan Africa, the estimated ratio of child neurologists is 0.01 per 100,000 people, and 27 of 54 African countries do not have a single child neurologist (J.W. and C.E.C.-B., unpublished data). An inadequate number of neurology training programmes and emigration of highly qualified individuals — the so-called ‘brain drain’ — also contribute to the shortage of neurologists in LMICs.

In many LMICs, the direct and indirect costs of medical treatment incurred by individuals are high, leading to catastrophic out-of-pocket expenditure that further aggravates the vicious cycle of poverty and disease. For instance, every year, 55 million people in India fall below the poverty line as a result of health-care costs[41]. Other challenges in LMICs that increase the burden of neurological disorders include overpopulation and a lack of material resources such as drugs and medical equipment. Most LMICs spend less than 3% of their gross domestic product on public health[42], and only small proportions of this percentage go towards brain health. LMICs are struggling to provide not only therapeutic care but also surveillance, diagnostic, prognostic, preventive, rehabilitative and palliative services to people with neurological disorders[11,26,43]. Non-inclusion of people living in LMICs in clinical trials presents another challenge, especially given the biological and non-biological variability in disease characteristics between countries. In addition, in many LMICs, there is a lack of awareness and widespread social stigma about neurological disorders, which can prevent individuals from seeking medical care[44,45]. Moreover, LMICs are particularly vulnerable to the effects of climate change and to air and water pollution, all of which can affect brain health[3]. Compared with HICs, LMICs experience slower progress in prognosis, diagnosis, treatment and care of all NCDs[46], which makes tackling the growing burden of neurological disorders in these countries a formidable challenge. Notably, underserved communities and ethnic minorities in HICs also face many of the challenges mentioned earlier, especially populations affected by colonization, slavery and systemic racism.

Neurological disorders and brain health

In addition to their epidemiological importance, neurological disorders are major determinants of brain health, as well as overall health. There is no consensus definition of ‘brain health’ and no universally accepted objective measure of brain health across the life course. Nonetheless, various researchers and organizations[47–53] have proposed definitions emphasizing the various domains of brain health (Table 1).

One study used a multistaged concept analysis method consisting of a literature review and an international survey, with a final analysis to integrate the findings into a working definition of brain health. Chen et al.[50] proposed the definition of brain health as “a lifelong dynamic state of cognitive, emotional, and motor domains underpinned by physiological processes; it is multi-dimensional and can be objectively measured and subjectively experienced; brain health is influenced by eco-biopsychosocial determinants, resulting in a continuum of quality of life and wellness.” This definition underscores the multidimensional nature of brain health, including the inherent difficulties of measuring it empirically, given that it is subjectively experienced, the fact that it is affected by several factors and its impact on the quality of human life[50].

Modelling their own definition after the WHO definition of health, Hachinski et al.[52] proposed a definition of brain health in adults as the “state of complete physical, mental, and social wellbeing through the continuous development and exercise of the brain.” In the 2022 position paper of WHO[51], brain health is defined as “the state of brain functioning across cognitive, sensory, social–emotional, behavioural and motor domains, allowing a person to realize their full potential over the life course, irrespective of the presence or absence of disorders.” The WHO definition recognizes that brain health encompasses neural development, plasticity, functioning and recovery across the lifetime of an individual[51,54].

Further to the definitions mentioned earlier, brain health also involves protection and promotion of brain function and is important

Table 1 | Definitions of brain health

Organization or authors	Definition
United States Centers for Disease Control and Prevention (2009)[47]	A healthy brain is one that "can perform all the mental processes that are collectively known as cognition, including the ability to learn new things, intuition, judgment, language, and remembering"
American Heart Association (AHA; 2017)[48]	Optimal brain health is "an optimal capacity to function adaptively in the environment. This could be assessed in terms of competencies across the domains of thinking, moving, and feeling, encompassing, for example, the abilities [to] pay attention, perceive, and recognize sensory input; to learn and remember; to communicate; to problem solve and make decisions; to have mobility; and to regulate emotional status." The AHA also incorporates an element of comparison with average cognitive performance among people of the same age who are free of brain disease or other organ system disease that adversely affects brain health
The NIH Cognitive and Emotional Health Project (2006)[53]	Cognitive health is defined as "the development and preservation of the multidimensional cognitive structure that allows the older adult to maintain social connectedness, an ongoing sense of purpose, and the abilities to function independently, to permit functional recovery from illness or injury, and to cope with residual functional deficits"
Chen et al. (2021)[50]	"A lifelong dynamic state of cognitive, emotional, and motor domains underpinned by physiological processes; it is multi-dimensional and can be objectively measured and subjectively experienced; brain health is influenced by eco-biopsychosocial determinants, resulting in a continuum of quality of life and wellness"
Wang et al. (2020)[49]	"The preservation of optimal brain integrity and mental and cognitive function and the absence of overt neurological disorders that affect normal brain function." Wang et al. also draw attention to some challenges of brain health research, including a lack of tools to assess or quantify brain health in a manner that ensures uniformity; incomplete knowledge regarding the mechanisms that underlie brain health and brain dysfunction and a lack of effective therapies to restore function and/or halt dysfunction in many neurological disorders
Hachinski et al. (2021)[52]	"A state of complete physical, mental, and social wellbeing through the continuous development and exercise of the brain"
WHO (2022)[51]	"The state of brain functioning across cognitive, sensory, social–emotional, behavioural and motor domains, allowing a person to realize their full potential over the life course, irrespective of the presence or absence of disorders." The WHO recognizes that brain health encompasses neural development, plasticity, functioning and recovery across the lifetime of an individual

for total and spiritual wellbeing. Spiritual wellbeing involves finding and living one's life purpose and understanding the values and beliefs that guide one's actions[8,9]. According to the seed of life model, which proposes a dualistic configuration of the human being comprising both a physical and spiritual domain referred to as spheres[9], the spiritual sphere involves a relationship with the transcendental and idealistic aspects of life, including connection to others and the meaning of life[9], but is not the same as religiosity[8]. Spiritual wellbeing can have a positive effect on brain health, mental health and overall physical health[10], which in turn could have positive effects on social and planetary health.

A 2018 article by Bradley et al.[55] set out to conceptualize a new definition of health that takes into account the body, mind and spirit. The authors drew on lessons from the Ancient Greeks, including Aristotle, who "saw that the striving of humanity was towards being well – a physical, mental and spiritual state where life flourished." The definition from Bradley et al.[55] describes health to be a dynamic quality of living, rather than a static state of being, that allows individuals to live a fulfilled life by fully using their body, mind and spirit each day. A quote from the Greek physician Herophilus stated that "when health is absent, wisdom cannot reveal itself, art cannot manifest, strength cannot fight, wealth becomes useless, and intelligence cannot be applied"[55]. This fundamental role of health in all aspects of human life is illustrated by the experience of the COVID-19 pandemic, which grounded the economy and major sectors of human activities, leading to unprecedented challenge to food systems, the working world, human travel and transportation of goods and considerable social disruption and insecurity[56].

Spirituality, including a sense of purpose and meaning in life[8–10], has been associated with prevention and better outcomes of dementia and other neurological diseases[9,57–59]. A systematic review identified several brain regions potentially associated with spirituality and religious practices and beliefs, including the medial frontal cortex, orbitofrontal cortex, precuneus, posterior cingulate cortex and caudate nucleus[57,60]. Scientific exploration and characterization of these brain regions could involve functional and anatomical mapping, trans-omic studies, functional imaging, neurophysiology, brain–computer interfaces, brain stimulation and computational neuroscience. Exploration of these brain regions could help us to unravel and harness spirituality for clinical interventions against various disorders, including mood, anxiety, psychotic, pain and vertiginous disorders[57,60]. Thus, both biophysical and psychospiritual models should be incorporated in defining brain health.

On the basis of the definitions and ideas discussed earlier, brain health can be described as the complete functioning of the brain across the life course to support the full physical, mental, social and spiritual wellbeing and quality of life of an individual towards attaining and maintaining the epitome of a meaningful, impactful, purposeful and productive life (Fig. 1). Brain health is essential for brain skills, which are in turn central to the development of brain capital and a brain economy, that is, an economy that demands cognitive, emotional and social skills over manual skills[61]. Brain capital encompasses the creativity, knowledge and skills that individuals accrue and improve on during their lifetime, which enable them to realize their potential and contribute productively and meaningfully to the economy and society at large[61]. Promotion and protection of brain health are central to the development of brain capital, which is itself essential for human capital development. Indeed, brain health is necessary for the attainment of the third SDG on health[6] (Fig. 2), which is central to the attainment of all other SDGs[1,6].

To promote brain health, in 2021, the European Academy of Neurology launched a Brain Health Strategy to support 47 national neurological societies across Europe in the implementation of the WHO IGAP, alongside other national brain health campaigns[62]. Moreover, especially in LMICs, brain capital is an asset and resource that can be developed at a time when natural resources are dwindling, the knowledge economy is growing and the world is moving towards a brain economy.

Over the past two decades, neuroscience research initiatives such as the Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative, the Human Brain Project, ERA-NET NEURON, the Human Affectome Project[63] and the Human Connectome Project have enhanced our understanding of the brain and its functions (Fig. 3). We have also seen huge advances in cognitive neuroscience[64], artificial intelligence, brain–computer interfaces, neuroimplants, neurostimulation, regenerative medicine, genomics, multi-omics, trans-omics (integrated analysis across the omics) and precision medicine. The remarkable extent to which the brain and spinal cord can reorganize and recover after injuries or stroke when neurotechnologies are embedded in a comprehensive and holistic rehabilitation programme is becoming increasingly evident[65]. Modern technologies such as artificial intelligence, signal processing and neurotechnology can model several functions of the brain and are emerging as useful tools to improve and repair brain function[66,67].

Despite the pivotal importance of neurological health to all SDGs, neurology has received far too little attention, with several countries still lacking comprehensive policies to support the brain health and overall health of their citizens[1]. Moreover, many more countries lack adequate neurological and mental health resources, including health personnel, and availability of drugs and appropriate neurological care for all ages[40]. Knowledge and technology transfer to LMICs, particularly of advanced neurotechnologies such as non-invasive brain–computer interfaces and brain stimulation, will be important to meet articles 4 and 25 of the UN Convention on the Rights of Persons with Disabilities. These articles oblige member states to promote research, development and availability of new technologies and devices to promote and ensure the effective societal participation of people affected by neurological and mental health disorders. As articulated in the WHO IGAP, much needs to be done globally to promote neurological and brain health over the life course.

Towards improving brain health

The neurological quadrangle

In alignment with the WHO IGAP and WHO Brain Health Initiative[52], here we present strategies for the global effort towards improving brain health, as articulated in what we have termed the neurological quadrangle[43] (Fig. 4). Modelled after the 'brain quadrangle' as a template to structure brain health interventions[68], the overall aims of the neurological quadrangle are to strengthen health policies, systems and services and to optimize health resources for the promotion of neurological health. This quadrangle could be adopted as a framework to achieve the WHO IGAP goals by 2030.

The four pillars of the neurological quadrangle aim to achieve equitable and inclusive surveillance, prevention, acute care and rehabilitation services for neurological disorders. The first pillar focuses on surveillance, research and innovation services for neurological disorders and the associated risk factors, alongside the quality and quantity of relevant health services at local, national and global levels. Development of meaningful objective measures of brain health that can be tracked across the lifespan is a central part of this pillar. The second pillar includes population-wide neurological health promotion, protection and preventive strategies. These strategies should leverage innovative evidence-based approaches, including digital and mobile health technologies, educational tools, social media and task shifting and sharing. The third pillar aims to achieve affordable, effective and timely delivery of treatment and acute care services worldwide. These services rely on accurate diagnosis and needs assessment and effective planning and organization. The fourth pillar promotes access to multidisciplinary rehabilitative and palliative care for chronic and terminal neurological disorders in diverse settings around the world.

The core of the neurological quadrangle, which lays the foundation for the four pillars, encompasses health systems and their enablers. The core is aimed at building and strengthening health systems and raising prioritization of neurological disorders. Reinforcement of governance, diplomacy, advocacy and population-wide intersectoral approaches will be vital to achieving these goals. Health systems can be strengthened by workforce training and capacity building, as well as improving information systems and the mobilization and application of resources. This core will support and synergize the activities of the four pillars[68] and ensure that the interventions are consumer-centric and, ideally, co-designed. Co-design should embrace self-determination, which is especially important for historically underserved and marginalized populations. The core also includes the development and application of innovative health technologies across all four pillars, as system enablers for patients.

Implementing the neurological quadrangle

Surveillance pillar. The surveillance, research and innovation pillar of the neurological quadrangle involves establishment of frameworks for equitable research and innovation and for regular disease surveillance. The surveillance framework should monitor disease distribution, determinants, trends and forecasts, as well as disease burden and economic costs. This pillar also involves evaluation of the quality and quantity of neurological health services at local, national and international levels. Equitable research requires needs-driven distribution

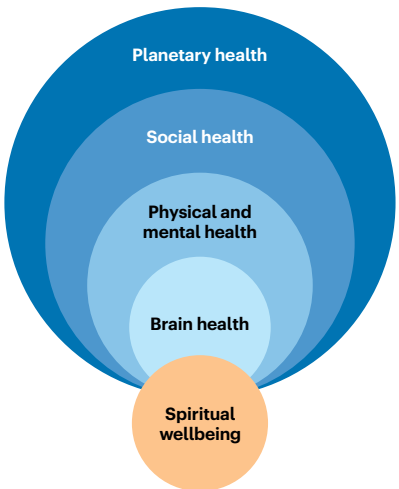

Fig. 1 | Interrelationships among the domains of health and wellbeing. Spiritual wellbeing involves finding and living one's life purpose and understanding the values and beliefs that guide one's actions[6,7]. Spiritual wellbeing has a positive effect on brain health, physical health and mental health[8], which in turn have positive effects on social and planetary health.

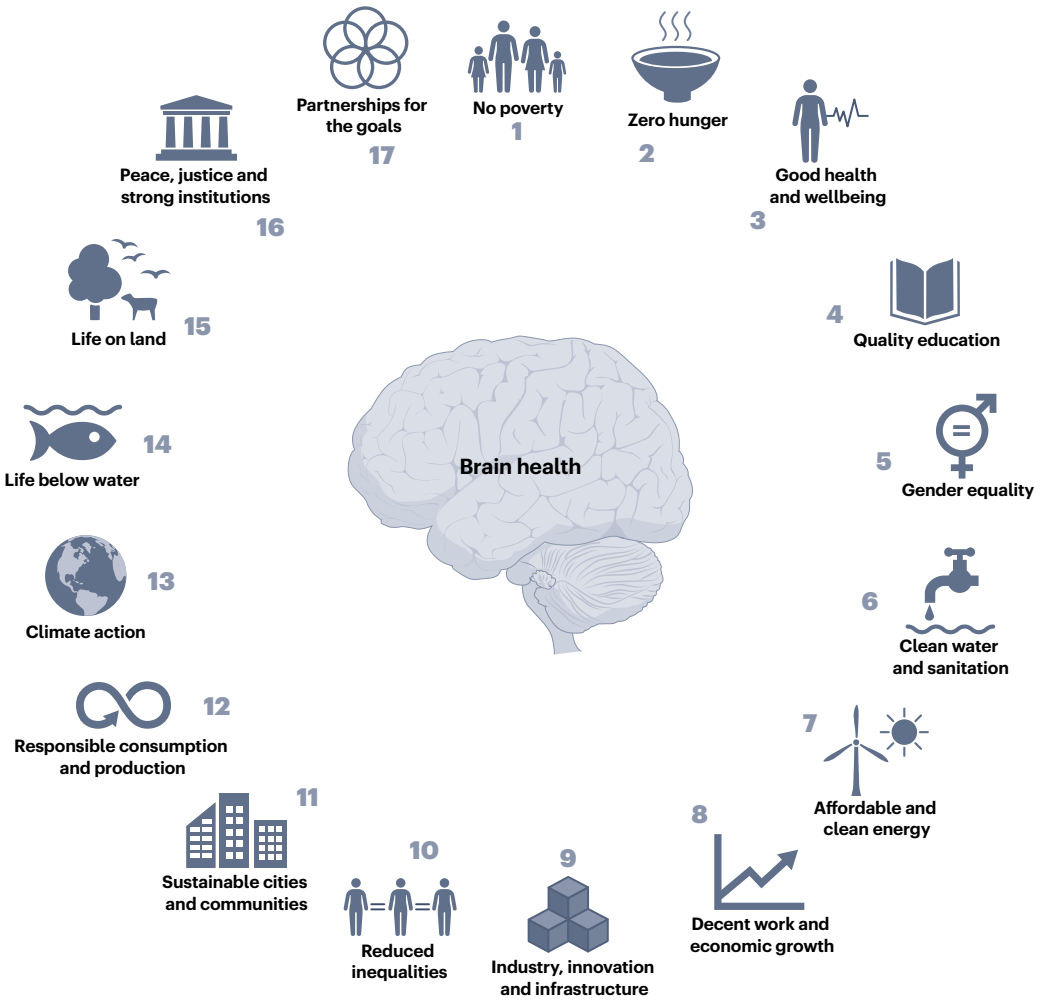

Fig. 2 | Brain health in the era of the Sustainable Development Goals. The figure shows the 17 Sustainable Development Goals (SDGs) set out by the United Nations as a call to action to end poverty and other deprivations, and address climate change, by improving health and education, reducing inequality and driving economic growth. Brain health is central to attaining all of these goals but is particularly important for SDG 3 (health), which itself is central to the other SDGs[6].

of resources without discrimination, to drive discoveries and innovative solutions that will have the greatest global impact. This research should include discovery science, precision medicine, data science, artificial intelligence and implementation science. These areas of research will be pivotal to the development of targeted interventions to promote, improve and monitor brain health across the lifespan. Examples of such interventions include novel biomarkers, diagnostic and prognostic tools and new treatments to improve brain health including drugs and vaccines, as well as tools to monitor the impact of these interventions.

Prevention pillar. The prevention pillar includes activities geared towards primordial, primary and secondary prevention of neurological disease and optimization of neurological health. Primordial prevention aims to avoid the emergence of risk factors for neurological disorders, and primary prevention aims to control risk factors that are already present in an individual who is yet to develop the disorder. This pillar also involves health promotion measures to boost the performance and resilience of a healthy brain and increase brain reserve, before the onset of any neurological disease. Enhancement of brain health is especially crucial because the brain has minimal capacity for regeneration and no option of organ transplantation. Neurological disease prevention requires improvement in our current understanding of neurological diseases, including disease-causing mechanisms and risk factors; application of this knowledge will help us to predict and forestall the occurrence of neurological disorders. For example, an estimated 40% of dementias might be delayed or prevented by risk factor modification[69], and up to 60% of strokes might be prevented by implementation of primary preventive strategies at individual and population levels, as recommended by the World Stroke Organization *Lancet Commission* on Stroke, published in collaboration with the WHO[14]. Preventive strategies include access to education and primary care, with the goal of controlling or eliminating modifiable disease risk factors. Examples of such strategies include hypertension screening and control programmes orchestrated by the WHO HEARTS package and World Hypertension League in collaboration with national governments and

Resolve To Save Lives, as well as digital technologies for stroke prevention[70]. Stroke prevention strategies are particularly important in LMICs, which have scarce resources and limited access to effective acute stroke care and rehabilitation services[35,71]. In addition, 25% of the epilepsy cases worldwide could be prevented by public health and primary care measures to prevent and treat perinatal insults, central nervous system (CNS) infections (such as neurocysticercosis), traumatic brain injuries and stroke[72].

Programmes aimed at protecting maternal health should be deployed through prenatal and perinatal care to promote brain health and prevent neurological disorders in fetal and early life. Such measures are also important for protecting brain health across the entire life course. These programmes should cover tobacco and substance abuse prevention and cessation; adequate perinatal care to prevent hypoxic–ischaemic perinatal brain injuries; vaccination programmes; maintenance and promotion of family health and wellbeing; nutritional interventions to incentivize healthy food value chains and tax unhealthy food; food security; promotion of clean air, potable water and recreational facilities; mitigation of the health impact of climate change and measures to improve and incentivize physical activities in schools, at home and at work[73]. These measures form part of 12 interventions proposed by the WHO to sustainably improve lives and wellbeing through healthy environments in the context of planetary health across the life course[3].

Given the progressive nature of neurometabolic, developmental and other genetic disorders, including visual and auditory disorders, neonatal screening and early diagnostic and intervention programmes are important[74]. Many inherited metabolic disorders can be treated by restoring homeostasis of a disrupted metabolic pathway. For some rare disorders, which might not be treatable, the early detection offered by neonatal screening can be life-changing and can prevent long-term cognitive and motor disability, or even death. Investment in strategies for early identification of affected individuals and for disease prevention through genetic counselling of families at risk will be important tools to prevent individual suffering, improve quality of life of patients and families and reduce economic costs. Disease-modifying therapies, in particular, high-cost genetic therapies, will have the greatest impact when administered early in the disease course, requiring reconfiguration of health systems to facilitate rapid diagnosis and pathways to specialist care[75].

Health diplomacy[76] and advocacy and population-wide educational interventions are essential for the prevention of neurological disorders with known modifiable risk factors, including stroke, dementia, neurocysticercosis and preventable epilepsy[77]. A major challenge for the prevention pillar is the incomplete understanding of risk factors and pathogenic mechanisms of neurological diseases, which hinders the development of targeted preventive interventions. For such conditions, early diagnosis and treatment becomes the next best option[78]. For example, the Multiple Sclerosis Brain Health Initiative advocates for timely detection and disease-modifying treatment to preserve neural function and maximize lifelong brain health[79].

Treatment and acute care pillar. The treatment and acute care pillar of brain health, in line with SDG 3 (health), calls for equitable access to high-quality essential health-care services (including early detection and diagnosis) and to safe, effective and affordable medicines, treatments and vaccines. This pillar entails implementation of universal health coverage and financial risk protection. Similarly, Strategic Objective 1 of the WHO IGAP includes global targets that call for appropriately funded health policies and social protection mechanisms to ensure access to diagnosis, treatment and care for people with neurological disorders[1]. Available services should extend to biomarker assessment and neuroradiological services for disease diagnosis and monitoring. To maintain diagnostic consistency across different geographical areas and settings, inequalities in availability of resources and services, which create disparities in the application of diagnostic criteria, need to be addressed. IGAP Strategic Objective 2 focuses specifically on effective, timely and responsive diagnosis, treatment and care around the world[1]. The two global targets outlined by IGAP state that by 2031, 75% of countries will include neurological disorders in their universal health-care benefits package, and 80% of countries will provide essential medicines and technologies to manage neurological disorders in primary care[1]. These targets will improve control of treatable neurological conditions such as epilepsy, 70% of cases of which are treatable with easy-to-use medications that could cost as little as US $5 per year per individual[72].

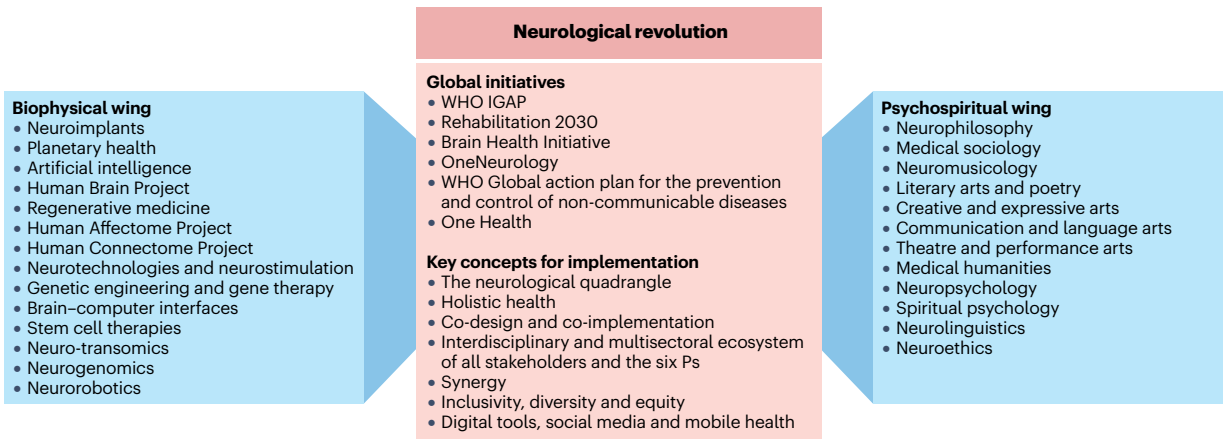

Fig. 3 | Developments in neurology and global initiatives propelling a 'neurological revolution'. A neurological revolution can be fostered by applying an interdisciplinary approach to the WHO Intersectoral Global Action Plan on Epilepsy and other Neurological Disorders 2022–2031 (IGAP), alongside other global health initiatives. A transdisciplinary scientific approach, incorporating arrays of biophysical and psychospiritual approaches, is required to define and understand the factors that contribute to brain health[52].

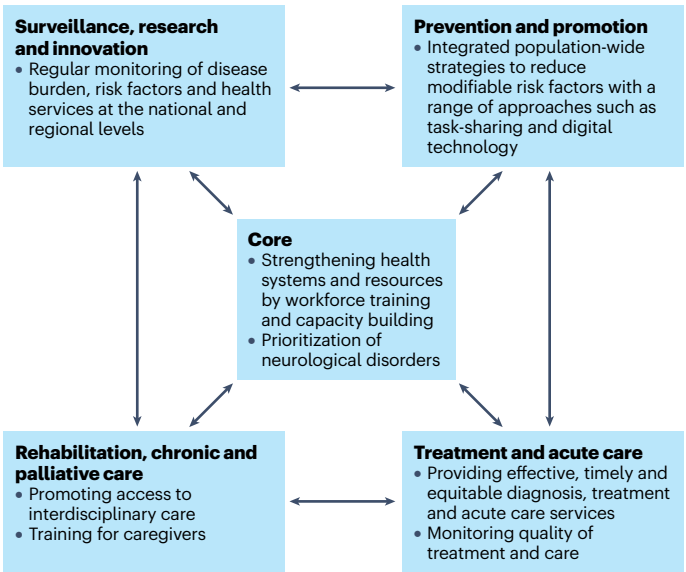

Fig. 4 | The neurological quadrangle. The neurological quadrangle could provide a framework to implement the WHO Intersectoral Global Action Plan on Epilepsy and other Neurological Disorders 2022–2031 (IGAP) to improve brain health and wellbeing across the lifespan. The quadrangle consists of four pillars — surveillance, prevention, acute care and rehabilitation — and a core, which lays the foundation for the pillars. The first pillar focuses on surveillance, research and innovation services for neurological disorders and their associated risk factors. The second pillar includes population-wide neurological health promotion, protection and preventive strategies. The third pillar aims to achieve affordable, effective and timely delivery of diagnostic, therapeutic and acute care services around the globe. The fourth pillar promotes access to multidisciplinary rehabilitative and palliative care for chronic and terminal neurological disorders in diverse settings. The core is aimed at building and strengthening health systems and enabling prioritization of neurological disorders by reinforcing governance, diplomacy, advocacy and population-wide intersectoral approaches for neurological health. The success of this framework relies on synergistic interactions among all aspects of the quadrangle.

Rehabilitation pillar. A lack of effective curative or disease-modifying therapies can limit the degree of efficacious treatment for numerous neurological disorders[78]. For such conditions, multidisciplinary rehabilitative and palliative care becomes imperative. The overall goal of rehabilitation, regardless of the specific neurological disease, is to optimize the functioning of a person to improve quality of life and maximize the ability to live a productive and meaningful life. In essence, the purpose of rehabilitation is to add years to life, add life to years, and add meaning to life. Management of disability, therefore, is an important consideration within the rehabilitation pillar. The WHO IGAP aims to reduce the disability associated with neurological disorders in line with the biopsychosocial approach of the WHO's International Classification of Functioning, Disability and Health[1,80]. This classification considers functioning and disability to be the result of interactions between neurological conditions and contextual factors, such as socio-economic and environmental factors, that influence an individual's access to services and participation in community life. Multidisciplinary palliative care services are also important for maintaining quality of life and to support patients and families as they face increasing challenges, including deterioration of health, death and bereavement[81].

Measures to address the rehabilitation pillar should aim to overcome limitations in existing services and build resilient health systems that provide accessible, affordable and effective rehabilitation along the continuum of care in diverse settings. To achieve this goal, rehabilitation must be integrated into national and subnational health priorities, planning, financing and evaluation, and a strong, multidisciplinary, contextually suitable rehabilitation workforce needs to be developed.

Interdisciplinary care could be expanded to involve newer relevant fields, including medical humanities, to offer holistic care. This approach will leverage the relative resilience of the spiritual sphere to neurological ailments (as observed in the 'disability paradox'), which could be tapped to aid recovery[8,9]. For example, the spiritual sphere is highly rated among stroke survivors probably owing to its documented role in the re-establishment of continuity of self along the path to recovery, self-rediscovery and self-rejuvenation after stroke[9,82,83]. This pathway is hypothetically guided by a sense of purpose in life and self-determination, which drives the processes of internal adaptation[9,82,83]. Internal adaptation involves re-prioritization of individual roles and needs to align with a sense of purpose and residual physical and mental functioning, as exemplified in the stroke recovery cycle[9,82,83]. These adaptations culminate in the formulation and deployment of coping strategies on the basis of residual and restored personal resources[9]. Specific approaches that could be explored include motivational and spiritual therapies, as well as arts and creative therapies (Fig. 3).

Challenges and solutions

Challenges to implementing the neurological quadrangle can be encountered at the systems, provider, patient and community levels. Table 2 summarizes the challenges at each level, stratified according to the core and pillars of the quadrangle. At the health systems level, potential challenges include inadequate policies and poor planning, infrastructural deficits, suboptimal health system organization, insufficient funding and workforce shortages. Challenges at the health-care provider level can include clinician resistance to change, overwhelming workload and burnout, training and/or skills gaps and poor motivation. Potential challenges at the patient and community levels include low health literacy levels, poor health-seeking behaviour, inadequate health insurance coverage and out-of-pocket payment for health services.

Potential solutions to the identified challenges are also highlighted in Table 2. They include stronger and better implemented health policies, increased advocacy for neurological health and leveraging of novel technologies and digital solutions. To provide equitable access to diagnostic facilities, drugs and medical devices, efforts should be made to diversify supply chains for pharmaceutical and medical equipment and to formulate intellectual property trade agreements. Personnel shortages could be addressed through training, capacity building and supervised task shifting and sharing. In addition, the brain drain could be slowed down through provision of incentives for workers by policy-makers. Universal health coverage and health equity should be prioritized by every policy-maker to improve access to diagnosis and care.

Efforts aimed at improving neurological services and optimizing brain health must also address the high levels of stigma and discrimination that accompany many neurological disorders. Stigmatization of individuals with a neurological disorder can often be worsened by other forms of discrimination, such as racism. The first global target of the IGAP identifies the need to address stigma and discrimination through intersectoral and interdisciplinary initiatives such as development of

Table 2 | Challenges to implementing the neurological quadrangle and proposed solutions

Level of implementation	Potential challenges					Possible solutions
	Surveillance and research	Prevention	Acute care	Rehabilitation and palliative care	Core	
Systems	Inadequate prioritization of neurological disorders and brain health; limited funding and other infrastructure for research and surveillance	High prevalence of unhealthy diets and other lifestyle factors that are potentially detrimental to neurological health; complete absence, inadequacy or insufficient implementation of policies that promote healthy dietary and lifestyle choices; inadequate risk factor screening for non-communicable diseases	Unavailability of emergency management systems for hyperacute and acute care; limited access to diagnostics and treatment; insufficient numbers of trained personnel; high cost of diagnostics and treatment, alongside inadequate health insurance coverage; lack of referral systems	Inadequate rehabilitation facilities and lack of trained therapists	Lack of awareness on the importance of meaningful involvement of patients with experiential knowledge	Involve patients and advocacy groups in decision-making to direct health care towards individual health needs, outcomes and experience; prioritize neurological disorders in line with the burden in each country; develop local and national data collection strategies, for example, disease registries and local pragmatic guidelines; perform cost–effectiveness analysis for various treatment options and allocate budgets accordingly; use social media for advocacy and education; leverage technological solutions, such as telemedicine, to bridge gaps in access; develop or reorganize infrastructure; provide effective training for physicians, nurses and other health workers; implement policies to promote healthy lifestyles, for example, risk factor screening exercises, and integrated programmes for non-communicable disease prevention
Provider	Poor awareness of the importance of health surveillance; overwhelming workload	Poor awareness of role of providers in health advocacy; overwhelming workload	Inadequate training; overwhelming workload; insufficient local data to guide and plan acute care; clinical inertia and/or provider reluctance to adopt new treatments	Inadequate numbers of trained personnel	Inadequate training; overwhelming workload; clinical inertia	Educate and train health-care providers, leveraging technology and digital tools for training and decision support systems for acute care; improve local data collection through local studies and registries; improve provider awareness regarding their roles in advocacy and disease prevention; telemedicine
Patient and community	Lack of awareness regarding the importance of health surveillance	Poor awareness of brain health and its implications for overall health; low health literacy levels and poor health-care-seeking behaviour; poor awareness of risk factors and opportunities for risk factor modification	Cultural and social beliefs might cause delays in seeking health care; high cost of treatment; logistical challenges, such as transportation issues and lack of health insurance, can hinder early presentation for acute care	Cultural and social beliefs might hinder use of rehabilitation services	Low health literacy; cultural and social beliefs; traditional or non-orthodox care systems; low demand for rehabilitation services owing to poor awareness; stigma; high costs of long-term care coupled with out-of-pocket payments	Improve brain health by promoting health education from reliable sources, including social media where appropriate; patient support groups; use public figures with neurological conditions to raise awareness and help with education; community engagement

national policies, protection of human rights for people living with epilepsy and other neurological disorders and promotion of awareness and advocacy campaigns[1].

Advocacy is an important tool in the implementation of the neurological quadrangle and IGAP[1] to improve neurological services and optimize brain health. Health diplomacy and advocacy and population-wide educational interventions will be pivotal for the prevention of neurological disorders such as CNS infections, epilepsy, sleep disorders and stroke[76,77,84,85]. Given the diversity of neurological disorders, disease-specific advocacy is a common approach to ensure adequate representation, even for rare conditions. However, disease-specific advocacy carries the risk of dividing public attention, confusing policymakers, losing momentum and wasting limited resources. Conversely, stakeholders working synergistically to advance common goals can

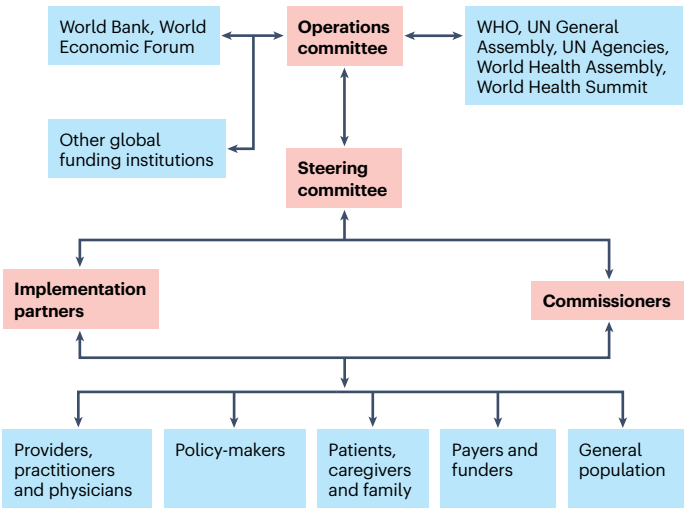

Fig. 5 | A global ecosystem to monitor and reduce the burden of neurological disorders. Synergistic action from a broad coalition of multisectoral stakeholders is required to address the global burden of neurological disorders. Key stakeholders include the six Ps: patients, health-care service and product providers, policy-makers, payers, implementation partners and the general population. Implementation partners include neurology organizations and societies, non-governmental agencies and ministries of health, and country ambassadors will act as commissioners. The World Bank and other funders and philanthropists will be approached for funding and support. Adapted versions of the global ecosystem can be adopted as regional and national ecosystems to suit the respective implementation environments[14].

provide more widespread benefits. Such synergistic efforts should cover all four pillars of the neurological quadrangle and emphasize the importance of patient-oriented care that is predictive, preventive, personalized and participatory[86], with sustainability and resilience at the heart of health systems. Crucially, synergies and collaboration for brain health should build on the principles of SDG 17, which emphasizes global partnerships[6]. This important SDG links directly with SDG 3 (health) and is essential for implementing the intersectoral, multidisease scope of the IGAP[1]. Important targets of SDG 17 that are relevant for implementation of the IGAP include resource mobilization, LMIC–HIC collaboration and multi-stakeholder engagement to share knowledge, technology and resources; capacity building, especially in the least developed countries and building on existing strengths through leveraging of available resources.

To maximize efforts to improve global brain health, synergy across disciplines, and among policy-makers, patient and caregiver support groups and advocates, is crucial. Across different neurological disorders, patients often experience similar challenges with regard to access to care; timely diagnosis, prognosis and management; discrimination and stigma; socio-economic difficulties and cultural barriers. Furthermore, many individuals have comorbidities of more than one neurological disorder and, though diverse, neurological disorders often share risk factors and underlying pathological processes. For example, stroke and dementia, two leading causes of neurological deaths and DALYs, share both risk factors and protective factors[87–91]. Similarly, seizures occur commonly in multiple brain disorders, either as a result of brain insults or through shared mechanisms[92]. These crossovers present unique opportunities for shared preventive strategies and alignment of disease management, and interdisciplinary synergy — for example, digitization of services and national investment in workforce capacity — is required to optimize health system efficiency.

Perhaps most important of all, given the increasing cultural importance being placed on interconnectedness of all life forms on earth (One Health/planetary health; Fig. 1) and a holistic approach to health, exercising an integrated, multisectoral and holistic approach to brain health is becoming increasingly important. This synergistic action must not only leverage new scientific knowledge and technological innovation but also build a broader ecosystem of stakeholders, including the 6Ps[14,93] (Fig. 5). Such ecosystems for co-creation, co-implementation and monitoring of pragmatic solutions for brain health are needed at local, national, regional and international levels to deliver transformative impact. These ecosystems can leverage the WHO IGAP and WHO Brain Health[52] programmes in synergy with the WHO One Health Initiative, which is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems.

Conclusions

A synergistic and holistic approach to neurological disorders and brain health is central to the attainment of the UN SDG 3 on health and indeed all SDGs[6] (Figs. 1 and 2). Insufficient attention to brain health will continue to exert a huge economic and developmental toll on all global populations and economies. As highlighted by this article, neurological disorders must be prioritized at local, regional and global levels by all stakeholders to achieve the greatest benefit for individuals who are directly affected and to lessen the burden on the wider society. Synergistic revolutionary action across the life course is urgently required in the four pillars of the neurological quadrangle — surveillance; primordial, primary and secondary prevention; treatment; and rehabilitation.

The WHO IGAP[1] and WHO Brain Health[52] initiatives are propelling neurology to the forefront of the global health and development agenda by harmonizing and consolidating global neurology activities and advocacy efforts into a powerful, united force. Sustainable ecosystems are needed in all countries to harness resources and facilitate interdisciplinary collaboration across the four pillars and core of the neurological quadrangle. This new paradigm, promoting neurological and brain health, could improve human health and sustainable development, particularly if combined with the innovative concepts of holistic, spiritual and planetary health. By improving brain health, this revolutionary call to action could foster a profound benefit to human wellbeing, welfare and wealth around the globe.

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