Building global capacity for brain and nervous system disorders research

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The global burden of neurological, neuropsychiatric, substance-use and neurodevelopmental disorders in low- and middle-income countries is worsened, not only by the lack of targeted research funding, but also by the lack of relevant in-country research capacity. Such capacity, from the individual to the national level, is necessary to address the problems within a local context. As for many health issues in these countries, the ability to address this burden requires development of research infrastructure and a trained cadre of clinicians and scientists who can ask the right questions, and conduct, manage, apply and disseminate research for practice and policy. This Review describes some of the evolving issues, knowledge and programmes focused on building research capacity in low- and middle-income countries in general and for brain and nervous system disorders in particular.

INDIVIDUAL LEVEL
At the core of capacity building is the training and mentoring of individuals to design and conduct research; to create or adapt research tools that are relevant to brain–disorders research; to form collaborations with scientists in their institution, elsewhere in the country, and internationally; and eventually to serve as mentors themselves for the next generation of scientists (most effectively if they are within their home countries or region). Increasingly, researchers also need training on how to interact effectively with policy and programme implementers to ensure that they and their practices are adapted to the practices and policies locally.

Capacity building at the individual level begins with mentors who counsel, provide career guidance, and advise on the teaching and sharing of ethical principles that instil integrity in research and care. Research–mentoring strategies and systems are context–driven, and often use apprenticeship or hands–on models, whereby individuals learn by doing. When little in–country research expertise and capacity exists, training may need to take place initially in a higher resource country. However, the goal should always be to have the research training in the context of the trainees’ home institution.

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In terms of systems, scientists initially educated in LMICs then trained in high-income countries say that they are accustomed to certain ways of providing and receiving feedback, and interacting within hierarchical relationships. When they return to their home academic environments, ideally they will adopt a hybrid mentoring style, combining positive attributes from both the country where they were trained and their home country, of which they have an awareness of local nuances, regarding local customs, politics and bureaucracy.

Questioning and vigorous debate are integral to the scientific process, but young investigators from cultures that emphasize deference in hierarchical relationships may experience a conflict between these two values when they return home.

In terms of research and clinical practice, performing a lumbar puncture to obtain cerebrospinal fluid (CSF), a requirement for the diagnosis of most CNS infections and some degenerative or developmental abnormalities, brain banking and autopsy can all be met with reluctance in LMICs. Extraction of fluids, tissue or organs for donation or banking for research purposes is associated with significant sociocultural barriers in some cultures. Several factors related to religion and culture, and issues related to distrust of the medical system, misunderstandings about religious stances and ignorance often complicate the process. Requests for brain or other organ banking for research purposes could raise concerns that agreeing to donation would discourage doctors from treating to save lives among relatives or that consenting to banking would result in premature removal of their or their relative’s organs.

To build capacity for these endeavours, mentors must be willing to not just advocate for these techniques, but also to address cultural barriers that may affect policies, as well as the discomfort of trainees who may not have experience of approaching relatives and patients about these procedures.

The National Institutes of Health Fogarty International Center Global Brain, NIDA International Fellowships and other programmes (see Supplementary Table) are designed to help catalyse research capacity development at an individual level (both as research training opportunities for young investigators, and as research pipeline opportunities for more advanced LMIC investigators) to help prevent the loss of crucial talent and expertise.

**INSTITUTIONAL LEVEL**

Institutional capacity building is the administrative foundation and is essential for establishing and sustaining initiatives intended to realize its vision14. Research infrastructure includes job positions that provide protected time for research, as well as robust laboratories and clinical spaces where diagnosis, treatment and research can be conducted. Research into brain disorders, especially stroke, CNS infections, trauma and neurodegenerative conditions requires the technology to assess structural neurological abnormalities; for example, computerized tomography or magnetic resonance imaging may be non-existent or prohibitively expensive in many LMIC settings. Although research-training grants typically provide the funding necessary to train new scientists and the equipment to increase laboratory capacity, larger infrastructure capacity-building endeavours, such as acquiring high-cost diagnostic neuroimaging or laboratory equipment, or constructing new laboratories, clinics or classrooms, require the financial commitment of institutions with support from funders (ideally, and eventually, at the country level for maximum sustainability).

Research and grants administration are crucial to the sustainability of research programmes within any institution, but good administrators can enhance the development of research capacity in resource-challenged institutions (Box 1).

**Networks**

Research and research-training networks enrich the research environment and build capacity by increasing collaborations and partnerships; expanding institutional perspectives from local and national levels to regional and perhaps the global level; and facilitating ideas exchange, dialogue and universal or standardized protocols for brain research15. Such networks are most effective when they attract not only individual scientists and academic institutions, but also non-governmental organizations (NGOs), corporations, policymakers, and/or philanthropists, to sustain and embed the research enterprise within a country that is focused on a health issue, such as NMDS disorders. One example is the neuroscience promotion association APRONES. This association was established by a group of neurologists to share knowledge of diseases of the nervous system in LMICs. Members are from Africa, Europe and the United States. The association encourages collaborative studies around the world, while building networks and ultimately research capacity16.

**NATIONAL LEVEL**

True sustainability of research capacity and its application requires a national commitment to the research enterprise and implementation of research results at the policy level, as well as a continuing dialogue between health practitioners, policymakers and researchers. However, often it is not until research and research-training networks are established that local government and NGOs recognize the benefit of talent and training to system-wide improvements and national human-resource development17. At that point, they take actions to sustain it.

According to the WHO1, work in support of the ethical review and public accountability of research is not keeping pace with best practices. Opportunities to create a shared framework for storing and sharing research data, tools and materials, have not been met with the same energy in the area of health as they have in other scientific fields. Furthermore, policymakers rarely understand research priorities or use evidence to inform their decisions.

Without country-level planning and action, along with guidance documents, health research in LMICs may be influenced more by the demands of foreign funders’ research and infrastructure interests than...
by the health priorities of the host country\textsuperscript{17}. In LMICs in general, and Africa specifically, increasing the value of health research requires evidence-informed actions to be taken by relevant authorities to ensure that health research is conspicuous in development agendas. It also requires defining, financing and monitoring a clear national plan for a future research enterprise focused on health. To achieve these goals, policymakers and public health and research--funding institutions can use principles adapted from the WHO Strategy on Research for Health\textsuperscript{3} as a guide. These provide the overall framework for research capacity and include reinforcing the research culture and organization; focusing research on key health challenges by setting priorities; strengthening national health research systems and building capacity; encouraging good research practice (setting standards) and consolidating links between health research and action (translation and evidence-based implementation).

Needs and opportunities for building and strengthening capacity for brain--disorders research are shown in Table 1. Although not exhaustive, they outline specific valuable approaches that can be used by high-income country and LMIC collaborators.

The Supplementary Table includes some organizations that are

| Table 1 | Approaches to building research capacity |
|-----------------|--------------------------------------------|
| **Category**    | **Activity**                               | **General and specific needs**                                      | **Anticipated benefits**                                      | **Specific approaches**                                      |
| Human capacity  | - Increase the number of clinician researchers | - Increased number of physicians and allied health professionals in research benefits all neuroscience researchers, including neurologists, neurosurgeons, infectious disease specialists, psychiatrists and other mental health practitioners | - Practical experience and opportunities for future training\textsuperscript{17} | - Create protected time and funding for research |
|                 | - Increase research capacity of clinicians and researchers through workshops and short courses; and advanced degrees in public health (for example, epidemiology, biostatistics, clinical trials, health services and implementation science), clinical and basic science research | - As the neurosciences have not received as much attention from research training grants, most areas would benefit from increased funding for research training | - Address the shared burdens of common conditions, including neurodegenerative disorders, stroke and epilepsy | - Multidisciplinary training and research |
|                 | - Sub-specialized training on specific skills related to nervous-system disorders | - Health-systems research is needed, which necessitates training in bioethics, research methodology, epidemiology, clinical trials, population-based methodology and intervention studies | - Development of multidisciplinary teams of health-care professionals to improve prevention, pre-hospital care, and clinical care in neuroscience, such as trauma, mental health or neurogenetics | - The Wellcome trust-DBT India alliance fellowship for clinicians and research scientists |
|                 | - Institutionalization of mentorship training | - Specific areas of neuroscience with unique needs, include mental health for which health-services research is crucial to increase the capacity of care services | - Wide spread mentorship training (for example, through programmes such as those of the NIH Fogarty International Center http://www.fic.nih.gov/) | - Innovation in science pursuit for inspired research programme |
| Infrastructure and tools | - Neuroimaging (for example, computerized tomography or magnetic resonance imaging) | - Outstanding mentoring is a prerequisite of any successful research-training programme | - Capacity for conducting neuroscience research will increase as trainees move into positions where they will start mentoring subsequent generations of trainees | - Wide spread mentorship training (for example, through the Fogarty Global Brain programme) |
|                 | - Genomic sequencing to detect SNPs in GWAS | - Most neurological conditions require neuroimaging to confirm a diagnosis, disease stage or to monitor progress | - Increasing numbers of scientists and the development of research teams, research culture and an increase in scientific literature and novel research | - Mentoring in the tools needed through flexible research and research-training programmes (for example, through the Fogarty Global Brain programme) |
|                 | - Increased laboratory capacity | - GWAS are used to identify genetic variations (SNPs) associated with neurological and psychological disorders, including addiction | - Increased availability of neuroimaging will lead to better definition of the burden of many neurological conditions, such as stroke, CNS infections, developmental, degenerative and genetic disorders, and trauma | - The US National Center for Biotechnology Information has developed the Database of Genotype and Phenotype, where genetic sequencing information can be deposited and accessed |
|                 | - Culturally appropriate assessment and screening tools | - Most studies of neurological diseases require at least a basic laboratory to process blood, cerebrospinal fluid or other human samples | - Detection of specific genes through GWAS can lead to a better understanding of the functional mechanisms that are biologically important in disease pathogenesis and, ultimately, to better treatments for neurological diseases | - Enhancement of laboratory capacity often requires the upgrade of electrical systems, and with larger laboratories may also require installation of air-conditioning systems |
|                 | - WHO and NIH databank of valid and reliable assessments for young people and adults. Each has an armamentarium of tools that are culturally appropriate | - With increasing complexity of studies, additional equipment is needed, such as polymerase chain reaction for detecting infectious pathogens or biosensors to detect environmental toxins | - Disorders such as epilepsy and schizophrenia would benefit from increased recognition of barriers identified through culturally appropriate screening tools | - NIH and WHO promote scientific discovery, and shared resources, that allow for data harmonization across many programmes |
|                 | - WHO and NIH databank of valid and reliable assessments for young people and adults. Each has an armamentarium of tools that are culturally appropriate | - Stigma, social and health disparities are more common with disorders such as epilepsy and schizophrenia | - Disorders such as epilepsy and schizophrenia would benefit from increased recognition of barriers identified through culturally appropriate screening tools | - Network meetings with special interest groups value the use of unified concepts of addiction and mental health, from DSM to ICD classifications cont. |
### Category | Activity | General and specific needs | Anticipated benefits | Specific approaches
--- | --- | --- | --- | ---
Technology | Incorporation of emerging POC diagnostics from both the development of cross-cultural tools to the use of the tools | POC diagnostics could permit rapid diagnosis of many neurological infections in the field, resulting in improved recognition and treatment | Miniaturization of diagnostic technologies for genomics, infectious agents and environmental markers will enable a better understanding of gene-environment interactions and lead to new therapeutic approaches | Better sharing of data and instrumentation is needed, as well as collaborative grants
| Access to electronic scientific literature | Common to all research is the need for understanding past and current scientific literature | Improved access to electronic scientific literature should lead to more scientifically sound research and often leads to the creation of journal clubs, which in turn strengthens the culture of research | The HINARI Access to Research in Health programme provides free or low cost access to 200 neuroscience journals for not-for-profits in LMICs, but the top ranking 50 journals are not available | Open access journals are available to everyone
| Introduction of mHealth technologies and e-learning strategies | Adoption of mobile technologies for surveillance, assessments and treatment are particularly needed in LMICs where cell phone ownership is rising rapidly, but access to conventional health care and health-care providers is limited | Reaching patients with disabling neurological conditions using cell phones may prove easier than conventional methods for providing health information | Share resources | Offer classes for students at reduced cost
| Increase Internet capacity | Adapt information and communication technologies to support research and research-training programmes | Video conferencing for direct communication between mentors, colleagues and training in diverse settings | Communication technologies include Skype, GoToMeeting, AdobeConnect, WhatsApp, Polycom and WebEx | Mentor LMIC partners through application processes.
| Pilot awards for LMIC researchers | Funding for research in LMICs is limited, but funding for neurological disease research is even more so | Providing funding to support pilot studies to LMIC colleagues and trainees should lead to increased research relevant to the LMIC setting and provide pilot data on which larger grant applications could be developed | Funds from national and international NGOs can increase research opportunities | Collaboration with foreign partners provides new research opportunities and support | PEPFAR, UNAIDS, WHO, and the Bill and Melinda Gates Foundation have made drugs and services significantly more accessible
| Increase governmental funding for research through universities and research institutions | Funds from national and international NGOs can increase research opportunities | Collaboration with foreign partners provides new research opportunities and support | Funds from national and international NGOs can increase research opportunities | Collaboration with foreign partners provides new research opportunities and support | PEPFAR, UNAIDS, WHO, and the Bill and Melinda Gates Foundation have made drugs and services significantly more accessible
| Research frameworks to support the implementation of the outcomes of well-designed studies relevant to neurological diseases | Evidence-based public health strategies to incorporate child neurodisability screening, clinical evaluation and rehabilitation packages into the health-care system | Maternal health programmes that work closely with early childhood programmes could ensure optimal pregnancy outcomes and develop effective interventions to enhance child development | Improved access to electronic scientific literature should lead to more scientifically sound research and often leads to the creation of journal clubs, which in turn strengthens the culture of research | Reaching patients with disabling neurological conditions using cell phones may prove easier than conventional methods for providing health information | The HINARI Access to Research in Health programme provides free or low cost access to 200 neuroscience journals for not-for-profits in LMICs, but the top ranking 50 journals are not available | Open access journals are available to everyone
| Capacity building in translational science and knowledge management | LMIC partners are asking for translational science training | Influence policymakers to redirect budget priorities to address brain disorders and their research | Increased Internet capacity | Increase governmental funding for research through universities and research institutions | Funds from national and international NGOs can increase research opportunities | Collaboration with foreign partners provides new research opportunities and support | PEPFAR, UNAIDS, WHO, and the Bill and Melinda Gates Foundation have made drugs and services significantly more accessible

### Human capacity challenges

Capacity building across countries and cultures for brain–disorders research is inherently a ‘messy’ processes when we consider the scope of research with global partners across completely different time zones, infrastructures, cultural norms, expectations and organizational research capacities. Differences in language and expression of research ideas can lead to confusion and misunderstanding. When choosing terminology for assessments on depression, for example, well-developed Western assessments use the words ‘feeling blue’ to indicate feelings of sadness. To discuss mania, the term ‘high’ might be used. These terms are idiomatic and do not translate well in many languages. Another example is the need for translators and interpreters in different sites within countries where multiple languages and dialects are spoken.

Research training includes emphasizing flexibility to address such cultural challenges to research and working within local and regional

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CNS, central nervous system; DSM, Diagnostic and Statistical Manual for Mental Disorder; GWAS, genome-wide association studies; ICD, International Classification of Diseases; LMIC, low- and middle-income countries; NGOs, non-governmental organizations; POC, point-of-care; SNP, single nucleotide polymorphisms; WHO, World Health Organization.
collaboration whereby they can help each other in the grant application
funding. Researchers have also set up channels of communication and
with presidents, deans and directors of institutes to advocate for more
ners have strengthened institutional support by setting up meetings
and limited access to scientific and technical information are also key
ument management capacities. These capacities vary widely across
board committees, grant-management personnel, and data and doc
To conduct research, LMIC institutions require institutional review
protocols that account for local cultural norms, while educating the
norms (the ESSENCE principles shown in Box 3 can help). For example,
when conducting a study on the prevalence of opiate use in Afghani-
stan, two female interviewers were needed to conduct interviews with
the female head of the household. Cultural norms dictated that the fe-
male interviewers had to be accompanied by a male team member who
would make the first contact with the household53. Designing research
protocols that account for local cultural norms, while educating the
high-income country and LMIC institutional review boards is neces-
sary and builds trust and understanding between collaborators over
time. Individual challenges can be resolved through open communica-
tion and sharing of expectations at the outset.

Infrastructure capacity challenges
To conduct research, LMIC institutions require institutional review
board committees, grant-management personnel, and data and doc-
ument management capacities. These capacities vary widely across
and within countries, but sufficient capacity in these areas is crucial
to ensure fidelity to research protocols. Financial resource limitations
and limited access to scientific and technical information are also key
challenges.

To overcome these barriers, high-income country and LMIC part-
ners have strengthened institutional support by setting up meetings
with presidents, deans and directors of institutes to advocate for more
resources and to become less reliant on outside high-income country
funding. Researchers have also set up channels of communication and
collaboration whereby they can help each other in the grant application

process for Western-based grants.

Investigators have also succeeded in seeking permanent access to
library resources through high-income country institutions for their
trainees. However, more sustainable access within and across LMICs to
bridge the global information divide is needed. One source is HINARI50.

Technology capacity challenges
Information and communication technology (ICT) has become in-
creasingly integrated into research and clinical training. ICT involves
a variety of technologies, including low-cost two-way voice, picture
and video communication; development of geographic information
systems, which are useful for planning interventions and mapping the
prevalence of neurological conditions and risk factors54,22; Internet-
and mobile-phone-based health-related interventions51, and Internet-
and mobile-phone-based data collection24,31.

Online courses and degree programmes that have become in-
corporated into most high-income country academic institutions
have particular utility in LMICs where training infrastructure may be
lacking or geographical barriers limit participation in conventionally
structured research training programmes. The development of mas-
ive open online courses (MOOCs) and bidirectional interactive vir-
tual spaces permit multidisciplinary partnerships between students,
faculty and mentors across institutions and countries. These provide
new practical opportunities for bidirectional training, presentations
and classroom-based discussions around the world (either as live or
recorded sessions).

The Internet allows research, clinical training and supervision to
take place across the globe, and although the content and quality of
the online material is important, the effectiveness of the supervision
depends on the quality of the input, and learning ultimately rests on
the ability and motivation of the trainee. Internet interventions have
the potential to reduce manpower requirements, but without sufficient
support, completion rates remain unacceptably low. There is a need to
rigorously evaluate the use of these technologies in brain-disorders re-
search training to ensure they are effective, acceptable and culturally
relevant.

Ethical challenges
The field of neuroethics is a component of bioethics that deals with
the investigation, treatment and research procedures that involve the
human brain and brain science. The International Neuroethics Society
(http://www.neuroethicssociety.org) was started to promote research
that would benefit people around the world.

Although all research training should include human subject re-
search ethics, teams that focus on brain-disorders research face unique
ethical challenges. People with neurological disorders are vulnerable,
sometimes cognitively or physically challenged and often stigmatized,
which creates special challenges when designing protocols that en-
sure ethical informed consent. It is essential to address these special

BOX 2 | ANATOMY OF A GLOBAL BRAIN RESEARCH FUNDING PROGRAMME
Achievements of the National Institutes of Health/Fogarty
International Centre coordinated global brain research programme
(http://www.fic.nih.gov/About/Staff/Policy-Planning-Evaluation/
Pages/fogarty-program-evaluation-brain-disorders.aspx).
The programme supports collaborative empirical research and
capacity building on brain and nervous-system diseases and
disorders identified by the applicants as relevant public health
challenges in their low- and middle-income countries (LMICs).

Programme’s achievements
Research conducted over 10 years in 45 LMICs, most of which are in
sub-Saharan Africa, Latin America and the Caribbean.
Topics were across the spectrum, from mental health and substance
use, to peripheral nervous system trauma and gene–environment
interactions.
During the first 10 years of the programme, participants published
435 peer-reviewed articles in 249 unique journals, as well as 14
books or chapters.
Grantees also produced unique tools for clinical assessment in the
LMIC context, developed and evaluated new interventions, and
identified novel laboratory tools or methods.
Almost half of the projects supported training for people, who were
not primary collaborators, in LMICs. The programme supported
in-depth instruction for at least 138 scientists, for an average of 23
months.
Projects included training or mentoring at the LMIC (or sometimes
a high-income country) site, in skills, methods or procedures that are
essential to research, including workshops on specific topics, or
clinical or research skills.
Achieved mandatory training in research ethics, which built and
sustained capacity in research ethics at most sites.

BOX 3 | SEVEN PRINCIPLES FOR STRENGTHENING RESEARCH CAPACITY
Based on the World Health Organization–TDR ESSENCE good
practice document series59
1. Network, collaborate, communicate and share experiences
2. Understand the local context and accurately evaluate existing
research capacity
3. Ensure local ownership and secure active support
4. Build in monitoring, evaluation and learning from the start
5. Establish robust research governance and support structure, and
promote effective leadership
6. Embed strong support, supervision and mentorship structures
7. Think long-term, be flexible and plan for continuity
challenges (some of which are similar to those faced by researchers working with populations affected by HIV/AIDS) in training curricula for research that is specific to brain disorders. The Fogarty funded Pakistani stroke research training programme has a dedicated neuroethics training module, in which every mentored project that involves mental health research has a bioethics programme (Box 4).

Use of functional magnetic resonance imaging (fMRI), near-infrared recording systems (NIRS), polygraphy to extract information, genetic testing and cognitive enhancement using drugs and brain stimulation are just a few examples of current and evolving technologies that raise moral and ethical questions. The application of these modern techniques has been gaining momentum in the developing world, thereby indicating an urgent need to integrate neuroethics training into the neuroresearch capacity building efforts in LMICs.

Metrics

A robust set of metrics is crucial to demonstrate the value of research capacity building to diverse stakeholders and to understand how to make research-training activities the most effective. Output measures include educational materials such as courses, modules and workshops; creation and transfer of new knowledge, such as prototypes and innovative protocols; and measuring trainee engagement indicators (for example, number of short-, medium- and long-term trainees taught, number of trainees completing courses or acquiring new skills and trainee feedback). As research training programmes mature, conventional metrics are needed, such as publications, grants, awards, memberships in societies, degrees awarded and faculty appointments.

Measuring the long-term impact of building research capacity is a significant challenge. Many funding agencies have strict guidelines for tracking career successes of funded scholars for up to 15 years after training and evaluation frameworks that can be built into programmes from the beginning to ensure trackable impacts (http://www.fic.nih.gov/About/Staff/Policy-Planning-Evaluation/Pages/evaluation-framework.aspx). Long-term impacts of successful capacity building include cultural competency of staff and faculty; increased involvement of staff and faculty in global health brain research; the extent to which former trainees hold positions of influence in their countries; leadership of former trainees in research and research collaborations; and increased knowledge of disorders and their significance locally and internationally.

CONCLUSIONS

Figure 1 summarizes some of the frameworks, components, pathways and tools involved in research capacity building. As described, research capacity building starts at the individual level. Although partnerships between high-income and LMICs are important, the goal is for research training, as well as research itself, to increasingly take place at the LMIC sites and for those sites to become research and training hubs in their own right.

Concurrent research capacity strengthening at the institutional and national levels is necessary to ensure research and career opportunities for, and the retention of, trained researchers. With respect to NMDs disorders in particular, targeted programmes provide opportunities for LMIC clinicians, faculty and trainees to gain new skills for conducting relevant research and to contribute to long-term sustainability of research conducted in LMICs (as the trainees become the trainers and attention is paid to institutional strengths and weaknesses). Although challenges exist, they can be managed and eventually reduced or overcome using principles and models learned and shared across programmes. Robust evaluations of capacity building activities with quantitative and qualitative measures should be conducted, shared and used to identify the most successful approaches and to allow iterative improvements in individual, institutional and national level NMDs research capacity.

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