REVIEW OPEN

Regional research priorities in brain and nervous system disorders

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The characteristics of neurological, psychiatric, developmental and substance-use disorders in low- and middle-income countries are unique and the burden that they have will be different from country to country. Many of the differences are explained by the wide variation in population demographics and size, poverty, conflict, culture, land area and quality, and genetics. Neurological, psychiatric, developmental and substance-use disorders that result from, or are worsened by, a lack of adequate nutrition and infectious disease still afflict much of sub-Saharan Africa, although disorders related to increasing longevity, such as stroke, are on the rise. In the Middle East and North Africa, major depressive disorders and post-traumatic stress disorder are a primary concern because of the conflict-ridden environment. Consanguinity is a serious concern that leads to the high prevalence of recessive disorders in the Middle East and North Africa and possibly other regions. The burden of these disorders in Latin American and Asian countries largely surrounds stroke and vascular disease, dementia and lifestyle factors that are influenced by genetics. Although much knowledge has been gained over the past 10 years, the epidemiology of the conditions in low- and middle-income countries still needs more research. Prevention and treatments could be better informed with more longitudinal studies of risk factors. Challenges and opportunities for ameliorating nervous-system disorders can benefit from both local and regional research collaborations. The lack of resources and infrastructure for health-care and related research, both in terms of personnel and equipment, along with the stigma associated with the physical or behavioural manifestations of some disorders have hampered progress in understanding the disease burden and improving brain health. Individual countries, and regions within countries, have specific needs in terms of research priorities.

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As outlined in the introduction to this series (see page S151), the proportion of the global burden of disease (GBD) due to neurological, mental health, developmental and substance-use (NMDS) disorders is rising worldwide[1]. The type of disorder and reason for increase varies across countries[2], regions and populations as indicated by the regional differences in disability adjusted life years (DALYs; a metric developed to take both mortality and morbidity measures into account). DALYs for a disease or health condition are calculated as the sum of the years of life lost (YLL) due to premature mortality in the population and the years lost due to disability (YLD) for people living with the health condition or its consequences (http://www.who.int/healthinfo/global_burden_disease/metrics_daly). The first regional use of DALYs, the regional patterns of disability-free life expectancy and disability-adjusted life expectancy, were reported by the Global Burden of Disease Study[3].

Opportunities to ameliorate nervous system disorders could be increased by both local and regional research collaborations. Lessons learned locally, and those learned in collaboration across regions and countries, may be adapted and applied to other areas, there may also be opportunities to leverage resources. Some disorders have physical boundaries, whereas others have sociocultural and economic contexts. Thus, the challenges faced in high-income countries are often different from those in low- or middle-income countries (LMICs) in type, characteristic or scale. Population demographics, genetics, income, religion, culture, language, ethnic origin, conflicts, land area and quality, and population size vary widely between and within LMICs. Although there is some commonality in the prevalence of certain brain disorders (Fig. 1), significant diversity exists with respect to the origin, manifestation and treatment strategies or options adopted across these regions. In this Review, we focus on sub-Saharan Africa, the Middle East and North Africa, Asia, South and Southeast Asia and Latin America[4,5]. We introduce a regional perspective with respect to NMDS disorders, highlighting what has been learned from epidemiological differences between LMICs as well as globally, while identifying specific needs, research priorities and the opportunities for collaboration among different LMICs (Tables 1–4).

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SUB-SAHARAN AFRICA

Malnutrition, from birth through to adulthood, seems to be the most significant contributor to disease burden and disability in sub-Saharan Africa[6]. Maternal malnutrition, including micronutrient deficiencies such as vitamins and iodine, impairs the development and function of the nervous system of offspring, and negative effects can persist in the next generation[6]. Other forms of maternal and environmental trauma during the perinatal period affect brain development and cause long-term changes in brain function. Neurological disorders caused by eating toxic foodstuffs are unique to sub-Saharan Africa. Cassava is an important food crop that contains endogenous neurotoxins and, if not properly prepared, can cause konzo — a peripheral polyneuropathy with prominent sensory loss and ataxia. Lathyrism that presents as spastic paraparesis is an equally debilitating neurological disorder caused by excessive ingestion of the grass pea *Lathyrus sativus* that contains the excitotoxic amino acid, β-N-oxalyl amino-L-alanine[6].

Use of psychostimulants is another major contributor to the burden of brain disorders in sub-Saharan Africa[7]. Of particular concern is the high prevalence of maternal alcohol and methamphetamine use in areas such as the Western Cape Province of South Africa. The incidence of fetal alcohol syndrome in some locations within this region is the highest in the world[8]. The increase of methamphetamine use in pregnant women in the Western Cape is of concern given the negative effects that the drug has on the developing fetus[9]. Khat use is of concern in East Africa[10,11], where 60–90% of men use the drug daily[12,13]. The consequences of habitual khat consumption include behavioural disturbances and toxic psychosis, which has a particular impact on the overall health of young adults.

The prevalence and incidence of epilepsy in sub-Saharan Africa countries is twofold higher than that of other countries[14–19]. The prevalence varies between 4.5 and 20.8 per 1,000 people, owing to the localized and high incidence of parasitic infections, poor perinatal care and poor access to treatment. The full burden of epilepsy in sub-Saharan Africa is difficult to assess and is likely to be under-reported because people with epilepsy are stigmatized and frequently left untreated[19]. Stroke is another concern among non-communicable disorders within sub-Saharan Africa — incidence is increasing at an alarming rate[20]. The prevalence of dementia in sub-Saharan Africa is reportedly much lower than in other regions[21,22]. However, these reports may not be a true reflection of the prevalence, which it is projected to increase with an increase in lifespan. Furthermore, as research extends into rural areas, diagnosis of unreported cases may reveal the true burden.

Sub-Saharan Africa has the highest burden of infectious diseases and the poorest public health infrastructure in the world[6,23]. Parasitic infections are also highest in this region and often have neurocognitive sequelae. HIV-associated neurological disorders area major burden, with more than 1.5-million children living with HIV and at risk of developing HIV-associated cognitive impairment and dementia[1,24]. Little is known of the effects of HIV and antiretroviral treatment on the developing brain. There is an urgent need for research on the longitudinal trajectory of neurodevelopment among children and adolescents who are perinatally infected with HIV[24]. Cognitive and psychiatric problems have been found to decrease antiretroviral treatment adherence and survival of adults with HIV in Zambia[25]. Neuroimaging and neurocognitive testing are well established in several regions within sub-Saharan Africa and have been used in cross-country collaborations to further our understanding of the spectrum of neurocognitive disorders in patients with HIV and to determine the effect of antiretroviral therapy on these individuals[26]. Subtle changes in white-matter integrity have been used for early diagnosis and monitoring progression of neurological disease in individuals with HIV[26].

MIDDLE EAST AND NORTH AFRICA

Many of the aetiological and treatment features of psychiatric disorders in the Middle East and North Africa are due, in part, to the unique environmental and cultural influences within the region. Over the past few decades, communities have been exposed to traumatic events including anti-government uprisings and wars, which has left many populations vulnerable to mood disorders, such as post-traumatic stress disorder (PTSD) and major depressive disorder (MDD). In comparison with the global estimate of 4.4% (ref. 27), depression prevalence in Iraq is 7.2% and is 15.3% in the Palestinian territories[28,29]. In fact, MDD is currently listed among the top three causes of YLDs in most of the countries within the Middle East and North Africa[2]. The statistics are similar for PTSD within the region.

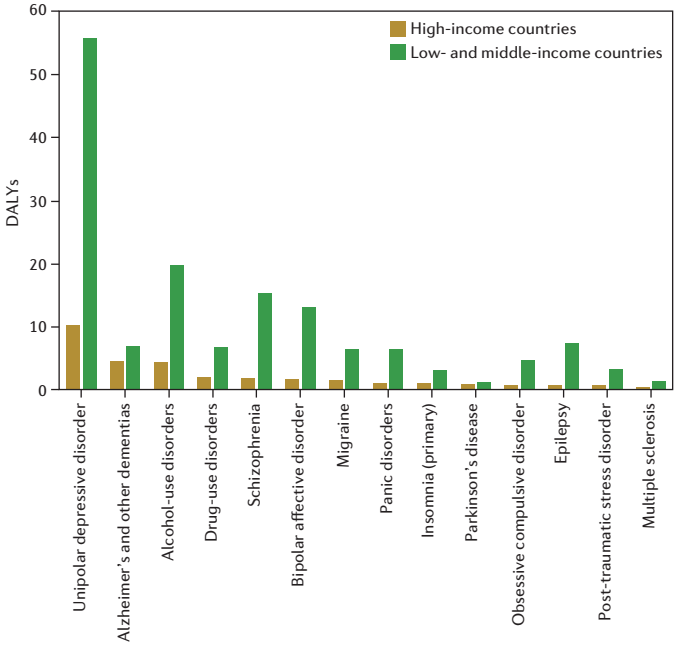

Figure 1 | Comparison of disability associated life years (DALYs) between high-income and low- and middle-income countries. The data were derived from the World Health Organization (http://www.who.int/healthinfo/global_burden_disease/metrics_daly/) and refs 4, 5.

Owing to the high rate of consanguinity in the region, the incidence of several recessively inherited genetic disorders, such as inherited deafness, is increasing[30–32]. For example, Bardet–Biedl syndrome, which includes many nervous system abnormalities, is common in most of the Arab countries, particularly in Kuwait. Whereas the syndrome typically affects 1 in 150,000 people in North America and Europe, the prevalence in Arab countries ranges from 1 in 13,500 to 1 in 30,000 people[30]. A national strategy is needed in this region to address this burden of genetic disease. Although services such as genetic screening exist, understanding the barriers to access and use requires implementation research and an understanding of sociocultural norms. This will help health workers to tailor services and educational campaigns that are culturally acceptable.

The prevalence of substance-use disorders varies between 7.25% and 14.5%, with cannabis being the most commonly used drug followed by alcohol[2,33]. Khat is also widely used as a stimulant in Yemen and the neighbouring countries within the Arabian Peninsula.

There is a need for population-based prevalence estimates of common neurological disorders in the Middle East and North Africa, with a special emphasis on epilepsy, because systematic epidemiological studies of epilepsy in Asia and Africa have not included this region[34]. Most published studies only report hospital-based samples[35]. For example, a review of seizure disorders in Arab countries indicated a median prevalence of 2.3 per 1,000 people (range, 0.9–6.5 per 1,000). These figures are very likely to underestimate the prevalence in a population of more than 350-million people[36], particularly because epilepsy is stigmatized within several communities[37].

LATIN AMERICA AND THE CARIBBEAN

Within the countries and territories of Latin America and the Caribbean (Central America, Mexico and the Latin Caribbean); the non-Latin Caribbean and South America there are sub-regional differences in the contribution of NMDS disorders to the total burden of disease measured in DALYs. Although DALYs owing to neurological disorders, including stroke, are low in the Andean Latin American sub-region, they are higher in the southern Caribbean sub-regions and even higher in tropical Latin America and the Caribbean. However, if one considers the total region, the burden of NMDS disorders accounts for 22.2% of the total DALYs. The overall weighted prevalence of mental health disorders in children in the region (12.7%) is significantly more than the prevalence (9.7%) seen in United Kingdom when similar diagnostic procedures are used[38]. Importantly, there is inadequate information on risk and protective factors that affect the incidence of mental health disorders in children living in developing countries in general and Latin America and the Caribbean in particular[39].

Unipolar depressive disorders (13.2%) and alcohol dependence (6.9%) constitute the most common psychiatric disorders[40] in Latin America and the Caribbean (Fig.1). The annual level of alcohol consumption (8.4 litres per capita annually) is the second highest in the world after Europe[41]. Alcohol consumption has been associated with roughly a third of intentional and non-intentional accidents[42]; traumatic brain injuries incurred from any type of accident have long-term implications for society and for the individual, including impaired attention, depression and economic costs to families[43].

As for other regions the current increasing trend in DALYs for non-communicable disorders[2] suggests that epilepsy and dementia are unique in terms of their increasing prevalence. Their prevalence or manifestation is increasing in Latin America and the Caribbean. The annual incidence of epilepsy according to a collection of 32 community-based studies is 77.7 to 190 per 100,000 people each year[44], compared with 30 to 50 per 100,000 people in high-income countries. Distribution of epilepsy across sub-regions of Latin America and the Caribbean also differs; one reason for this is the direct association between epilepsy and the distribution of neurocysticercosis[45]. Dementia is also widespread[46,47], but pockets of early onset Alzheimer's disease in families are apparent in Caribbean Hispanic people who originate from Puerto Rico or the Dominican Republic[21]. Studies on familial types of dementia in Latin American countries such as Colombia (Alzheimer's disease) and Venezuela (Huntington's disease) have shown that both non-genetic (nurture) and unrelated genetic factors may have a major role in influencing phenotypes[48–50]. This suggests that even highly penetrant autosomal dominant diseases may be modified by environment or lifestyle factors. Although not unique to the region, it is worth noting that stroke is the leading cause of death in Ecuador, and in other Latin American countries[51]. Little is known about the prevalence of any of these disorders among indigenous Andean or Amazonian populations.

ASIA

Sub-regions of Asia comprise East and Southeast Asia, and incorporate the Association of Southeast Asian Nations as well as China, whereas South Asia consists of sub-Himalayan countries, including Afghanistan, Bangladesh, India, Pakistan and Sri Lanka. About two-thirds of the world's population resides on the Asian continent. India and China, because of their size and economic impact, have a major influence on the health and trends of the region, and in shaping global health statistics, however they are catalogued. Asia's ethnic diversity, and widely disparate socioeconomic development lead to significant variations in the prevalence and burden of NMDS disorders. An epidemiological study[52] of epilepsy in 23 Asian countries revealed the lifetime prevalence of epilepsy to be 1.5 to 14 per 1,000 people. Infections of the nervous system often contribute to epilepsy and prevention of these infections is needed to reduce the burden of the condition.

Another major concern is the rising prevalence of dementia; although the number of patients with dementia is predicted to increase by 100% between 2001 and 2040 in developed countries, dementia is predicted to increase by more than 300% in India, China, South Asia and the Western Pacific region[21]. In India alone, there are 3.7 million people with dementia and the numbers are expected to double by 2030 (ref. 53). In addition, the high burden of cardiovascular risk factors in developing countries, including India, contributes to cerebrovascular disease such as vascular dementia[54].

Asia, in particular South Asia, has the highest stroke mortality in the world[55]. Within Asia, there is a wide variation in stroke prevalence[56]. Rural parts of South Asia have lower stroke prevalence than urban areas[56], and this needs to be examined further in future research[57]. In China, the incidence of stroke differs geographically. A higher incidence of stroke is seen in northern and western areas, and is associated with a higher prevalence of hypertension and obesity[58]. Barriers to preventing and reducing mortality and disability due to stroke are the lack of infrastructure, such as dedicated stroke care units, and awareness[57].

Tobacco use — a leading cause of stroke — is a major public health issue for East and Southeast Asia. Half of the world's tobacco consumption takes place in Asia[59]. Men are more likely to smoke than women; and prevalence rates for males range across countries from 36% in Singapore to 64% in Laos[60]. Although the neurological and other health implications of smoking are well known, many Asian people still smoke. Public health measures to reduce smoking are just beginning; for example, in June 2005 and October 2008, India and Beijing banned indoor smoking in public places and offices, respectively.

COMMON RESEARCH NEEDS AND CHALLENGES

There are several commonalities within LMICs in terms of disease prevalence and the public health and research challenges, although considerable ethnic and geographical diversity exists.

Lack of robust epidemiological studies

Epidemiological studies, preferably longitudinal, designed to identify disease burden and risk or protective factors for NMDS disorders, are one of the most important research needs in LMICs. These need to be complemented by research on health systems and sociocultural effects, and clinical trials to determine the best interventional strategies. Furthermore, rapid urbanization and the associated demographic and sociocultural changes in LMICs should be studied with respect to their impact on the course and outcome of different brain disorders, especially mental health illnesses and substance misuse. A careful analysis of the possible interaction between demographic and sociocultural changes, and biological factors is essential to initiate remedial steps to contain the progression of these disorders.

Disproportionate distribution of scientists

Some countries have a disproportionate share of scientists, with investment and output concentrated in only a few places. In general, Latin America produces more neuroscience and mental health disorder publications than the Middle East and Africa. Similar variation is seen in the number of neuroscience publications produced in Asia (Fig. 2). Between 1996 and 2013, India consistently produced the most neuroscience and mental health research publications. Figures also reveal that 9.2% of institutions in India produce 80.1% of the publications. Among Latin American and Caribbean countries, Brazil now accounts for more than two-thirds of South America's entire research output, although in terms of articles per capita, it is broadly similar to Argentina, Uruguay and Chile. One could leverage this situation by promoting intraregional research collaborations to enhance research capacity and infrastructure. The top 10 African countries in terms of health-research publications from 2000 to 2014 are South Africa, Nigeria, Kenya, Uganda, Tanzania, Ethiopia, Ghana, Cameroon, Malawi and Senegal[61]. Although these trends comprised all health research, it is likely that mental health publications are ranked similarly in sub-Saharan Africa.

Table 1 | Neurological, mental health, developmental and substance-use disorders and specific burden of disease in sub-Saharan Africa

Condition or disease	Key affected countries	Burden of disease	Impact of condition or disease
Nutrition: malnutrition	All SSA	• 204 million people suffer from hunger[80–82] • Highest prevalence of stunting in the world is in East Africa (42%) and West Africa 36% based on the WHO Child Growth Standards[83] • 22% of children are underweight in West Africa[83]	• Maternal malnutrition impairs the development and function of the nervous system of offspring and negative effects persist in the next generation[6] • Malnutrition in infants and children affects their growth and cognitive development[6,84]
Nutrition: the toxic nutritional neurological disorders konzo (cassava) and lathyrism (grass pea)	Cameroon, Central African Republic, Democratic Republic of Congo, Tanzania, Ethiopia and Mozambique	• Reported estimates show there are around 6,500 cases of cassava toxicity; unofficial reports estimate the number of cases to be at least 100,000 (ref. 85)	• Leads to difficulty in walking[84] and peripheral polyneuropathy with prominent sensory loss and ataxia[6]
	Ethiopia		• Malnutrition may increase the negative impact of food borne toxins and causes irreversible spasticity[86].
Substance use: cannabis, methamphetamine, khat, alcohol, and opiods or heroin	West and Central Africa (notably), and South Africa	• Cannabis use is higher than the global average (12.4% versus 3.8%)[87] • Cannabis is the most popular illicit drug followed by cocaine	• 1 in 18 problem drug users receive treatment; most of those in treatment are cannabis users[87]
	South Africa	• Increased use of methamphetamine during pregnancy[8,9,88] • General increase in drug use[87]	• Structural (volume reductions in the striatum and increases in limbic areas of the brain) and functional deficits as well as cognitive and behavioural abnormalities have been described in infants and children exposed to methamphetamine prenatally[9] • Violent behaviour in adults • Cognitive dysfunction[89]
	Tanzania, Kenya, Uganda, Ethiopia, Eritrea and Somalia	• 60–90% of East African males use khat daily[10–13,89]	• Chronic khat use may have a long-term deleterious effect on working memory[90]
	South Africa	• Self-reported prevalence of alcohol abuse is 36.9% • Fetal alcohol syndrome in the local Western Cape population is the highest in the world[8]	• Negative effects on the developing fetus[9] • Fetal alcohol syndrome, growth retardation and cognitive dysfunction[8]
	West and Central Africa and South Africa	• Annual prevalence of heroin use is above the global average[88] • 0.92–2.29 million people used opiates in the past year[87]	• An increasing role as a transit area for drug trafficking and increased crime rate[87]
Epilepsy	All SSA	• Prevalence varies between 4.5 and 20.8 per 1,000 people; about twice that elsewhere[14–19]	• Impaired cognitive function due to effect of seizures on the developing brain[91] • Stigma and social isolation[19]
Stroke	All SSA	• Community-based studies revealed an age-standardized annual stroke incidence rate of up to 316 per 100,000 of the population, and age-standardized prevalence rates of up to 981 per 100,000 (ref. 92) • 65% of all neurological admissions to hospitals are stroke related in the West African sub-region[92]	• Increased burden to society
Dementia	Nigeria, Democratic Republic of Congo, Senegal, Central African Republic, Tanzania, Zambia and Kenya	• Prevalence is between <1% and 10.1% in population-based studies and up to 47.8% in hospital-based studies[93]	• A burden to family and society
HIV-associated neurological conditions	South Africa, Kenya, Nigeria, Zambia, Malawi, Cameroon, Botswana and Uganda,	• 1.5-million children are living with HIV and are at risk of developing HIV-associated cognitive impairment and dementia[3,24] • Prevalence of HIV-related neurocognitive impairment ranged from <1% to 80% in hospital-based studies[93]	• HIV-related dementia is a particular concern, and burden, in SSA as people live longer with the disease • Children infected with HIV perinatally do not perform as well as non-infected children on cognitive tests and are at much higher risk for psychiatric disorders later in life[24]

SSA, sub-Saharan Africa; WHO, World Health Organization. The 2014 population estimates for sub-Saharan Africa were 961.5 million (http://data.worldbank.org/region/SSA)

Insufficient resources for treatment and research

Most countries allocate less than 5% of their health-care budget to the treatment of brain disorders[62,63]. For example the Middle East and North Africa, Palestine, Qatar and Egypt, spend only 2.5%, 1% and less than 1% on brain-disorder treatment, respectively[64]. The number of mental health professionals available in most LMICs is also very low. For example, there are only 1.44 psychiatrists per 100,000 people in Egypt. In India, 52% of the districts do not have psychiatric facilities, and there is an acute shortage of psychiatrists, psychologists and psychiatric social workers[65]. Hence people with neuropsychiatric disorders remain largely undiagnosed and even when they are diagnosed, they do not have access to sustainable, affordable treatment and optimal medical care[66]. Although a recent World Bank report indicates that disease burden that results from non-communicable causes, including mental health disorders, has increased substantially, with major depressive disorders at the top of the list (http://www.healthdata.org/gbd/data)[2] there is a severe lack of resources, particularly of trained personnel and training facilities[67]. Given the severe fiscal and human-resource constraints for treatment, it is not surprising that research is lagging. The current research gap between developed and developing nations is reflected in the mental health research output, with LMICs contributing to only 6% of international research articles[68].

Brain drain

Brain drain is the loss of highly trained people, constituting another big challenge to LMICs, and widening the research gap between high-income countries and LMICs. The reasons cited by researchers for their exodus are a dearth of funding, poor facilities, and limited or a lack of peer groups to provide intellectual stimulation[69]. Although it may be argued that brain drain is a common problem in LMICs across disciplines, neuroscience research is particularly affected. This is because unlike core disciplines such as chemistry, physics or mathematics,

Table 2 | Neurological, mental health, developmental and substance-use disorders and specific burden of disease in South Asia and Southeast Asia

Condition or disease	Key affected countries	Burden of disease	Impact of condition or disease
Mood disorders	Vietnam, Cambodia and South Asia countries	• Depression is the second most common NMDS disorder in Vietnam (2.8% prevalence) and Cambodia (16.7% prevalence); there is a relatively high prevalence (23.6%) in elderly Chinese[69,94,95] • Anxiety is the most common NMDS disorder in Cambodia (27.4% prevalence)[2,5] • Prevalence of 16/1,000 population in India[96] • Unipolar depression ranks among the top 10 disorders[2]	• Substantial impact on society in general and family in particular • Patients with psychiatric disorders under diagnosed and undertreated due to scarcity of physicians[97] coupled with absence of evidence for effectiveness of treatment[98] • People with dysthymia have impaired quality of life and poor marital adjustment[99]
Dementia	All Asia	• Predicted to increase by more than 300% in India, China, South Asia and the Western Pacific region[21] • 9 million Chinese have dementia[100] • The rate in people over 60 was 3.4% in Thailand and 3.5% in Indonesia[101] • China and India are predicted to have the largest number of dementia cases in the next decade[21,100] • An estimated 3.7 million Indians have dementia and the numbers are expected to double by 2030 (ref.102)	• People with dementia who live with families puts significant burden on carers. None of the carers receive carer benefits and have high levels of psychological morbidity[102] • Annual cost of dementia in China is US$2,384 per patient annually[103]
Stroke	All Asia	• Prevalence of 45–471 per 100,000 people in South Asia[56] • Annual stroke mortality in China is 1.6 million, approximately 157 per 100,000, which has exceeded heart disease as the leading cause of death and adult disability[104] • Among a sample of five ASEAN countries (Indonesia, Myanmar, Vietnam, Thailand and Malaysia), stroke was the top cause of death[105] • Stroke mortality in South Asia is the highest in the world, accounting for more than 40% of global stroke deaths[57] • Mortality in South Asia is 73 per 100,000 of the population[57]	• Leading cause of death, long-term disability • Incidence of stroke differs geographically in China — there is a higher incidence in northern and western areas, which are associated with higher prevalence of hypertension and obesity[58] • Rural parts of South Asia have a lower stroke prevalence compared with urban areas[56] • There are less than 100 stroke care units in South Asia[57], leading to poor care for patients and increased morbidity and mortality • Barriers to stroke thrombolysis in South Asia include a lack of infrastructure, lack of awareness and a lack of affordability[57], leading to increase in morbidity and mortality
Traumatic brain injury	All Asia	• 44% of the world's road deaths occur in Asia[106] • The incidence rate of TBI in India is 160 per 100,000; 1.6 million people will sustain a TBI[106]	• India has the highest rate of TBI due to falls, and accounts for 50% of global falls[106]
Tobacco use	East and Southeast Asia	• Prevalence of male smokers ranges from 36% in Singapore to 64% in Laos[60]; the rate is lower in women[58] • Smoking in children aged between 13 and 15 is common in ASEAN[60] • Half of the world's tobacco is consumed in Asia[59] • South Asia has the highest use of smokeless tobacco worldwide[59]	• Chronic nicotine consumption induces neuro-adaptations in the brain's reward system that result in nicotine dependence[107] • Withdrawal from nicotine can include somatic symptoms (for example, jumping, shaking, abdominal constrictions, chewing, scratching, and facial tremors) or affective symptoms (for example anhedonia)[107] • Past smokers are prone to relapse for weeks, months or even years after cessation[107] • Nicotine affects mood and cognition by stimulating nicotinic acetylcholine receptors on neurons in the brain's mesolimbic reward system[107]

ASEAN, Association of Southeast Asian Nations; NMDS, neurological, mental health, developmental and substance-use; TBI, traumatic brain injury. The 2014 population estimates for South Asia were 1.692 billion and those for East Asia and Pacific region were 2.02 billion

neuroscience is an interdisciplinary field and most LMICs do not have adequate training capacity. This, combined with the fact that the expensive infrastructure needed for some areas of brain research is often not available, drives many researchers from LMICs to migrate to high-income countries.

REGION SPECIFIC RESEARCH NEEDS AND CHALLENGES

There are specific needs across the regions that constitute LMICs, which have to be addressed in a region- and/or country specific manner.

Identification of risk and protective factors

There is an immediate need to characterize population groups that have increased susceptibility or resilience to brain disorders or better clinical outcomes, which could lead to the identification of disease-modifying factors and interventions in other populations. Opportunities for research have been observed in different regions. For example, the course and outcome of schizophrenia is better understood in India than in other countries[70]. The lifetime prevalence of PTSD as a major depressive disorder is not significantly greater in Southeast Asia compared with other parts of the world[1], despite the region being a natural disasters-prone region. As a region with significant population growth trends, the likely increase in the number of people with childhood and adolescent disorders (including learning disabilities) at one end of the spectrum and increasing lifespan that leads to higher incidence of age-related neurodegenerative disorders (including dementia) at the other end make it imperative that resources are channelled to research aimed at identifying risk and protective factors[5,71–73].

Integration of traditional methods of treatment

Assessing the efficacy of indigenous, traditional Chinese medicine and Indian Ayurveda medicine for brain disorders is important. Integrating traditional Buddhist practices in the treatment of psychiatric disorders, such as the integration of mindfulness techniques into cognitive behavioural therapy, has created new intervention approaches including mindfulness-based cognitive therapy[74], mindfulness-based stress reduction[75], and dialectical behaviour therapy[76]. Similarly yoga, as an addition to pharmacological interventions, is beneficial in the treatment of schizophrenia and depression[77,78].

Collaborations and knowledge generation

Opportunities have been made possible by improvements in infrastructure in sub-Saharan Africa, which sets the stage for cross-country collaboration. For example, in addition to South Africa, several countries have neuroimaging facilities, which can be used to analyse brain structure and function to aid diagnosis and treatment. Malawi has excellent electroencephalography (EEG) services and the capacity to conduct longitudinal studies. Zambia has very good imaging

Table 3 | Neurological, mental health, developmental and substance-use disorders and specific burden of disease in Latin America and the Caribbean

Condition or disease	Key affected countries	Burden of disease	Manifestation of condition or disease
Unipolar depressive disorder	All LAC	• One of the most common mental illness[39], constituting 13.2% of the burden of total DALYs • Represents 35.7% among psychiatric disorders and is more prevalent among lower-income groups[105]	• Typical manifestations are irritability, difficulty with concentration, fatigue or lack of energy, feelings of hopelessness and/or helplessness and sleep problems
Substance use: alcohol and tobacco	All LAC	• One of the most common psychiatric disorders[39], constituting 6.9% burden of total DALYS • Chile has the highest consumption rate of alcohol and tobacco[40]	• Alcohol consumption is a trigger of violence and accidents and is associated with 33% of intentional accidents and 26% of non-intentional accidents[41] • Both associated with acute as well as long-term chronic conditions that range from brain damage, high blood pressure and stroke to liver and muscle diseases[108]
	All LAC (higher in South America)	• Prevalence of smoking in men is 31% and in women is 17%[109]	
Traumatic brain injury	All LAC	• The region has one of the highest rates of injury mortality in the world[110–112] • Has the highest incidence rates of traumatic brain injury caused by violence[106]	
Epilepsy	Honduras, Panamá, Chile, Peru and Colombia	• 17.8 (range, 6–43.2) per 1,000 people • Incidence is 77.7–190 per 100,000 people per year[44], whereas in high-income countries it is 30–50 per 100,000	• Epilepsy is characterized by the appearance of primary generalized or partial seizures that begin with a widespread electrical discharge that involves one or both sides of the brain at once. Hereditary factors are important in many of these seizures
Dementia	All LAC including large family groups in the Dominican Republic, Colombia, and Venezuela	• 6% of those over 60 years are affected[21] • Affects 2 million people, and likely to increase[47]	

DALYs, disability adjusted life years; LAC, Latin America and the Caribbean. The 2014 population estimates for Latin America were 521.9 million and for the Caribbean were 7.0 million

Table 4 | Neurological, mental health, developmental and substance-use disorders and specific burden of disease in the Middle East and North Africa

Condition or disease	Key affected countries	Burden of disease	Impact of condition or disease
Unipolar depressive disorder	All countries	• Prevalence between 5–10%[113] • 15.3% Palestinian adults and children have depression[28] • The lifetime prevalence in Iraq is 7.2%[27]	• Women are more likely to have higher rates of depression than men • Disability, marital dysfunction, loss of employment and risk of suicide[113]
Post-traumatic stress disorder	Conflict zone countries	• 36% of adults in Iraq suffer from psychological trauma as a result of violence[114] • A rate of 23.2% has been reported in Palestinian populations in the Gaza strip and Nablus district in the West Bank[28] • Prevalence of 37.1% for Palestinian children[115]	• Disability, loss of employment, disrupted family relationships and risk of substance misuse
Substance-use disorders (including nicotine, cannabis, alcohol and opiates)	All countries	• 80% of men and 67.8% of women in Yemen have used khat during their lifetime • There has been an increase in the prevalence of substance use in the Arabian Peninsula and East Africa, particularly among young adults and females • Tramadol use is a serious, growing public health problem in Egypt and other Middle East and North African countries (8.8% use among school children in Egypt)[116] • Cannabis is the most commonly used drug • In a 10 country study the tobacco smoking rate was 31.2%. The highest rates were in Jordan, Lebanon, Syria and Turkey[117]	• Khat is implicated in depression, anxiety, psychosis and cognitive dysfunction[91,118] • Early first drug use leads to more drug problems later in life[119]
Recessively inherited genetic diseases	All countries	• Incidence is related to high consanguinity rates[30–32]	• Increased need for medical care • Reduced lifespan • Increased family burden[30,31]
Epilepsy	All countries	• Median prevalence is estimated to be 2.3 per 1,000 (ref. 36) • In 23 Asian countries lifetime prevalence of epilepsy was 1.5 to 14 per 1,000 (ref. 54)	Prevalence is likely to be underreported because of stigma associated with the illness

The 2014 population estimates Middle East and North Africa were 351.4 million. Population data from World Bank and aggregated by http://data.okfn.org/data/core/population

and neurophysiology (EEG and nerve conduction velocity) facilities for adults and children, as well as the capacity for population-based studies in rural and urban centres and longitudinal cohort studies. In South Africa, a wide range of research techniques have been developed, including EEG, electromyography, magnetic resonance imaging, diffusion tensor imaging, structural imaging, magnetic resonance spectroscopy, positron emission tomography and transcranial magnetic stimulation.

Health budgets and research funding

A lack of adequate funding opportunities for neuroscience research in LMICs is a major hindrance to moving the field forward. The disproportionate designation of health spending in relation to variable national gross domestic product in LMICs makes it difficult to sustain or even designate research budgets[23]. For example, the order of the top three countries in sub-Saharan Africa — South Africa, Nigeria and Kenya — in terms of health research publications has remained unchanged for

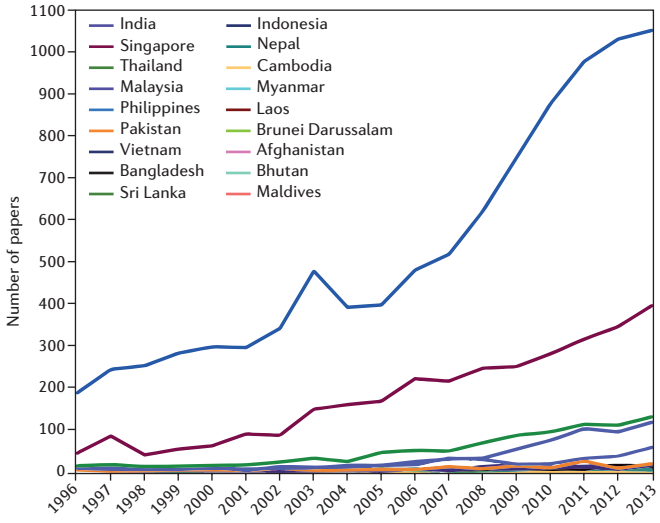

Figure 2 | Number of neuroscience papers in international peer-reviewed journals published by authors from Asian counties per year. The data were retrieved from http://www.scimagojr.com.

the past 14 years, because of financial constraints imposed by total expenditure on health and the national gross domestic product[61]. Funding for NMDS disorders research is variable and depends on the priorities of the government agencies that fund health and/or science and technology research in general (where these exist). Three steps could be taken to promote neuroscience research in LMICs. First, governmental funding for research through universities and research institutions should be enhanced and encouraged. Second, funds from national and international non-governmental organizations (NGOs; which contribute up to 20% of all external aid for health services in developing countries, http://www.imva.org/Pages/biblfrm.htm) could be used to increase research opportunities in health and medicine, including epidemiology, clinical research, public health services and policy research. Third, increased collaboration with regional or international partners could lead to more research opportunities and support.

CONCLUSIONS

Regional variations in the challenges posed by NMDS disorders among LMICs means that research priorities need to be addressed country-by-country, and by regions within countries. There are significant gaps between the resources needed for research and those that are currently available, and a pressing need to strengthen human-resource capacity and research infrastructure, while promoting collaboration. Global demographic trends point to LMICs as the main work force of the future[79]; it is, therefore, imperative to act expeditiously to reduce the enormous burden of brain disorders in these countries. The loss of human potential and cost of inaction are unacceptably high.

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ADDITIONAL INFORMATION