



GLOBAL HEALTH AND NEUROSCIENCE

Global Burden of Brain Disorders

Brain disorders have far-reaching impact, affecting people of all age groups from all geographic locations. According to the World Health Organization (WHO), an estimated 1 billion people worldwide suffer from neurological and psychiatric disorders. These disorders account for 6.3 percent of the total burden of disease. As many as 6.8 million people die annually from brain disorders, accounting for 12 percent of global deaths. Brain disorders are considered one of the greatest threats to public health, and yet there are many gaps in the understanding of these conditions.

Moreover, mental disorders such as depression and schizophrenia are among the leading causes of disability in the United States, Canada, and Western Europe for ages 15 to 44 — prime working years. A recent report conducted by the WHO, World Bank, and Harvard University indicates mental disorders may account for more than 15 percent of the burden of disease in established market economies.

Economic Hardship

In addition to human suffering, these disorders cause tremendous economic hardship for individuals and society: the loss of gainful employment, the caretaker's loss of family income, the cost of medications, and the need for other medical services. Some estimates place the economic burden of brain-related illness for 2008 at over \$2 trillion worldwide. Another recent study indicated that the economic burden of serious mental health conditions in the United States may top \$317 billion, including health-care costs, loss of earnings, and disability payments, but not including associated costs such as incarceration or homelessness.

Given the lack of health resources in developing nations and the expense of modern medicine, costs in those parts of the world are especially debilitating. Moreover, the absence of brain-related disorders from official cause of death tallies means they are often neglected in developing nations. And the stigma and discrimination that accompany neurological disorders often cause patients to go untreated.

For instance, according to WHO, while some 50 million people worldwide suffer from epilepsy, 90



As the world population grows and ages rapidly, the global scientific community is working to develop new advances in medical research to offset the burden of disease.

percent of affected individuals in developing nations fail to receive appropriate treatment. Nearly 70 percent of those affected could become seizure-free with appropriate antiepileptic drug treatment, thereby decreasing stigma and increasing their ability to lead normal lives.

As the global population continues to age due to increased life expectancy, worldwide neurological disease prevalence is expected to increase dramatically. Brain disorders are especially common among the elderly, and age-related brain disorders, like dementia and Alzheimer's disease, pose a particular problem. In the United States, these disorders were the subject of a major policy evaluation and report led by co-chairs Newt Gingrich, former Republican speaker of the U.S. House of Representatives, and Bob Kerrey, a former Democratic senator and governor from the state of Nebraska.

Approaching a Tipping Point

The number of people suffering from dementia is already estimated to be in the tens of millions. WHO estimates the incidence of Alzheimer's disease and other dementias will increase 66 percent by 2030,

and another study suggested about 43 percent of all cases worldwide need a high level of care, like a nursing home.

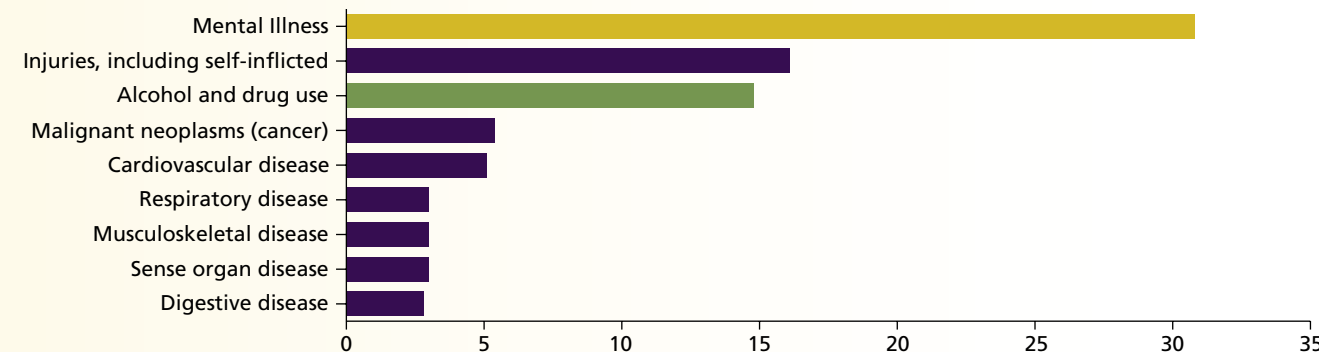
Finding effective ways to target and treat these debilitating conditions is a priority for the global health community. In the United States alone, delaying the onset of Alzheimer's disease by five years could save \$50 billion in annual health-care costs, and researchers believe interventions that delay disease onset and progression by just one year would result in 9.2 million fewer cases of disease in 2050. They note that nearly all of the decline would be "attributable to decreases in persons needing high level of care."

Age-related brain disorders affect entire families and society-at-large. The National Institute on Aging reports that in 2006, nearly 500 million people worldwide were 65 and older; by 2030, that figure is expected to climb to 1 billion. The

number of elderly people in the developing world is expected to jump 140 percent by 2030.

The proportion of elderly people in industrialized nations also will swell. In the European Union (EU), where state-provided health-care programs are the norm, those over 65 outnumber those under 14 — the latter figure has dropped 21 percent in 25 years. While there are now four working persons for every pensioner in the EU, by 2050 there will be only two. Governments are grappling with how to provide adequate long-term care for the elderly — and how to pay for it.

Researchers continue to decipher the mysteries of these brain diseases and disorders. Now more than ever, neuroscience research and a broader commitment to biomedical research is nothing less than a global imperative with monumental personal, economic, and social implications.



The burden of disease is measured in disability-adjusted life years, a public health metric for assessing how a disease adversely affects society through mortality and loss of health.



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Unraveling Alzheimer's Disease

Alzheimer's disease is an emerging problem in the developing world, according to researchers. As populations grow and life expectancies rise, the number of people suffering from age-related neurological diseases like Alzheimer's may skyrocket. However, research is pointing the way to promising new treatments.

Alzheimer's Disease in India

India offers one example of the global impact of Alzheimer's disease. According to the World Health Organization, average life expectancy in India is now 63 years of age — quickly approaching 65, when vulnerability to Alzheimer's disease increases. The United Nations projects that by the year 2050, life expectancy in India will rise to 73, and there will be 221 million Indian citizens who are 65 or older.

According to the Alzheimer's Association, one in eight people over the age of 65 develops Alzheimer's disease. So, by 2050, more than 27 million Indians may be living with the disease. The challenge of caring for so many Alzheimer's patients

is daunting — there are currently fewer than 1,000 neurologists in the entire country.

Alzheimer's Disease Research

These predictions make unraveling the biology of Alzheimer's disease all the more important. Ongoing research is helping to identify the biological bases of memory loss, cognitive decline, and brain cell death in Alzheimer's disease.

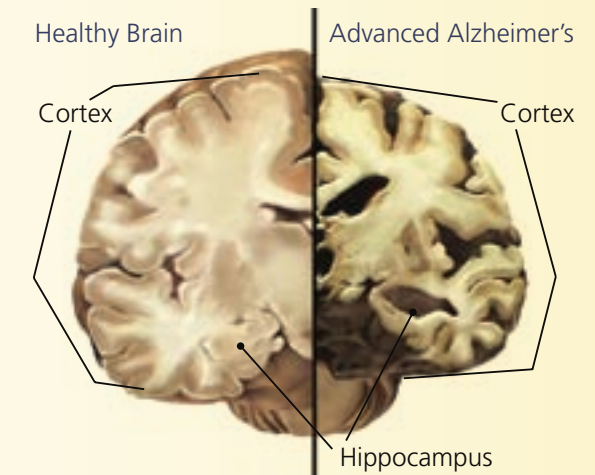
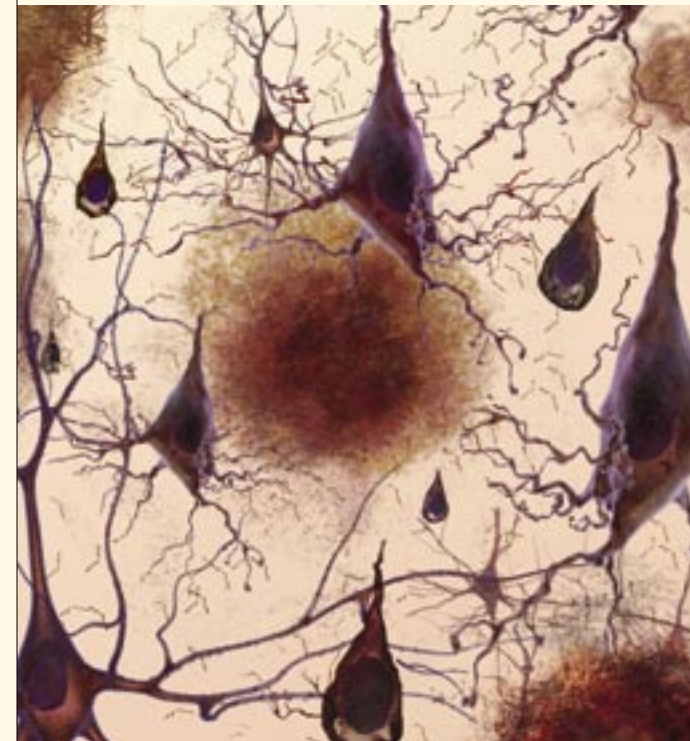
Many researchers are examining the protein deposits that litter Alzheimer's disease brains for clues to the cause of disease. Alzheimer's disease brains contain plaques composed of large deposits of a protein called amyloid-beta. The plaques themselves were once believed to be responsible for disrupting brain cell communication; however, recent research implicates earlier forms and smaller amounts of amyloid-beta. According to new research in animal models of Alzheimer's disease, treatments targeting amyloid-beta may prevent or delay disease progression.

Alzheimer's disease brains also include aggregates of the tau protein called neurofibrillary tangles. Like amyloid plaques, these protein clumps may be at the heart of

the Alzheimer's disease process. Researchers are now looking for ways to limit protein aggregation and tangle formation.

Advances in genetics are helping to identify people most at risk for developing Alzheimer's disease and the molecules and cellular processes involved in disease onset. Researchers have identified three genes (*APP*, *PSEN1*, and *PSEN2*) that cause early-onset Alzheimer's disease, which strikes before the age of 65. Although scientists agree that an array of genes likely contribute to and confer increased risk for the more common, later-onset form of the disease, only one gene (*APOE*) is currently known to do so. Researchers are now investigating how *APOE* is involved in the Alzheimer's disease process.

Scientists also are identifying medical conditions and lifestyle factors that increase the risk of Alzheimer's disease. For example, people with Type 2 diabetes may be at increased risk of developing Alzheimer's disease. Damage to the blood vessels that supply the brain also may increase Alzheimer's disease risk. Together, these findings suggest that maintaining



Left: Healthy nerve cells communicate across a space called the synapse. In Alzheimer's disease, however, the presence of plaques (in brown) and tangles make for a toxic environment in which cells wither and normal communication ceases. **Above:** As Alzheimer's disease progresses, it kills brain cells mainly in the hippocampus and cortex, which leads to impairments in learning, memory, and thinking.

healthy weight, blood pressure, and cholesterol may reduce the risk for Alzheimer's disease and other forms of dementia.

Additional research suggests that Alzheimer's disease may kill brain cells by hijacking a process involved in normal brain development. During development, the brain makes too many brain cell connections. Like overgrown trees, the ones that are not needed are "pruned" back. Researchers recently found the precursor protein that produces amyloid-beta also produces a protein fragment that activates the pruning process.

Deprived of their cellular connections, many mature brain cells die. So, the new finding suggests that Alzheimer's disease kills brain cells by activating the pruning process at the wrong time. Blocking this pruning process might therefore be beneficial to at-risk adults.

Global Opportunity

Although researchers hope to stop the expansion of Alzheimer's disease in the developing world, they recognize that the global community offers unique opportunities for Alzheimer's research. By studying populations with rich cultural and genetic diversity, researchers may gain new insights into the causes of

disease, specifically the genetic and lifestyle factors that protect against or enhance disease risk.

Is Alzheimer's disease preventable? Researchers are not sure. But because it strikes late in life, they recognize that even delaying disease onset by several years would greatly limit its reach. Achieving this goal will require the efforts of a global community of scientists and clinicians, sensitive to both the similarities and unique needs of patients around the world.