Q&A

Answering Your Questions About

The Brain

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

The Dana Alliance for Brain Initiatives

The Dana Alliance for Brain Initiatives is a nonprofit organization committed to advancing public awareness about the progress and promise of brain research and to disseminating information on the brain in an understandable and accessible fashion.

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-INTRODUCTION-
THE CROWN OF CREATION

The human brain is the most complex structure in nature, a masterwork of evolution.

Compacted in its 3-pound mass of creased and folded tissue are nearly a hundred billion nerve cells, intricately linked to one another by trillions of connections, or synapses — more than the number of stars in the Milky Way. Electrical impulses and chemical signals travel ceaselessly through this tightly coiled system, cell to cell, across broad areas of the brain.

Unimaginably complex yet supremely organized, this hive of activity is responsible for every aspect of our experience. Each thought, emotion, physical sensation and act has its origin in the brain, from the mere awareness of touch to the most sophisticated concept. That we are conscious of the world, and that we can live in the world — thanks to the automatic operations of our hearts, lungs and other organs — we owe to our brains.

Over the centuries, we humans have used our brains to decipher the mysteries of our universe. Perhaps the most ambitious undertaking of all has been the attempt to understand the brain itself. At an accelerating pace, researchers are probing how it works, and what can go wrong.

Q: HOW DOES THE BRAIN WORK?

The brain is a multilayered web of cells: nerve cells (neurons) and vastly more numerous glial cells that stabilize the chemical environment and regulate and protect neurons.

The outermost layer, the cerebral cortex, is a fraction of an inch thick but contains 70 percent of all neurons. This most evolved part of the brain is divided into lobes specialized to regulate sensory experience, language and memory, and our sense of space. The frontal lobe is the most distinctively human region, responsible for judgment, planning and decision making.

Beneath the cortex are areas such as the basal ganglia, which controls movement; the limbic system, central to emotion; and the hippocampus, a keystone of memory.

The primitive brainstem regulates balance, coordination and life-sustaining processes such as breathing and heartbeat.

Throughout the brain, neurons communicate with one another through interlocking circuits. When a neuron is stimulated, it generates a tiny electrical current, which passes down a fiber, or axon. The end of the axon releases neurotransmitters — chemicals that cross a microscopic gap, or synapse — to stimulate other neurons nearby.

The process may be repeated thousands of times to create a circuit of electrical signals that produces movement, emotion, a sensory experience or thought.

Actually, a neuron typically communicates with many others simultaneously, and will or won't fire depending on the sum of

signals it receives. Neuron-to-neuron activity extends widely, linking lobes and levels of the brain. Bundles of axons, “white matter,” efficiently carry signals from region to region, like long-distance cables.

In recent years, this connectivity has become a focus of research as scientists explicate how the brain is wired and piece together the intricate orchestration of inner activity that ebbs and flows as we go about our lives — how reading, for example, integrates vision, language, emotion and reasoning centers.

At a projected cost of $4.5 billion, the BRAIN initiative is pushing this effort to its ultimate goal: Map the whole brain, neuron by neuron, and determine how these connections work in health and disease. The project is designed as a public-private endeavor, with initial funding from the federal government.

Q: HOW DO GENES SHAPE THE BRAIN?

The cells and chemicals of the brain are largely protein, and genes are the blueprints from which proteins are constructed.

Humans have 20,000 to 25,000 genes: spirals of DNA, tightly coiled on 23 pairs of chromosomes within the nucleus of each cell. Only a small proportion of genes are turned on in any cell at any given time. In the brain, the on-off process plays a role in such diverse areas as development, memory and addiction.

Genetically, we are far more alike than different. It is estimated that between 99 and 99.9 percent of the DNA we each possess is identical.

But these small differences are crucial: They completely determine some traits, such as eye color, and contribute (along with environmental influences) to many others, such as height and weight — and disease risk.

Techniques such as comparing identical twins (whose genes are all alike) to fraternal twins (just half alike), and association studies (comparing genes in people with and without a trait or disease) help researchers understand the role of genes.

In most brain-related phenomena — e.g., intelligence, personality — genes and environment interact. The same is true with brain diseases: Specific genes have been linked to Parkinson's and Alzheimer's diseases and amyotrophic lateral sclerosis (ALS, or Lou Gehrig's disease), for example, but factors such as environmental toxins are frequently implicated.

Although some familial strains are caused by single mutations, brain diseases are usually polygenic — multiple genes contribute to increased risk. Over 100 genes have been associated with schizophrenia, for example. (Huntington's disease is an exception: Mutation in a single gene is always responsible.)

Beyond helping us understand the brain, genetic research provides insights into the biology underlying its ills. For instance, linking a new gene to Parkinson's disease may suggest a new target for drug development.

GENES THAT MAKE US HUMAN

A newcomer to brain research, *evolutionary neurogenomics* compares human genes with those of our closest primate relatives for clues to the capacities that make our brain unique.

Because these distinctively human genes are, in some cases, also linked to brain disorders, this research may someday improve treatment for conditions such as autism.

Q: HOW DOES THE BRAIN DEVELOP?

The brain is a lifelong work in progress. Development is most rapid before birth, maintains a furious pace in infancy and continues briskly through childhood and adolescence, but never ceases altogether.

In the third week of gestation, genes switch on to turn some of the embryo's stem cells — "blank slate" cells with the potential to become any kind of tissue — into neurons and glia. These newly formed cells multiply, migrate and connect with one another, guided by chemical signals into the webwork of brain anatomy. By week seven, primitive forms of the cortex, cerebellum and brainstem are apparent.

Birth is only the beginning. The brain adds volume at an initial rate of 1 percent per day, growing by two-thirds in the first three months. To fuel its development, it requires 43 percent of the body's daily energy intake until puberty — which, some experts say, explains why physical growth takes so long in humans, compared with other species.

Neurons aren't added — in fact, we have more at birth than in adulthood — but grow and connect as specialized circuits form. Sensory centers emerge early, while the hippocampus and amygdala, primitive regions important in emotion and memory, aren't fully functional until age 3 — which is why we retain virtually no memories of infancy.

Childhood development is a dynamic brain-world interaction. During "critical" periods when regions regulating senses, emotions and language are amped up to make synapses, they must

receive appropriate environmental stimulation to connect properly.

Development in adolescence defines brain circuits more sharply, adding new synapses, pruning unnecessary ones and strengthening those that remain. Sensory, language and emotional centers mature. Axons add an insulating sheath of myelin to transmit messages more efficiently.

As adolescence ends, the brain still needs fine-tuning, as indicated by frequent risk taking and poor judgment displayed by some in their early 20s. That the prefrontal cortex, seat of planning and decision making, won't mature fully for another decade partly explains this behavior, but connections between brain regions also must strengthen to give the intellect meaningful control over emotional impulse.

WHEN DEVELOPMENT GOES WRONG

Mishaps in this complex process before birth or early in childhood result in neurodevelopmental disorders, such as intellectual disability, autism and attention deficit hyperactivity disorder (ADHD). Some suggest that schizophrenia, which typically appears in late teens, develops in a similar way.

Causes of neurodevelopmental disorders may include genetics, toxic exposure, infection and trauma. Research into these problems may facilitate earlier intervention and improve treatment.

Q: HOW DOES THE BRAIN CONNECT US TO THE WORLD?

We often focus on the brain as the seat of consciousness, but it's also a control center that maintains life. Through nerve signals and hormones modified by feedback from the organs

and chemical levels it regulates, the brain's *autonomic nervous system* keeps breathing, heartbeat, digestion and other bodily functions running properly, and chemicals in body fluids at the right concentration.

The hypothalamus, located just above the brainstem, is a key structure: It makes the body responsive to emotion and stress, and to information about the world around us.

The brain connects us to that world through systems sensitive to its various aspects — sight, sound, touch, taste and smell. Each of these sensory systems is organized in a roughly equivalent fashion: an organ designed to respond to physical stimulation; cells that transform sensation to nerve impulses, usually by releasing a chemical that activates the corresponding nerve; and a neural network to process the signal.

Each of the senses has a cortical area dedicated to it — the temporal lobe for hearing and the occipital for sight, for example. Within the cortex, sensory signals may branch out to tell us in detail what's out there. For visual images, for example, separate brain areas interpret size, position, color and shape; some are specialized for faces, some for places or words.

PERCEPTION IS AN ACTIVE PROCESS

The brain doesn't passively receive sensory data, but picks out what's relevant and fills in the blanks — allowing us to follow conversation in a noisy room, for example. This information may engage memory, emotion and language centers as we interpret and respond to what we see, hear, taste, smell and feel.

It's a two-way street. Our brain selects and amplifies some sensory details and inhibits others, according to our mood and mindset. We see and hear the world differently depending on whether we're upset or happy.

Q: HOW DO WE LEARN AND REMEMBER?

The brain changes constantly in response to experience. Learning is a matter of such changes: The acquisition of new information and new skills reconfigures brain circuitry.

When neurons connect, their synapses fill with neurotransmitters as electrical signals flow between them. For a brief time, this circuit is primed for restimulation. The brain's ability to "hold" patterns in this way lets us keep a phone number in mind while making a call, or a witty remark as we formulate our rejoinder.

This *working memory* represents a transient kind of learning. But retaining what we've learned requires structural brain changes: Synapses become larger as proteins are produced to strengthen the connection. Sometimes, new neurons appear — neurogenesis — along with capillaries to nourish the circuit.

While long-term memories are encoded in the same brain areas that originally process information — for example, we record what we saw in the visual cortex — the hippocampus and surrounding structures play a key role in establishing them.

Repeatedly reactivating the same circuit through practice or conscious effort — memorization — is the usual way to make learning last. "Neurons that fire together, wire together," neuroscientists say. But even a single experience with emotional impact can alter brain patterns enough to give the memory formidable staying power.

It's sometimes better to forget: Tormenting memories lie behind phobias and post-traumatic stress disorder (PTSD). Research has shown that when memories are recalled, they are briefly

unstable and can often be changed or even unlearned. Understanding the links between the hippocampus and amygdala eventually may lead to drug treatment to switch a memory's emotional charge from negative to positive.

THE BRAIN LEARNS TO READ

Learning a complex skill strengthens connections within and between brain regions. Visual areas specialized for shape recognition, and pathways that identify sounds and relate them to language, are better integrated in children — and adults — after they learn to read.

Q: WHAT DOES TECHNOLOGY DO TO THE BRAIN?

Modern technology has transformed how we live — and not entirely for the better. Many experts worry that the relentless lure of smartphones and computers has shortened attention span, stunted memory, undermined imagination and even promoted psychiatric ills and violence.

Does digital technology actually change how our brains are wired — particularly during the critically formative childhood and adolescent years? Researchers are actively seeking answers.

One phenomenon of interest is device-driven *multitasking*. Checking emails while listening to a lecture, talking on the phone while driving — how does the brain juggle simultaneous demands?

By rapidly switching between them, apparently. Imaging studies suggest that multitasking means shutting down one brain circuit

and activating another, while short-term memory holds the line. The ability diminishes with age, but at any age it's less efficient than doing one thing at a time.

Even smart students perform more poorly if they use electronic devices for nonacademic purposes during class. Surprisingly, habitual multitaskers are worse at ignoring distractions and switching between tasks. They are also vulnerable to depression and anxiety, according to some studies.

Another concern has been the negative impact of video games, a digital pursuit that engages some 90 percent of children and adolescents. Research has linked violent games to teen aggressiveness, as well as depression and risky behaviors such as reckless driving and smoking. One study found reduced activity in brain areas that keep emotion and aggression under control.

On the positive side, pro-social video games that involve cooperation have been shown to increase empathy and helpfulness.

BRAIN MEETS MACHINE

The effect of technology on the brain is most dramatic when they're in direct contact. The shining star among *brain-machine interface* (BMI) devices is the cochlear implant, whose tiny electrodes stimulate auditory nerve fibers, enabling profoundly deaf people to hear well enough to understand language.

An artificial retina to help the sight-impaired is also available, and BMI devices to give robotic limbs to the paralyzed are in the research pipeline.

Q: WHAT HAPPENS WHEN THE BRAIN IS INJURED?

Though encased in bone and cushioned by fluid, the brain is vulnerable to injury from without and within. Interruption of its blood supply — stroke — means subtle or devastating damage. And a blow to the head can cause traumatic brain injury (TBI).

Tissue destruction is not instantaneous. After ischemic stroke (the most common kind, caused by a blood clot), neurons completely deprived of blood die quickly, but a larger group are impaired but salvageable for hours, even days, until a complex chain of molecular events kills them. This is why immediate treatment is essential: Time lost is brain lost.

Better understanding this process, researchers hope, will provide tools to halt the cascade.

TBI initiates a similar chain of events. The role of astrocytes (brain cells that support and regulate neurons) and immune cells in both limiting and exacerbating damage has become evident, and manipulating them to improve outcome is a focus of research.

Memory problems, depression and neurological symptoms such as seizures have been linked to TBI, along with increased Alzheimer's risk. Repeated injury, as may be suffered by boxers or professional football players, can lead to chronic traumatic encephalopathy, a progressive degenerative brain disease.

Consequences of even mild TBI, including concussion, have only recently been recognized. Concussions too slight to cause loss of consciousness can still be destructive, and the repeated impact of head blows without concussion (e.g., "heading" the

ball in soccer) may alter brain structure. Young, developing brains seem particularly vulnerable.

TBI research has led to rule changes in professional and amateur sports, and the development of blood tests to detect concussions that might otherwise be overlooked (by measuring compounds released by damaged neurons, for example).

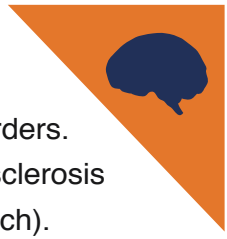
Brain cells killed by stroke or TBI can't be resuscitated, but the brain is adaptable: Other circuits reshape themselves to take over functions of damaged areas, and new cell growth — neurogenesis — replaces some tissue.

After stroke or TBI, the ability to regenerate transiently heightens, as growth factors and stem cells migrate to damaged areas. Rehabilitation works best in the first months post-injury, although further progress remains possible, for several years at least.

Researchers are looking further to the possibility of restoring the extraordinary neuroplasticity of early life "critical periods," when sensory, motor and language networks organize themselves in response to stimulation. Putting parts of the injured brain back in this mode (perhaps by manipulating neurotransmitters with drugs) might vastly enhance recovery.

Q: WHAT ARE NEURODEGENERATIVE DISEASES?

In neurodegenerative diseases, neurons deteriorate, malfunction and die. The most common are Alzheimer's disease and Parkinson's disease, which afflict 5 million and 1 million Americans, respectively, according to the Harvard NeuroDiscovery



Center, a research group that focuses on these disorders. Other neurodegenerative diseases include multiple sclerosis (400,000), Huntington's disease and ALS (30,000 each).

The occurrence of Alzheimer's and Parkinson's increases with age, although "early onset" variants occur as well.

The diseases start in different parts of the brain and cause different symptoms: Alzheimer's first hits the hippocampus and cortex and impairs memory and thinking; loss of dopamine-producing neurons in the basal ganglia makes movement problems predominate in Parkinson's. Symptoms worsen and broaden as neurons die throughout the brain.

Finding treatments to halt or reverse neurodegenerative diseases is the ultimate goal of much brain research. But before we can treat these diseases, we first need to understand them.

Most neurodegenerative diseases involve malformed or over-produced proteins that clump in the neuron: beta-amyloid in Alzheimer's, alpha-synuclein in Parkinson's and huntingtin in Huntington's. They are believed to play a role (as yet unclear) in cell malfunction and death.

Recent discoveries have highlighted another protein, tau, as a culprit common to neurodegenerative diseases (and TBI). Tau is essential for basic processes within the cell, so abnormalities can have profound consequences.

In their efforts to understand neurodegenerative diseases, researchers have broadened their investigations to include glia, the "other brain cells" that support and regulate neurons. They're looking beyond the brain, too, at body processes such as glucose metabolism, which appears to link Alzheimer's and diabetes. How exactly are these diseases related to aging?

Why do some people live long lives and never develop them? Identifying “protective” genes or lifestyle factors may provide insights into prevention and cure.

BIOMARKERS

Neurodegenerative diseases start killing neurons long before symptoms appear. Their visible effects progress slowly. Researchers seek biomarkers, such as compounds in blood or the fluid surrounding the spinal cord, that will reveal disease activity earlier and more efficiently show whether experimental drugs work.

Extensive research campaigns such as the Alzheimer’s Disease Neuroimaging Initiative (a public-private partnership) and the NIH-funded Parkinson’s Disease Biomarker Program are spearheading these efforts.

Q: WHAT HAPPENS TO THE BRAIN IN MENTAL ILLNESS AND ADDICTION?

Depression, anxiety, schizophrenia, PTSD — according to the federal Substance Abuse and Mental Health Services Administration, nearly one in four Americans suffers from a diagnosable mental disorder in a single year. Enormous progress has been made in treating these conditions, and most afflicted people are greatly helped by today’s medication and psychotherapy. But even now, only a minority achieves full remission, and the search for more effective treatments is intense.

Mental illnesses are brain diseases: Behind tormenting moods, endless worry or disordered thoughts are imbalanced neurochemicals and malfunctioning neural pathways.

The fear circuit, centered on the amygdala, is essential for survival, but disturbances result in anxiety disorders such as

panic and PTSD. Depression involves dysregulation of complex mood circuitry that links memory and emotion centers with specific cerebral cortex sites. Connections to a network regulating the capacity for enjoyment are altered as well.

The reward pathway, which enlists the neurotransmitter dopamine to steer us toward natural pleasures like sex and food, goes awry in another mental illness: addiction. Alcoholism and drug dependence, as well as behavior such as uncontrollable gambling, share abnormal activation of this midbrain circuit, which powerfully influences regions regulating memory, emotion and judgment.

A picture of the biochemistry of mental illness that is emerging from research suggests interactions among a growing number of neurotransmitters, and processes involving inflammation, glucose metabolism and the stress response.

In clarifying what goes wrong, researchers hope to lay the groundwork for improved, individualized treatment for mental illness. In the past few decades, new approaches that alter brain function directly, such as transcranial magnetic stimulation, have joined the arsenal of options.

Prevention is better than cure. While stress and trauma raise the risk of depression, anxiety disorders and PTSD, some people sail through unscathed. Studying the neurobiology of *resilience* could lead to drugs or therapies to enhance this bounce-back ability.

PSYCHOTHERAPY CHANGES THE BRAIN

Psychology is also biology. Imaging research shows altered brain activation patterns after successful psychotherapy for depression and anxiety disorders — changes similar to those seen with effective drug treatment.

Q: HOW DOES NEURO-IMAGING HELP DIAGNOSE AND TREAT BRAIN DISEASES?

Technology that provides a window on the brain is a key research tool. A burgeoning array of imaging techniques has improved our understanding of how the brain works.

Some of these techniques have become clinical mainstays as well. Magnetic resonance imaging (MRI) and computerized tomography (CT), which give highly detailed pictures of brain structure, are the methods of choice to diagnose stroke, detect tumors and assess TBI.

In planning surgery, a high-resolution MRI is invaluable for precisely outlining tumors and defining clusters of neurons to be destroyed when epilepsy can't be controlled with medication. Functional MRI (fMRI) and positron emission tomography (PET), which depict brain activity, are often enlisted as well to identify vital centers and circuits that the surgeon must avoid. Diffusion tensor imaging (DTI) to map critical white matter tracts is sometimes used similarly.

A cutting-edge innovation enlists robotic surgery to destroy tumors or seizure-generating areas under active MRI guidance, while the patient is in the scanner.

With chemicals that attach to beta amyloid, doctors can now use PET scans to assess the extent to which this protein, a major factor in Alzheimer's disease, is deposited in the brain. While Alzheimer's can't be diagnosed on the basis of PET alone, it adds important information when the clinical picture is unclear.

PET and related imaging tests provide a glimpse of dopamine activity in key brain areas to help distinguish Parkinson's disease from disorders that look similar but require different treatment.

THE BRAIN'S MOST HUMAN SIDE

New research explores uniquely human concerns.

Neuroethics investigates brain activity behind moral judgment and behavior. Findings have begun to influence thinking about justice and responsibility, and may improve strategies to prevent crime.

Neuroesthetics plumbs how the brain makes and responds to art. Researchers delineate the rich networks engaged when we hear music or are moved by a painting, and explore what happens when musicians improvise and beginners learn to draw.

Q: HOW CAN I KEEP MY BRAIN YOUNG AND HEALTHY?

To a great extent, your brain's health is in your hands. Experts estimate that just 30 percent of aging is genetically programmed. The rest depends on the cumulative impact of inner and outer environments — factors we can largely control.

Like all organs, the brain changes over time. Although the rate varies enormously among individuals, in general it shrinks slightly and the cortex thins. We lose some neurons — probably not many — and connections between those that remain become less dense. Neurotransmitters dwindle. A thinning axon-insulating sheath makes communication between regions less efficient.

The good news is that for most healthy people, these changes cause little decline in mental function. Learning may demand more effort, and working memory may lose its edge, but we still retain new information and skills.

Processing speed slows — it takes longer to retrieve memories, respond to stimuli and make choices — but some experts say this reflects, in part, *strengths* of the aging brain: a richer trove of facts and experience to sort through and connect. Researchers have also begun to explore the neurobiology of *wisdom*, a capacity often associated with age.

Since the brain is made for change, it remains particularly adaptable throughout life: It's never too early or too late to mitigate the impact of brain aging. The same lifestyle changes that promote brain health and keep it younger longer also strengthen systems throughout the body that sustain the brain.

Lifestyle changes with the most support from brain research include:

Stay active. Recent research indicates that exercise helps maintain memory and improve mood at any age. It increases the brain's blood supply, preserves white matter integrity and stimulates neurotrophic compounds that support neuron growth and function. Evidence suggests it reduces Alzheimer's and Parkinson's disease risk. Aim for 30 minutes daily of walking, biking or swimming, and maintain a generally active lifestyle.

Keep mentally engaged. Learning forms new connections between neurons at any age, and keeps brain chemicals flowing. Richer neuron networks provide a backup, or "cognitive reserve," to preserve brain function longer despite damage by stroke or disease. Exploring unfamiliar ground — for example, learning a foreign language or musical instrument — seems especially valuable.

Stay connected. A strong social network that includes close relationships is linked with better overall health and longevity. Just interacting with people in their variety and unpredictability is great mental exercise.

Research suggests that self-efficacy — feeling that what you do makes a difference — maintains cognitive capacities. People who believe their lives have purpose stay sharp and live longer. Spiritual or religious activities, or studying philosophy, can promote the purpose-driven life for many.

Protect your arteries. Keep cholesterol, blood pressure and weight at healthy levels, and control stress to keep your brain well fed and oxygenated by a strong circulatory system. A balanced diet based on moderate consumption of healthy fats and carbohydrates, rich in vegetables and fruits, and low in salt promotes brain health and reduces risk of brain-disabling diseases such as stroke and diabetes.

BRAIN MYTHS TO FORGET

We use just 10 percent of our brains. This grossly erroneous belief may have originated in early researchers' inability to understand the brain's diverse functions, and is perpetuated by the fact that only some regions are visibly active at any one time.

We lose thousands of neurons daily and can't replace them. Brain cell loss is limited in healthy aging, and new neurons are constantly made in the hippocampus and elsewhere. Neuron number remains reasonably constant throughout life.

Memory decline is inevitable with age. Some healthy octogenarians retain remarkable memories, while 50-year-olds can experience noticeable slippage. Genes and lifestyle probably account for the differences.

TEN WAYS YOU CAN BECOME A BRAIN ADVOCATE

Stay informed on the brain. Read articles and books and watch science programs that discuss new advances in brain research.

Participate in Brain Awareness Week. Search for an event in your area or find out how to get involved as a partner in the campaign at **www.dana.org/BAW.**

Spread the word. Let your friends, neighbors and co-workers know how important you think brain research is to you and your community. If you are a parent, encourage your children's schools to incorporate the brain into the classroom. Find resources at **www.dana.org/kids.**

Use social media. Connect with the Dana Foundation and other like-minded organizations, and share brain research updates with your friends and family on social media platforms.

Contact your representatives to share information on important advances in brain research with them. Don't assume that they are up to date in their knowledge. If you think an article or piece of information about the brain is interesting, it is likely they will, too. Find your representatives at **www.house.gov.**

Donate your time and support to the organizations or advocacy groups of your choice.

Support local colleges and universities that have active teaching and research programs in neuroscience.

Alert the media. Write to newspapers and broadcasters to let them know that you appreciate their coverage of the brain. Or contact local media outlets to encourage increased coverage on the brain. Letters to the editor and opinion pieces are very effective ways of sharing your views. Tips for reaching out to the media can be found on the Brain Awareness Week website, **www.dana.org/BAW.**

Participate in a clinical trial. Scientists learn from studies about how normal brains function. Search the National Institutes of Health's listing of trials at **www.clinicaltrials.gov.**

Be a role model by living a brain-healthy life. Learn more at **www.dana.org/SuccessfulAging.**

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