A Brief History of Brain Study

4000bc-- The first known writing on the brain is found in ancient Sumerian records from this period. The anonymous writer describes the euphoric mind-altering sensations caused by ingesting the common poppy plant.

2500bc-- The ancient Egyptians believed that the heart is the most important organ in the body. To them, it is the essence of life as well as the source of good and evil. This reverence for the heart is seen in the Egyptian funerary guide, The Book of the Dead, which instructs that a dead man's heart must be weighed against feathers to determine the balance of good to evil it contains. The brain, on the other hand, is considered a minor, unimportant organ. They discard it during the embalming process even as they ceremoniously preserve other organsfor mummification. Despite this decided lack of interest, an ancient Egyptian record known as the Edwin Smith Surgical Papyrus contains the first written account of the anatomy of the brain. Written by an unknown physician, the papyrus documents twenty-six cases of brain injury along with various treatment recommendations.

2000bc-- Archealogical evidence from this time suggests that trepanation, a form of primitive brain surgery that involved boring a hole into the skull, was widely practiced by prehistoric man. Trepanized skulls with evidence of healing have been found at many sites, suggesting that the subjects of these operations survived. In South America, pre-Incan civilizations performed trepanation using surgical tools made of bronze and sharp-edged volcanic rock. The sheer number of trepanized skulls found at such sites indicates that this surgery was commonplace. The reason for the frequency of trepanation is not known, but archaeologists suspect that it was used for both spiritual and magical reasons, as well as to treat headaches, epilepsy and mental illness.

450bc-- Alcmaeon, an early Greek physician, is the first to use anatomic dissection of animals as a basis for his theories. He concludes from his studies that the brain, not the heart, is the central organ of sensation and thought. This idea directly contradicts the accepted theory of his time which holds that the heart is the true seat of intelligence. Alcmaeon also suggests that the optic nerves are light-bearing paths to the brain and that the eye itself contains light. This fanciful theory of the eye as a container of light is believed by many neuroscientists until the middle of the 18th century.

335bc-- Aristotle states that the organ of thought and sensation is the heart and that the brain is merely a radiator designed to cool it. He claims, however, that the organ of thought is not the same as the basis for thought. The basis for thought, which he calls the rational soul, is immaterial and can not be found anywhere within the body. Aristotle's theories about memory ultimately prove to be more successful. He correctly surmises that the processes involved in short term memory (immediate recall) differ distinctly from those involved in long-term memory.

300bc-- Herophilus and Erasistratus, two of the major Alexandrian biologists, are the first to dissect a human body and compared it with other animals. They write the first detailed account of the structure of the brain and heart, and conclude that the seat of intelligence lies in the ventricles of the brain. They also discover the nervous system, which they classify into different types of nerves. In this classification, they make the important distinction between motor and sensory nerves.

170bc-- Galen, a physician to the Roman gladiators, proposes that the brain is a glandular organ that contains four vital fluids or humors-- blood, phlegm, choler, and black bile. He believes that a person's temperament and the functioning of his body are directly affected by the balance of these humors. For example, he argues that a person with an excess of black bile will have a melancholy temperament while a person with too much blood will be sanguine. Galen also states that the important mental faculties (memory, emotion, the senses and cognition) are situated in the ventricles of the brain. Galen's theory of the bodily humors is enormously influential and remains the dominant theory for more than twelve hundred years.

1100ad-- Brain studies cease during the Middle Ages due to a church ban on human dissection and the study of anatomy. Despite this restriction, primitive brain surgery continues to be performed by enterprising barbers who roam the countryside offering to remove the "stone of madness" or "pierre de follie" from the skulls of the mentally ill. The only true surgeons of this period are educated clerics who practice medicine, but carefully eschew anatomical studies so as not to run afoul of the church ban against the desecration of the body. [Hieronymous Bosch, The Extraction of the Stone of Madness]

1543-- Andreas Vesalius, a Renaissance anatomist, publishes De humani corporis fabrica (On the Workings of the Human Body), one of the first known neuroscience textbooks. Lavishly illustrated, it contains major sections on the workings of the nerves and the brain. Vesalius also disputes the prevailing doctrine that the higher functions of the brain are situated, reside in the ventricles. He has discovered in his dissection studies that the brains of many animals (and all mammals), have the same ventricles as humans. Since animals have no soul, he reasons, the ventricles must not be the key to higher brain functions such as emotion and memory.

1649-- Rene Descartes, a French philosopher and mathematician, proposes the idea that the brain functions like a machine. He claims that the nerves are filled with "animal spirits" that carry motor and sensory information to the ventricles of the brain much in the same way that hydraulic fluid travels through machines. Yet despite his belief that the hydraulic fluid movement theory explains brain function and behavior in animals, he concludes that it can not account for some of the higher mental faculties found in man such as intellect and emotion. Instead, he argues for a dualistic system in which the organ of the brain is distinguished from the immaterial "mind." In his view, it is the mind, not the brain, which contains a person's thoughts and desires or "soul." He also concludes that the pineal gland acting as a valve controls the flow of information to the body or mind.

1664-- Thomas Willis, a professor at Oxford, writes the first monograph on brain anatomy and physiology, Cerebri Anatome. In his book, he states that the cerebral hemispheres, which constitute 70% of the human brain, determine thought and action and are completely separate from the part of the brain that controls basic motor functions like walking. He **also locates specific mental functions** within the corpus callosum, corpus striatum and the cerebellum and introduces the words; 'neurology,' 'hemisphere,' 'lobe,' 'pyramid,' 'corpus striatum,' and 'penduncle' into the modern vocabulary. His work is influential in leading future neuroscientists to study the functional contributions of individual brain parts.

1791-- Luigi Galvani, an Italian physiologist, conducts experiments in which he causes frog muscles to twitch by touching them with wires. He believes that this twitching proves that electricity is flowing from the frog's muscles to the nerve. This theory is later disproved when further studies show that the electricity in Galvani's experiment was actually produced by a chemical reaction caused by acids present on the frog's skin. Even so, his work is an important first step toward the modern understanding of the electrical basis of neural activity.

1808-- Franz Joseph Gall, a German anatomist, founds the study of phrenology, which holds that a person's character and personality can be discerned by reading the configuration of bumps on his head. Gall states that the brain is composed of thirty-one personality organs, each with a specific mental function and each found at a specific location in the cerebral convolutions of the brain. He draws his conclusions from studies in which he examines the heads of specific groups of individuals, who he believes represent "the extremes of society" such as criminals or clergyman. One of the basic premises of phrenology is that the larger a particular convolution in a person's brain the greater the role that particular personality attribute will play in his character. According to Gall, combativeness, courage, the instinct to fight and the tendency to oppose could be found in "the posterior part of the inferior temporal convolution" while cautiousness, foresight, circumspection and the organ of melancholy lurked in the "supra-marginal convolution". As peculiar as these theories may seem, they were widely accepted at the time, perhaps because phrenology claimed to offer a method to objectively assess and judge the character of others. At the height of the phrenology craze, some people suggested that politicians should be chosen based on the shape of their skulls while others claimed to be able to detect signs of latent delinquency in children based on the bumps on their heads.

1811-- Charles Bell, a Scottish surgen, establishes that the nerves for each of the senses can be traced from specific areas of the brain to their end organs. For example, he makes distinctions between the cranial nerve, which is connected to chewing, and the cranial nerve, which controls muscles of expression. He also demonstrates that motor and sensory functions are anatomically separated in the spinal roots. Previously, it had been believed that the two functions were combined.

1817-- James Parkinson publishes an Essay on the Shaking Plasy, which decribes the degenerative disease of the nervous system that now bears his name. Parkinson states that the syndrome is characterized by an involuntary tremor in the limbs combined with difficulty in initiating and controlling movements. He notes that although it is physically debilitating, the disease generally does not affect the mental lucidity of the patient. Today Parkinsonism is widely studied by neuroscientists because of the insight it provides into the brain mechanisms that translate thoughts and intentions into physical actions.

1848-- Phineas Gage, a railrod worker, survives a bizarre accident in which the frontal lobe of his brain is pierced by an iron rod during an explosion. Although he eventually recovers, he experiences profound mood and behavior changes. By all accounts, a quiet, industrious worker before the accident, Gage becomes a surly, combative man who can not hold down a job. This famous case, now found in countless neuroscience textbooks, was an important milestone in the study of the brain's anatomy because it suggested that key parts of the personality resided in the frontal lobe. These findings indirectly lead to the development of the procedure called lobotomy, which was based on the theory that removing portions of the frontal lobe could cure mental derangement and depression.

1862-- Paul Broca, a neurological clinician and researcher, determines the location of the speech center of the brain. He bases his findings on his study of an institutionalized patient in Paris, France, who had suffered a stroke as the result of a syphilitic lesion on the left frontal lobe of his brain. This patient could understand language, but had lost his capacity for speech. In fact, he was called "Tan" because this was the only syllable he could still speak. Broca's work with Tan and other brain-damaged patients convinces him that the integrity of the left frontal lobe is crucial to speech and that damage to this region results in aphasia. He eventually pinpoints the site of the speech center of the brain as being in the third gyrus of the prefrontal cortex. This section of the frontal lobe is now known as Broca's area.

1869-- Sir Francis Galton publishes his work, Hereditary Genius, which claims that intelligence is an inherited trait and that high levels of intellectual achievement follow genealogical lines. Galton also makes the first scientific attempt to measure intelligence. In 1888, he sets up an "anthropometric laboratory" in which he uses the rather dubious measures of visual acuity, auditory accuracy, and breathing capacity to assess levels of intelligence.

1872-- Charles Darwin adds to the study of human psychology with the publication of his book, The Expression of the Emotions in Man and Animals. In it, he carefully traces the origins of emotional responses and facial expressions in humans and animals, making note of the striking similarities between species. While researching the book, Darwin conducted several experiments designed to induce anger or fear, using his children as subjects so that he could record their responses. Later, in an unpublished notebook, Darwin proposes the theory that blushing is a clear indication of consciousness. He notes that of all the animals only humans blush and claims that this is because they are the only ones capable of self-consciously imagining what others are thinking of them.

1874-- Carl Weinke publishes Der Aphasische Symptomencomplex, an important work on aphasia. Like Broca, Wernicke's work centers on stroke victims with language difficulties, but his focus is not on those who have lost the ability to speak, but rather on a subset of aphasics who speak incomprehensibly. Some of these patients can convey meaningful thoughts but have lost their ability to speak grammatically. Often they drop connective words such as "and," "if" or "but" so that their speech has an abrupt telegraphic quality. Others can speak fluently but their speech seems to lack specific content as if they are no longer able to choose the precise words they mean. Weinke's findings suggest that these particular kinds of aphasia, as distinct from the variety Broca described, result from damage to the area where the temporal and parietal lobes meet in the posterior of the brain's left hemisphere. This part of the brain is now known as Wernicke's area.

1875-- Wilhelm Wundt sets up the first lab devoted to study human behavior in Leipzig, Germany, and suggests that psychology should be regarded as a complementary scientific discipline to anatomy and physiology. Wundt is deeply interested in philosophy as well, and many of his students at the lab, known as the Institute for Experimental Psychology, are men who have studied philosophy at other German universities. At the Institute, students are taught a wide range of philosophic and psychologic subjects including the study of attention and sensory processes. Wundt's Institute becomes the model for most of the psychological laboratories established in Europe in subsequent years.

1896-- Emil Kraepelin, a practicing psychiatrist, is the first to describe manic depression as a separate illness from schizophrenia (then known as dementia praecox). He also introduces the terms neurosis and psychosis into the modern vocabulary.

1899-- Aspirin, a derivative of salicyclic acid, is first marketed by the Bayer Drug company as a pain-reliever. It will not become available without a prescription until 1915.

1900-- Sigmund Freud publishes his groundbreaking work, The Interpretation of Dreams. In it, Freud describes dreams as "the royal road" to the unconscious mind, where repressed desires and urges are played out nightly. His central theory is that the unconscious mind drives much of human behavior even though civilized society stresses the importance of overriding primitive impulses with morality and reason. Yet this constant tension between a person's repressed drives and his expected social actions often causes psychological distress. Freud suggests that one of the ways this tension is resolved is through the fantasy world of dreams. He also draws an important distinction between the manifest and latent content of dreams. In his view, the manifest content is the remembered elements of the dream or its apparent narrative. The latent content is the underlying thoughts and wishes the dream represents. Freud argues that this latent content of dreams is based on fantasies related to the emotional experiences of childhood. Through psychoanalysis or "dreamwork," a patient is able to uncover the unconscious wishes or motives that lie behind a particular dream and so gain a greater understanding of himself.

1905-- Alfred Binet, a leading French psychologist, disputes Galton's use of sensory discrimination as a measure of intelligence. He claims that individual differences in intelligence can be detected only through measures of complex processes such as memory, imagination, attention and comprehension. In 1904, Binet is appointed to a commission concerned with how to integrate retarded children into the public school system in Paris. The committee decides that special education programs should be provided for them and proposes that a system be designed for identifying retarded children entering school. Binet sets out to develop a scale that can differentiate children who are slow learners from children who are learning at a normal rate. He collaborates with Theodore Simon, a young physician who has worked with retarded children in the past. The result is a scale designed to measure a variety of higher mental processes such as memory and imagination. To test their scale, Binet and Simon draw samples of children from schools, hospitals, orphanages, and asylums. They use these samples to try out the various cognitive tests they have designed with the goal of selecting those tests that clearly discriminate between the slightly retarded and the normal school population. In 1905, Binet and Simon introduce their intelligence scale and provide guidelines for its administration. They stress that the scale is appropriate only for assessing whether or not a child is of normal or inferior intelligence and is not designed to uncover the psychologically unstable or insane.

1906-- Santiago Ramon y Cajal and Camille Golgi win the Nobel for their work on the structure and function of nerve cells. Their research details the basic changes that neurons undergo during the functioning of the nervous system and describes the mechanisms that govern the connective processes of nerve cells within the nervous system. Cajal is also the first to isolate the nerve cells located near the surface of the brain, which are now known as Cajal's cells.

1911-- Henry Head, a British neuroscientist, publishes Studies in Neurology. In it, he disputes the prevailing theories about aphasia and argues that speech is not a localized function. He also conducts important studies with the Irish neurologist, Sir Gordon Holmes, on the neurophysiology of sensory perception in the cerebral cortex, focusing particularly on patients' spatial perceptions of their own bodies.

1921-- Hermann Rorschach, a Swiss psychiatrist, develops the ink blot test. The Rorschach test, as it is now called, consists of ten standardized ink blots. Half of the ink blots are in black and white and the other half are in color. A subject is asked to describe what he sees in the visually ambiguous pictures and then his responses are analyzed or "scored" by the test giver. The test contains three scoring areas -- location, determinants and content. Location refers to how much and which part of the ink blot is described. Determinants refers to the patient's description of the blot's shape or color. Content, the most straightforward of the categories, refers to the types of objects described. Many psychiatrists have found animal and human sightings to be particularly useful clues to patients' psyches. The Rorschach test, once widely used as an "open-ended" test for personality traits and disorders, has fallen out of favor in recent years because it is so difficult to independently validate the results.

1929-- Hans Berger demonstrates the first human electroencephalograph, an instrument for measuring and recording the electrical activity of the brain. Commonly known as the EEG or brainwave test, Berger's invention is now used routinely as a diagnostic test in neurology and psychiatry and as a common tool in brain research.

1932-- Lord Edgar Adrian and Sir Charles Sherrington win the Nobel Prize in Medicine for their research on neuron function which details the mechanisms by which nerves transmit messages.

1934-- Egas Moni, a Portuguese neurologist, performs a series of prefrontal leucotomies as a treatment for depression. Leucotomy, the precursor to the more extensive lobotomy, involves severing the connections between the prefrontal cortex and the rest of the brain. Of the twenty-seven patients who have the surgery, twenty recover from depression and the other seven show improvement. Unfortunately, many also suffer from profound personality changes just as Phineas Gage did after his accidental leucotomy in 1848.

1936-- Walter Freeman performs the first lobotomy in the United States.

1938-- Albert Hofmann synthesizes LSD while conducting research on the ergot fungus. The ergot fungus contains a kind of lysergic acid with hallucinatory properties which can be transformed into LSD. Ergot fungus, which often affected grain and was milled into bread and may have caused thousands to hallucinate. Some scholars suggest that its mind-altering effects may have contributed to making the Middle Ages a time of superstition and religious hysteria.

1944-- Joseph Erlanger and Herbert Spencer Gasser share the Nobel Prize for their discoveries relating to the highly differentiated functions of individual nerve fibers.

1949-- Walter Rudolph Hess wins the Nobel Prize for his work on the interbrain, which includes the hypothalamus, subthalamus and parts of the thalamus. His research shows that the interbrain is responsible for coordinating the activities of the body's internal organs.

1950-- Karl Spenser Lashley, an American neuropsychologist, conducts a series of experiments designed to uncover the neural components of memory, which he called engrams. He works extensively with rats trying to discover where their memory is situated. In one experiment, he systematically removes different percentages of rats' brains and then tests them in mazes they have run many times before. The result is a gradual, but consistent, decline in their ability to remember the twists and turns of the maze. From these findings, Lashley concludes that there is no singular site for memory in the brain, but rather that it is a holistic process made up of the sum of many neural connections.

1953-- Nathaniel Kleitman and Eugene Aserinsky describe rapid eye movement (REM) sleep, a phenomenon they stumbled on while doing research on the sleeping patterns of children. Until then, scientists had assumed that the brain was passive and inactive during sleep. Aserinsky used an EEG to record the brain activity of a sleeping person and discovered that the electrical pattern was remarkably similar to that of someone who was awake. In contrast, the electrical waves between periods of REM sleep were slow and even, suggesting a brain at rest. Researchers now believe that people experience two kinds of sleep, orthodox and paradoxical, that alternate throughout the night in intervals of about 100 minutes. Orthodox sleep occupies 80% of the night and does not involve rapid eye movement. Paradoxical sleep (known as REM sleep) makes up the rest of the time and involves bodily movement as well as rapid eye movement. Newborns spend more than 20% of their sleep in the REM phase, which has led researchers to suspect that this part of sleep involves some sort of learning process.

1961-- Georg Von Bekesy wins the Nobel Prize for his work on the function of the cochlea, a division of the inner ear. His research details the physical mechanism of stimulation within the cochlea, thus tracing the perception of sound to its fundamental anatomical elements.

1963-- John Carew Eccles, Alan Lloyd Hodgkin and Andrew Fielding Huxley share the Nobel Prize for their work on the mechanisms of the neuron cell membranes. They discovered the chemical means by which impulses are communicated or repressed by the nervous system.

1967-- Ragnar Granit, Haldan Keffer Hartline and George Wald share the Nobel Prize in Physiology or Medicine for their discoveries concerning the primary physiological and chemical visual processes in the eye. Their research details how the eye passes images to the brain.

1970-- Julius Axelrod, Ulf von Euler, and Sir Bernard Katz share the Nobel Prize for their discoveries concerning the storage, release, and inactivation of catecholamine neurotransmitters and the effect of psychoactive drugs on this process.

1974-- M.E.Phelps, E.J.Hoffman and M.M.Ter Pogossian develop the first Positron Emission Topography (or PET) scanner, a machine that provides visual information about the activity of the brain. A patient undergoing a PET scan is administered a substance that includes radioactive atoms that emit positively charged particles known as positrons. The gamma radiation that results from this process is sensed by detectors and converted into computer-generated images of the brain as it would appear in cross-section. Doctors use PET scans to monitor such things as blood flow and oxygen utilization in the brain.

1977-- Roger C.L. Guillemin and Andrew Schally are co-recipients of the Nobel Prize which they also share with Rosalyn Yalow. Schally and Guillemin are honored for their discoveries concerning the production of peptide hormones in the brain. Yalow is recognized for her work in the development of radioimmunoassays, a technique for determining the amounts of peptide and other hormones are present in the body. Schally's research centers on the hormones produced by the hypothalamus, the part of the brain that controls temperature, hunger, and thirst, as well as those produced by the pituitary gland. Guillemin's work focuses on the function of the hypothalamus in relation to the pituitary gland, a gland in the brain that regulates many bodily functions. Their discoveries have helped to increase the understanding of glandular diseases.

1981-- Torsten Wiesel and David Hubel are co-recipients of the Nobel Prize for Physiology which they also share with Roger Sperry. Wiesel and Hubel's research centers on how visual information is transmitted from the retina to the brain. Sperry's work concerns the specialization of functions within the cerebral hemispheres of the brain.

1987-- Fluoxetine (Prozac) is introduced and becomes a widespread and controversial treatment for depression. Though the precise mechanisms of the drug are unknown, Prozac belongs to a class of antidepressants that work by enhancing the effects of the chemical neurotransmitter, serotonin. Serotonin creates a sense of well-being when it is released which suggests that people suffering from clinical depression may have abnormally low amounts of it. Prozac alters the brain chemistry of depressed people by allowing more serotonin to remain in their brains, thus alleviating the despair and hopelessness that characterizes this illness.

1991-- Erwin Neher and Bert Sakmann share the Nobel Prize for their work on the function of single ion channels which increased understanding of how cells communicate with each other. Single ion channels are like tunnels that run from the inside of the cell to the outside. Cells communicate with each other using the 20 to 40 ion channels they have. Neher and Sakmann developed a thin, glass micro-pipette, one thousandth of a millimeter in diameter, which allowed them to view these ions as electrical currents.

1994-- Alfred G. Gilman and Martin Rodbell share the Nobel Prize for their discovery of G-protein coupled receptors and their role in signal transduction. G-proteins are important because they act as a kind of internal switchboard for the body's various communication pathways. For this reason, they are sometimes described as "biological traffic lights." The G-proteins within a cell respond to signals outside the cell such as light, smells, neurotransmitters, or hormones, and then translate these signals into internal cellular activities. Misfires in the G-proteins switchboard system can lead to the development of diseases such as diabetes, cholera and whooping cough.

1997-- Stanley B. Prusiner wins the Nobel Prize for his discovery of a new genre of infectious agents known as prions. Normally, prions exist as harmless cellular proteins. However, they possess an innate capacity to convert their structures into highly stable configurations that can lead to the formation of harmful particles. Prusiner's research implicated prions as infectious agents in several brain diseases that cause dementia in humans and animals. Prusiner's discovery of this new principle of biological infection has also helped to provide important insights into the mechanisms underlying other types of dementia-related diseases, such as Alzheimer's.

2000-- Arvid Carlsson, Paul Greengard and Eric Kandel share the Nobel Prize for their discoveries concerning signal transduction in the nervous system. Signal transduction occurs when a message from one nerve cell is transmitted to another through a chemical transmitter. It takes place at special points of contact, called synapses. Each nerve cell can have thousands of such contacts with other nerve cells. Carlsson, Greengard, and Kandel's research focuses on one type of signal transduction between nerve cells, known as slow synaptic transmission. Their discoveries have contributed to a greater understanding of the normal function of the brain as well as how disturbances in this signal transduction can give rise to neurologic and psychiatric diseases.