India plans for interdisciplinary neuroscience research center

Neuroscience research in India tends to attract mostly biologists and doctors and few scientists from other disciplines. Even the National Brain Research Centre (NBRC) set up in 1999 has found it difficult to attract faculty from other science disciplines to its location at Manesar near Delhi, says NBRC director Vijayalakshmi Ravindranath.

Much of this could change with a new multidisciplinary neuroscience research center planned at the Indian Institute of Science in Bangalore.

The decision to set up the new center, with experts from departments as varied as electrical communication engineering, computer sciences, mathematics and chemistry, was formally approved by the institute's council in June and is inspired by the Harvard University model. The Indian Institute of Science may provide an initial seed fund of about $425,000 (20 million rupees), says its director Padmanabhan Balaram.

Work on the new center has kick-started with the appointment of its first head, Ravindranath, who is expected to leave her post as NBRC director in early 2009.

Faculty recruitment has begun, and research is slated to start by next spring, says Balaram.

India has considerable scientific strengths in computational biology, image processing and cell biology, but its involvement in neuroscience research is scattered, Balaram notes.

"The idea is to leverage the existing expertise in a large, university-type institution and bring together people of diverse backgrounds to work on frontier areas of neuroscience," Ravindranath told *Nature Medicine*. "We want to see which model works better: creating small institutions of excellence in isolation or creating centers within big institutes and universities."

Ravindranath says India can no longer afford to ignore the rise in degenerative disorders related to aging.

According to UN estimates, the number of people aged 60 years and older in India is expected to shoot up from 77 million in 2000 to 324 million by 2050, thanks to a huge rise in population and increased longevity due to improved healthcare. The country is also witnessing a shift in disease burden from infectious diseases to noncommunicable diseases, such as diabetes and heart disease, and age-related disorders.

There are additional reasons for India to expand its neuroscience research. With almost half of its children undernourished, studies on how malnutrition affects brain structure, development and function are crucial. "It is also important to determine whether undernutrition in mothers during pregnancy and lactation makes the brain [of babies] more vulnerable to later stresses, and also the critical time period when brain damage can be reversed by restoring adequate nutrition," she says.

Similarly, some developing countries such as India have a high burden of the mosquito-borne Japanese encephalitis, which involves inflammation of the brain and kills children. Cases of epilepsy, too, are more numerous compared to industrialized countries.

Research in the Indian population could also offer insights into other intriguing observations—the nationwide incidence of stroke in persons under 40 years of age is higher in India than in Western nations, but the incidence of Alzheimer's is lower, and treatment for schizophrenia gives better results. The biological basis for these differences between Indian and Caucasian populations is not understood yet, notes Ravindranath.

The new center will probably benefit from the fact that Bangalore is home to India's publicly-funded National Institute of Mental Health and Neurosciences (NIMHANS), a leading center for treatment of brain and nerve disorders. "We hope to form a bridge between NIMHANS's clinical expertise and the Indian Institute of Science's academic expertise," says Ravindranath.

India today presents a "unique window to observe how rapid social and lifestyle changes impact disease burden and progression in developing countries, especially aging-related disorders," she adds.

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Publication is positively skewed

Positive results of clinical trials for drugs or devices have a higher chance of getting published in the medical literature than negative trials, according to an investigation into the publication status of the trials submitted to the US Food and Drug Administration (FDA) as part of the 90 new drug approval applications approved by the agency between 1998 and 2000. Notably, when the authors of the study split up their analysis by trial type, they found that clinical trial sponsors publish the results from pivotal trials (an industry term that refers to those trials that show whether a drug or device really works) only 76% of the time (*PLoS Med.*, doi:10.1371/journal.pmed.0050191; 2008).

Overall, of the 909 trials they found related to the 90 drug applications, only 43% of all the trials conducted were published within five years after FDA approval of the drug or device.

The studies that found a statistically significant difference were more than three times as likely to be published. According to study co-author Ida Sim, director of the Center for Clinical and Translational Informatics at the University of California, San Francisco, this leads to a phenomenon called 'positive publication bias', which is a serious problem, because it can make a drug or device appear in the literature to be more effective than it really is.

Sim explains, "We have this idea of practicing evidence-based medicine, which is predicated on having a full and complete evidence base. But when the evidence base is skewed, we can't really do this."

In a paper published this year, experts suggest that the FDA Amendments Act of 2007 has improved transparency, because the law mandates that sponsors or primary investigators of clinical trials for approved drugs post a summary of their results in a national open-access database (*Science* **319**, 1340–1342; 2008).

The lead author of the report, Deborah Zarin, oversees the ClinicalTrials.gov registry at the National Library of Medicine of the National Institutes of Health and is in charge of ensuring the results are posted in compliance with what the new law. According to Zarin, "for the trials that are covered by this law, the results database should have a big impact on disseminating medical knowledge, because the results have to be publicly available."

But not every type of clinical trial is covered by the legislation, nor does it directly affect medical journals. Although Sim applauds the FDA Amendments Act of 2007, she adds that it "doesn't address the issue of not publishing trials in medical journals. They remain one of the most influential and biased sources of information."

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