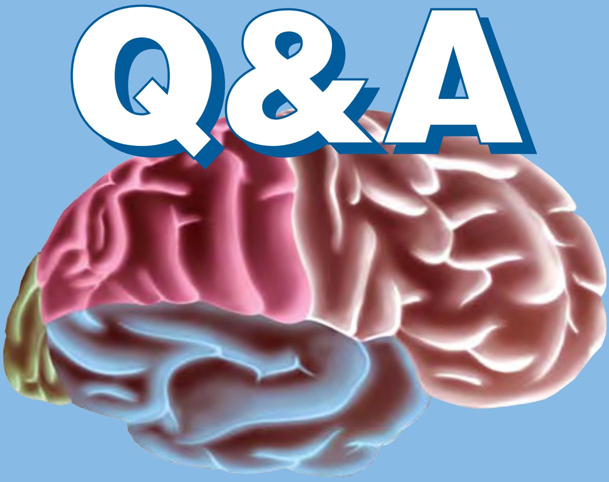
Answering Your Questions About Brain Research



Discover how research is advancing our understanding of the brain in health and disease.

Learn more from the answers to some commonly asked questions about the brain.

The Dana Alliance for Brain Initiatives

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The Dana Alliance for Brain Initiatives *has a vision. The Alliance imagines a world in which the scourge of brain disorders is overcome. The unprecedented advances in neuroscience research over the past several years have helped make this optimistic vision seem more possible. Harnessing the healing potential of the immense knowledge we've gained about the brain to conquer its diseases is the next great frontier of neuroscience.*

In this brochure, we share with you some of that knowledge, in answers to some commonly asked questions about the brain. Explore with us the growing advances in brain research, and join us in imagining the possibilities that can emerge from a deeper understanding of the brain.

The Dana Alliance for Brain Initiatives is a non-profit organization of more than 200 leading neuroscientists, including ten Nobel laureates. The Dana Alliance is committed to advancing public awareness about the progress and benefits of brain research and to disseminating information on the brain in an understandable and accessible fashion. Supported entirely by the Dana Foundation, the Dana Alliance does not fund research or make grants.

THE HUMAN BRAIN *has mystified people throughout history. Though it weighs a mere three pounds and is small enough to hold in our hands, it is our body's most vital organ. Its complex network of 100 billion or more nerve cells orchestrates every aspect of our thoughts, perception, and behavior. More than anything else, our brain defines who we are.*

Disorders of the brain account for more disability worldwide than any other group of illnesses, causing immense suffering and a great burden to individuals and societies. Finding ways to prevent or cure brain diseases is a primary goal of neuroscience research. Reaching it requires an ever-improving understanding of the brain's normal functioning, as well as what goes wrong in disease.*

Q. Can our experiences change our brain?

A. Scientists now know that the brain is remarkably "plastic:" it continues to change throughout life in accordance with our experiences. It is also clear that our surroundings influence our experiences, to a large degree driving our behavior and thinking as we adapt to our environment. Our brain, in turn, reflects our behavior, since behaviors are the sum total of patterns of neural activation. In essence, then, brain, behavior, and environment are all intricately linked in an interactive loop: changes in the environment lead to changes in behavior, which lead to changes in the brain.

*Source: World Health Organization

The "wiring-up" of our brain begins in early development. While our genetic blueprint largely drives this wiring in the womb, a newborn baby's brain sponges up new information from its environment and rapidly sprouts billions of nerve cell connections ("synapses") in response, eventually pruning some of them. New findings reveal that the brain undergoes a second wave of dramatic synapse growth during adolescence, followed by another round of pruning to strengthen synapses that are used routinely and eliminate those that are not. Even into old age, the brain continues to fine-tune itself in response to new learning and novel experiences.

The brain is capable of changing its structure in a number of ways. Synapses become stronger and denser. Tiny blood vessels increase in size and number to bring more blood flow to the brain. Myelin, the fatty sheath that wraps around nerve connections, thickens, helping enhance the flow of nerve signals. New nerve cells are even born in certain brain areas, and with the right environmental influences, the new cells migrate, differentiate, and form synapses with other cells, a process known as "neurogenesis." Scientists have linked neurogenesis to learning, and have shown that stimulating environments increase the rate of neurogenesis. Together, these findings paint a picture of a dynamic, adaptable brain that is ever changing, ever responding to our experiences and our surroundings.

Q. How can "basic" neuroscience research help to find cures for neurological disorders?

A. A better understanding of the brain at every level – molecules, cells, and neural systems – is critical to finding better treatments and, perhaps more important, ways to prevent disease altogether. If we understand how the brain functions in normal states, we should be better able to "fix" it when something goes wrong.

So-called "basic research" to unravel the fundamental mechanisms of brain processes in health as well as in disease is a primary driver of clinical research aimed at developing new drugs or therapeutic strategies. For example, basic studies of how brain cells communicate with one another and how the brain encodes memories have contributed greatly to the development of pharmacologic compounds that treat disrupted neural processes. This approach is beginning to pay off in investigational therapies for Parkinson's and Alzheimer's disease. In psychiatric illnesses, investigating the brain pathways underlying depression and obsessive-compulsive disorder is providing clues about how best to select treatment based on the neural systems involved.

Q. What capacity does the brain have to repair itself after injury or disease?

A. It has long been accepted dogma that the central nervous system does not regenerate itself after traumatic injury or widespread cell death. This is supported by the fact that people with severe head or spinal cord trauma are generally not able to recover their pre-injury level of function. However, recent discoveries – including the revelations that adult brains can form new nerve cells and that immature neural stem cells can migrate to injured areas of animals' brains – have forced a reconsideration of this accepted principle. In addition, improved understanding of how nerve cell connections are formed in early brain development has fueled hope that these developmental processes might be recapitulated to repair the damaged nervous system.

Scientists are just beginning to understand how these innate repair mechanisms might be harnessed to treat disease. On the leading edge of this research are so-called "bound limb" strategies for recovering from a stroke that has caused paralysis or weakness on one side of the body, in which doctors immobilize the unweakened arm or leg to force use of the weakened limb. Devices that re-create the mechanics of walking are used to promote recovery from spinal cord injury. Both of these approaches seek to induce a reorganization of neural systems in order to compensate for damaged nerve connections.

Q. Is memory loss an early sign of Alzheimer's disease?

A. Memory loss is one of the earliest symptoms of Alzheimer's disease and other types of dementia, but occasional forgetfulness is also a perfectly normal part of life. Certain types of memory slips, such as forgetting names or where we parked the car, are common even among the young. In fact, in young and old alike, stress, sleep problems, certain prescription medicines, and depression are associated with memory difficulties. On the other hand, memory problems that significantly impair day-to-day functioning are cause for concern and should be evaluated by a qualified medical professional. Using the best tools and psychological tests, skilled clinicians can diagnose Alzheimer's with 90 percent accuracy.

The search is on for ways to diagnose Alzheimer's earlier, even before symptoms may be apparent. Recent promising developments include using PET imaging to see and track the amyloid plaques in the brain that characterize Alzheimer's disease, and biological tests to look for disease "markers" in the blood. Earlier diagnosis will be increasingly important as new therapies become available, since they – like treatments already on the market – may be most effective when begun in early stages of the disease.

For the garden-variety memory slips that many of us may increasingly notice as we get older, the best advice scientists give is to cope by adapting our habits and following a brain-healthy lifestyle (see also page 14). Memory training tips and programs, detailed in many good books by neuroscientists, can help us learn how to compensate for age-related changes in memory and other cognitive functions.

BRAIN TIP:

As we get older, it may take us longer to learn and store new information, so concentration becomes increasingly important. Try to reduce distractions and minimize interferences when learning new information. Write down and verbally repeat important things, and organize objects you use frequently (like car keys), so you'll always know where to look for them.

Q. How have brain-imaging methods such as PET and MRI affected neuroscience research and clinical care?

A. Techniques that capture pictures of the living human brain at work have become fundamental tools of neuroscience research and increasingly influence how doctors diagnose and treat brain disorders. The advent of "functional" imaging, which looks at both structure and patterns of brain activity, galvanized the young field of cognitive neuroscience, which investigates the interactions of brain, learning, and behavior. Clinical researchers are also beginning to employ brain scans to track the changes underlying neurological diseases and measure the effects of treatments.

The clinical use of brain imaging in disease management has also grown, driven by broader availability of scanning devices and novel techniques that have fostered new applications for imaging. For example, neurologists are increasingly using brain scans to differentiate Alzheimer's disease from other forms of dementia. In a major development, the government-funded Medicare program now accepts PET scans as a reimbursable adjunct to Alzheimer's diagnosis. Doctors may also use scans to determine the extent of damage to the brain from stroke, head trauma, or multiple sclerosis, to characterize brain tumors, and to guide neurosurgeons operating on the brain.

Emerging clinical uses include identifying the brain regions from which epileptic seizures emanate and confirming diagnoses of neurodegenerative diseases such as Parkinson's or Huntington's. In psychiatric disorders, scientists are applying functional neuroimaging methods to track disrupted brain pathways in depression, bipolar disorder, schizophrenia, and obsessive-compulsive disorder. While still investigational, such studies can reveal correlations between brain changes and disease symptoms or treatment response, information that may eventually help doctors better tailor treatments to individual needs.

Q. Can stroke be prevented?

A. Brain experts are convinced that many strokes can be prevented with proper attention to lifestyle factors that increase risk, including smoking, obesity, excessive alcohol use, diabetes, high blood pressure, and physical inactivity. While genetics do play a role (family members of people who have had a stroke are at increased risk), environmental factors may tip the balance in susceptible individuals. Better awareness of stroke prevention could have a huge impact on public health, since stroke is the second leading cause of death and disability worldwide.*

When stroke does strike, it's critical to get medical help immediately. Time lost is brain lost, as stroke experts say, and the only drug currently available for acute stroke must be administered within a few hours.

*Source: World Health Organization

Stroke often disables rather than kills, causing paralysis, muscle spasticity, and cognitive impairments. New approaches to enhancing recovery from stroke capitalize on the growing knowledge about the brain's innate capacity to reorganize itself in response to training.

BRAIN TIP:
Stroke, also known as a "brain attack," is a medical emergency, and should be treated with the same urgency as a heart attack. If you or someone you know experiences any of the following symptoms, seek help immediately: sudden numbness, paralysis, or weakness in the face, arms, or legs; sudden difficulty talking or understanding speech; sudden confusion; vision disturbances; dizziness; or severe, unexplained headaches.

Q. How might stem cells and other tools of "regenerative medicine" be used to treat brain diseases?

A. Fueled by the hope that stem cells may have the capacity to rebuild virtually any damaged or diseased tissue in the body, regenerative medicine has emerged as one of the most promising areas of biomedical research. But many fundamental questions need to be answered before we can realize the clinical potential of regenerative therapies. For example, we don't yet fully understand the signals and biochemical factors that drive stem cell generation and determine what type of cell they will become.

Stem cells derived from “blastocysts,” the balls of cells that form a few days after an egg is fertilized, have the potential to become any cell type in the body. So-called “adult” stem cells, including those formed in the brain, appear to be more organ-specific. Understanding why could enable scientists to grow the cells under conditions that would produce the desired type of cell, such as dopamine neurons for treating Parkinson’s disease.

Scientists are already testing some therapies based on neural stem cells or the factors that promote their growth in animal models of a number of neurological disorders, including stroke, epilepsy, Alzheimer’s disease, Parkinson’s, and amyotrophic lateral sclerosis (ALS, or Lou Gehrig’s disease). Early clinical trials are underway in humans to test nerve growth factor (NGF) for Alzheimer’s, and glial-derived neurotrophic factor (GDNF) for Parkinson’s. How best to get these “growth factors” into the brain is one of many obstacles that scientists are trying to overcome. Some researchers use harmless viruses as a type of Trojan horse vehicle for therapies, while others believe stem cells themselves may be able to deliver therapeutic chemicals to target areas of the brain.

While experts caution that the clinical use of stem-cell based therapies is still years away, and that the field is hampered by contentious political and ethical issues as well as scientific barriers, most are also convinced that it is only a matter of time before the promise of regenerative medicine is realized.

Q. Do we know what causes mental illnesses, or how best to treat them?

A. Mental illnesses take many forms: debilitating sadness in depression; uncontrollable repetitive actions in obsessive-compulsive disorder; disordered thinking in schizophrenia; or manic highs and deep lows in bipolar disorder. Despite their wide variance in symptoms and still largely unknown causes, all of these conditions have one thing in common: a disruption in brain circuitry. In depression, for example, scientists have traced aberrant brain pathways using brain-imaging scans, and have found imbalances in brain chemicals such as serotonin or norepinephrine. Similar kinds of neural dysfunction are believed to underlie many mental disorders.

What makes any one person susceptible to mental illness is still an open question. Genetic and environmental influences – "nature" and "nurture" – interact in complex ways in each of us. It is likely that many genes are involved, each conferring a degree of risk, and environmental triggers may set the disease process in motion in genetically susceptible individuals.

Despite the gaps in knowledge, effective treatments are available for most mental illnesses. Seeking help from a qualified medical professional – preferably one who specializes in the particular illness in question – is critical to getting the best care. When administered by experienced professionals, medications and psychological therapies can alleviate debilitating symptoms in many cases and make it possible for people to cope with their condition and regain a level of "normal" functioning.

BRAIN TIP:

A major government-funded clinical trial has found that adolescents with depression benefit most frequently from a combination of cognitive-behavioral therapy, a type of "talk therapy," and antidepressant medications. Talk therapy may be particularly important for teens with suicidal tendencies.

Q. Is there anything I can do to keep my brain healthy in older age?

A. It is increasingly clear that how we live our lives on a day-to-day basis strongly influences how well our brain ages. While our genetic make-up also plays a role in brain health – many diseases of the aging brain may be at least partly due to gene mutations – the lifestyle choices we make throughout life are critical. A number of long-term studies, some still ongoing, have tracked older adults' activities and habits to determine what distinguishes people who retain good mental faculties into old age from those who fare less well. Some of the characteristics that stand out above others include:

- Staying mentally active by engaging the brain in stimulating and challenging activities that force us to use our brain in novel ways;
- Staying physically active through regular exercise (e.g., 30 minutes or more of brisk walking three times a week) or by pursuing active leisure activities that get you out and moving;
- Having a sense of effectiveness in the world and control over our lives, including feeling that we contribute to our families and/or society, and feeling good about ourselves;
- Maintaining a strong network of social connections, including regular contact with friends, family, and other people in our community and beyond.

Scientists have also uncovered interesting correlations between heart health and brain health. It turns out that many of the things we associate with heart-healthy living are also good for the brain. In addition to exercise, this includes keeping weight, cholesterol, and blood glucose levels in check; managing stress so that it doesn't overwhelm us; and eating a healthy diet with plenty of antioxidant vitamins (especially vitamins A, C, and E, found in many fruits and vegetables) and omega-3 fatty acids (found in fatty fish like swordfish, salmon, tuna, and mackerel).

The bottom line is that the things we do every day can and do make a difference in how well our memory and learning abilities hold up as we age. Simple changes can make a big impact, and there is no better time than the present to embark on a brain-healthy lifestyle.

Q. What do alcohol and illicit drugs do to the brain?

A. Whether it's nicotine, alcohol, prescription painkillers, cocaine, or heroin, addictive substances change the brain in fundamental ways. All of these substances act on "reward pathways" in the brain, releasing a rush of neurochemicals to produce a euphoric high. With continued use, the underlying brain circuits physically change. In people at risk, this drives a destructive cycle of compulsive drug craving and usage aimed at recreating the high. (Some people are more susceptible to this cycle than others, for complex reasons.) An addict may become so focused on “drug-seeking” that everything else in life is secondary. Without treatment, quitting is difficult or impossible.

Despite the recent availability of new therapies for addiction, only a small proportion of people who need treatment actually get it. This may be partly due to the stubborn misconception that addiction represents a flaw in an individual’s personality, a myth that may prevent people from seeking help to quit and stay off drugs or alcohol. Individuals who manage to quit face a life-long battle to resist starting again, leading experts to define addiction as a chronic, relapsing disorder.

By unraveling the brain circuitry underlying addiction, scientists have identified new targets for therapies that might quell the compulsion to use drugs or ease withdrawal. Continuing research in this area is a crucial public health goal: substance abuse has wide-ranging consequences for families, communities, and society at large, directly affecting an estimated 22 million Americans and carrying an economic price tag of more than $245 billion annually, according to government estimates.

Q. How can brain research improve the treatment of pain?

A. Despite recent advances in understanding how the brain processes and responds to pain, experts say pain continues to be grossly under-treated in this country. The biggest treatment gaps are in chronic pain conditions such as neuropathic pain (a common complication of diabetes), cancer pain, and a range of other disabling problems. Together, these conditions affect an estimated 86 million Americans and cost U.S. businesses some $90 billion annually, according to the American Chronic Pain Association.

When pain is chronic, the body's normal physiological response to pain stimuli goes awry, and the chemical signals that transmit pain sensations to the brain become stuck in the "on" position. In searching for a solution, scientists have set their sights on a number of molecules that transmit or amplify pain signals. The most promising targets are those that are used exclusively for sending pain messages to the spinal cord, since targeting these would not interfere with the normal (and necessary) response to acute pain. A number of clinical trials are now underway to test the effectiveness and safety of this new generation of possible treatments for chronic pain.

Q. How is the brain involved in the immune system?

A. Immune cells, which constitute the body's biological defense against infections and toxins, have many things in common with nerve cells. Like nerve cells, immune cells communicate with one another through connections called synapses. They also have "memory," a molecular switch that enables them to remember an infectious agent and single it out for attack if it tries to invade the body. In addition, it is now clear that substances known to be important for nerve cell maintenance and survival also support immune system functioning.

Scientists are still working to determine to what extent, and how, the brain influences or controls immune system functions, questions that will have important implications for nervous system disorders. We know that the immune system helps to prevent diseases such as measles and encephalitis that attack the brain, and recent work suggests that immune system activation following trauma such as stroke or spinal cord injury may be part of the body's attempt to contain the damage.

Unfortunately, immune responses in the brain can quickly spiral out of control and cause further harm. In degenerative diseases like Parkinson's, Alzheimer's, or multiple sclerosis, immune cells may misidentify deteriorating nerve cells as "foreign" and attack them, which may worsen the disease. This also appears to happen in spinal cord injury, where immune cells travel to the site of injury and attack the damaged spinal cord cells. Our increasing understanding of these complex interactions between the brain and the immune system is revealing targets for therapeutic interventions. For instance, scientists are currently investigating various vaccines that might arrest or slow the progress of brain tumor growth or Alzheimer's disease, and clinical trials of an immune therapy for spinal cord injury are underway.

BRAIN TIP:

While acute stress can actually enhance immune functioning short-term, chronic stress takes a toll on the immune system and may make our body less able to respond appropriately to health threats. If you find yourself chronically stressed out, take steps to change the situations that are causing you stress, and learn how to better manage stress with proven techniques such as exercise, meditation, deep breathing, biofeedback, or relaxation therapies.

Q. What are neurodegenerative diseases and how might they be treated?

A. Neurodegenerative diseases, which include Alzheimer's, Parkinson's, Huntington's, and amyotrophic lateral sclerosis (ALS), are all marked by the progressive degeneration and death of nerve cells in distinct regions of the brain. Scientists have identified a number of common neurodegenerative disease mechanisms. For example, each of these conditions involves "protein aggregation," abnormal build-up of certain proteins in the brain (e.g., amyloid in Alzheimer's). Each also seems to target specific subsets of nerve cells, such as dopamine cells in Parkinson's, or motor neurons in ALS and Huntington's. Mechanisms such as oxidative stress, inflammatory processes, and "cell suicide," or apoptosis, may also be part of the problem in each of these diseases.

These common links suggest possible therapies that might be used to slow, stop, or prevent nerve-cell degeneration and fuel hope that advances in one neurodegenerative disease may be applicable to others. Therapeutic approaches that scientists are pursuing include transplanting cells to replace those that are damaged or using growth factors to enhance survival of those remaining, applying immune therapies to interrupt dangerous inflammatory responses, and targeting so-called molecular "chaperones" that act as facilitators of cell degeneration.

Q. **How can we prevent the misuse of discoveries about the brain, such as those that suggest how learning and cognition might be enhanced?**

A. The ethical use and application of neuroscience findings is a growing concern, especially as scientists come closer to understanding how the brain learns and how learning might be enhanced pharmacologically. Should we use these new understandings to boost learning in the average person? What's to stop college students looking to ace their final exams from using drugs developed to treat attention deficit disorders, or in the future, medications designed to enhance memory in people with Alzheimer's?

"Neuroethical" questions take on new urgency as neuroscience research moves forward. The Dana Alliance for Brain Initiatives is a leader in a global effort to convene top experts in neuroscience, bioethics, law, and policy-making to bring such questions to the forefront of public debate. The goal is to begin to set standards and form basic guidelines that will enable society to respond appropriately to the ethical ramifications of new knowledge about the brain.

Q. What purpose does sleep serve for the brain?

A. We don’t yet know the full answer to this fundamental question, but neuroscience is providing intriguing clues. It is increasingly clear that adequate sleep is necessary to consolidate certain types of memories and to improve performance on various learning tasks. If we are deprived of sleep, we don’t learn as well. Recent brain research indicates that so-called “slow-wave” sleep, a type of non-REM sleep that generally occurs early in the night, is particularly crucial to learning. Sleeping within 30 hours of new learning seems to be essential, although some studies suggest that brief, 60- to 90-minute naps produce as much improvement in practiced behaviors as a full eight hours of sleep, so long as the naps include both slow-wave and REM sleep.

Anyone who has ever pulled an all-nighter knows that lack of sleep can impair learning, memory, attention, and decision-making, making it difficult to perform even simple tasks. Our risk of accidents is also greater when we don’t sleep well. While the average person requires about 8 hours of sleep per night, surveys suggest that America is sleep-deprived. As many as one-fifth of us say daytime sleepiness keeps us from performing at our peak, and nearly as many report having fallen asleep during driving. Chronic lack of sleep or abrupt changes in sleep patterns could signal an underlying problem that warrants evaluation by a qualified sleep doctor.

BRAIN TIP:

If you want to perform your best, strive for a full night's sleep. The National Sleep Foundation offers these tips for better sleep:

- Consume less or no caffeine and avoid alcohol.
- Drink fewer fluids before going to sleep.
- Avoid heavy meals close to bedtime.
- Avoid nicotine.
- Exercise regularly, but do so in the daytime and not too close to bedtime.
- Try a relaxing routine, like soaking in hot water (a hot tub or bath) before bedtime.
- Establish a regular bedtime and wake-time schedule.

Q. How can I become involved in supporting brain research?

A. Here are some ways that you can support brain research:

- Join in the activities of Brain Awareness Week. For news of dates and events in your area, check our Web site: www.dana.org/brainweek.
- Donate your time and support to the brain organization or advocacy group of your choice.
- If you or someone you love has a brain disorder, stay informed of the latest developments in treatments and clinical trials, and ask your doctor about them.
- Write to your Congressional representatives to let them know that you think brain research is a good investment.
- Stay informed on the brain. Read articles and books and watch science programs that discuss new advances in brain research.
- Volunteer to be a research subject for a brain study at an accredited research institution. Studies about how the normal brain functions are crucial to finding the answers to brain disorders.
- Write to newspapers and broadcasters to let them know that you follow and appreciate their media coverage of the brain.

The Dana Web site, **www.dana.org**, offers free resources, accessible information and news about the brain, links to many other brain-focused organizations, and special sections for kids and seniors. Some resources include:

- *The Progress Report on Brain Research,* an authoritative annual review of major developments across neuroscience;
- *Brain Connections,* a list of nearly 300 organizations and advocacy groups devoted to specific brain disorders;
- *BrainWork*, a bi-monthly newsletter that reports news and features in neuroscience research;
- *The Brain in the News*, a monthly publication that reprints brain-related articles from major newspapers;
- *Immunology in the News*, which reprints immunology related articles from major newspapers and journals;
- *It's Mindboggling!*, a pamphlet filled with information about the brain in a fun format of games, riddles, and puzzles (also available in Spanish);
- *Staying Sharp*, a series of booklets on brain topics including *Memory Loss and Aging*, *Depression*, *Chronic Health Issues*, *Quality of Life*, and *Learning Throughout Life*;
- *Neuroethics: Mapping the Field* (Dana Press, 2003; $10.95), records the proceedings of a landmark 2002 conference;
- *Beyond Therapy: Biotechnology and the Pursuit of Happiness* (Dana Press, 2003; $10.95), an authoritative report on issues surrounding the use of biotechnology to enhance performance.

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