Oxidative stress in human brain ageing

The human brain is the main source of nerve function in the body. It is the epicentre of the nervous system and controls all of the main neural functions of the human body (Lewiset al, 1998, 479-483). When assessing brain function, there are many different areas that are addressed, but one main area of concern is the actual aging of the brain. As the brain ages, the functions that it performs are broken down and degraded. The nerves become slower and the motor functions are less precise. Short term and long term memory is negatively affected and the overall brain function is broken down.

Many people attribute all of these detrimental effects to old age and poor health, when in reality oxidative stress and free radicals are the main causes of loss of brain function. Throughout this paper, actual brain function patterns will be examined, followed by some common reasons for brain function degradation. Then oxidative stress and its effects on the human brain will be looked at, along with a few of the common diseases and health problems that are associated with brain aging and loss of brain function.

The Brain: an Overview

The human brain is a mass of nerve tissue, synaptic gaps, and nerves (Lewis et al, 1998, 479-483). All of these parts work together to form what is known as the human brain. The brain is the main centre of nerve function in the body. The nervous system is controlled solely by the brain itself, which works as a kind of packaging centre for the messages that are delivered to each nerve cell by the body. However, the brain would not function properly if it were not for the job performed by each cell and its consequent parts. A cell is made up of the nerve cell itself, the synapse, and dendrite. Each dendrite

is connected to the next dendrite by a small opening that allows the passage of chemicals such as Potassium and in order for proper neural functioning. The chemicals move along the dendritic pathway and form a gradient at the synaptic gap. The gradient then allows the chemical to trickle across the gap, which then causes the nerve to deliver its message (usually a message for a muscle to contract). If a gradient does not exist, then the message is not sent and the function is not performed properly. If a problem arises in the nervous system then it is usually due to the fact that the chemical gradient is incorrect at a particular synaptic gap, creating either a muscle seizure or some other undesirable reaction.

The main nerve cord of the body, known as the spinal column, is made up of layer upon layer of nerve cells. This mass of nerves serves as the pathway for all of the major neural messages of the body. It allows the chemical messages packaged by the brain to be transported to various parts of the body, and vice versa. All of the neural messages of the human body are delivered in a matter of seconds, that is why it does not seem as if there is along delay in between a particular stimuli and the consequent reaction. Branching out from the spinal cord itself are the various nervous pathways of the body. There are nerves that stretch all of the way to the fingertips and toes, but they all return to the spinal cord to deliver various stimulus messages. Each of the various nervous pathways is also made up of layers of nerve cells. All of the nerve cells of the body work together to form messages that are interpreted by the brain. The brain is able to decide what priority is needed to be appropriately assigned to each task and then takes action to perform those actions.

Brain Function

There are basically three main functions of the brain: memory, interpretation of data, and motor function control. Not only is the brain a packaging and interpretation centre for the neural messages of the human body, but it is also a storage bank for information. The brain stores information from everyday life using chemical reactions in the cerebrum to create memories. This information is then available for the rest of the brain's life, regardless of whether a person can actually pull the information up to examine it.

The brain serves its main purpose of data interpretation by deciphering the messages and stimulus information that the human body encounters every day. Each and every piece of information that the body comes into contact with is sent through the brain to either store the information, cause a reaction to a stimulus, or to disregard it. This interpretation process is very exact, yet extremely fast. The entire process seems instantaneous, from the introduction of the information all the way to the interpretation results/stimuli reaction.

Finally, the brain controls all of the muscles of the body and consequently all motor control of the human body. Every movement, be it voluntary or involuntary is controlled by the brain. Each function of the muscles is perfectly coordinated and timed so that the abducting muscles work perfectly with the adducting muscles to produce useful movement. The brain coordinates each twitch of any muscle in the entire musculature system so that no energy is wasted in useless movement. Because the body is constantly in a delicate balance, it is necessary for the brain to be even more precise than the world's most sophisticated computer when dealing with the

body’s homeostasis. The body has many involuntary muscle movements that are necessary for life, but need not be thought about to be performed each time. A couple of these movements are such things as the contraction and expansion of the diaphragm in the stomach to allow respiration and the beating of the heart. However, other muscles and functions are also controlled by the brain, such as the movement in walking, swimming, or running. The contraction of the bladder and other voluntary, yet unthought of muscle contractions are also controlled by the brain.

Stressors of the Brain

In every cell of the body, there are what are known as redox reactions (OXIS Research, 2003, 2). Basically, a redox reaction is an oxidation-reduction chemical reaction in which one compound is oxidized (loses electrons) and another compound is reduced (gains electrons) (Zumdahl, 1991, 216-220). Redox reactions are essential for survival and for the proper function of various organ systems in the body.

While redox reactions may be essential for survival, they can produce what are known as free radicals (OXIS Research, 2003, 2). A free radical is defined as any type of chemical existence that can stand alone and survive on its own without the need for any other chemicals to continue the life of the chemical (OXIS Research, 2003, 2). Free radicals contain unpaired electrons, which make the chemical very unstable (OXIS Research, 2003, 2). The unpaired electrons tend to try to pair with any other free electrons to achieve a stable outer electron ring (usually eight electrons). Therefore, the unstable free radicals are always trying to pair up with any and all organic chemicals that they come into contact with. Free radicals can be increased in

the body by exercise and environmental stresses. They tend to be stored in the fat cells of the body and are released when fat is burned. The free radicals are then spread all throughout the body where they can then react with other organic substrates (OXIS Research, 2003, 1). These organic substrates include DNA and various proteins as well (OXIS Research, 2003, 1). The oxidation of these molecules can damage them and cause a great number of diseases (OXIS Research, 2003, 1).

There are several different organ systems that are predisposed to free radical damage. These organ systems include the circulatory system, the pulmonary system, the eye, the reproductive system, and the brain (OXIS Research, 2003, 2). While it is true that every organ system could be examined and an oxidative stress Achilles heel could be found, the brain is especially susceptible to free radical damage (OXIS Research, 2003, 2). Oxidative stress is a term that is used when dealing with a build up of ROS chemicals (OXIS Research, 2003, 2). ROS stands for Reactive Oxygen Species and refers to many chemical oxygen derivatives (OXIS Research, 2003, 2). The build up of these chemicals can cause an imbalance of oxidant activity in the system (i. e. the brain) and can lead to several negative health effects including premature aging of the system and any number of diseases (OXIS Research, 2003, 2).

The oxidative reactions that take place in the body and especially the brain are regulated by a system known as the Antioxidant Defence System, or ADS for short (OXIS Research, 2003, 2). This system is a conglomerate of many different approaches to keeping free radical production and collection to a minimum in the body. The ADS contains antioxidant chemicals as well as a

number of enzymes that can not only limit and control the overall production of oxidative reactions, but actually target damaged molecules for the purpose of replacement or repair (OXIS Research, 2003, 2). The actual antioxidants are either internally synthesized or are ingested by the organism via various fruits, vegetables, and grains (OXIS Research, 2003, 2). Antioxidants are categorized into two different categories: Scavenger oxidants and prevention antioxidants (OXIS Research, 2003, 2). Scavenger antioxidants remove the ROS molecules from the body and include both small antioxidants (Vitamin C and glutamine) and large antioxidants that need to be synthesized by cells in the body before they can be used to protect the organ systems (OXIS Research, 2003, 2). Prevention antioxidants such as ferritin and myoglobin are designed to prevent the formation of new oxidants and free radicals (OXIS Research, 2003, 2). They work by binding to the various free radicals to protect the proteins that are essential in the organ system (OXIS Research, 2003, 2). This group includes such chemicals as metallothionine, albumin, and transferrin (OXIS Research, 2003, 2).

It is obvious that free radicals are at least a necessary evil in the body when it comes to the completion of certain processes. In order for proper functioning of the various life systems of the human body, it is necessary to have the by products of the processes (generally free radicals)present in the system. However, this does not mean that free radicals are safe or needed. Most of the time the body’s systems of removal (ADS, etc.) will take care of the overabundance of free radicals, however at times it is possible for even the ADS system to be overpowered by a great influx of free radicals. This phenomenon can be due to the production of energy by mitochondria or

some other natural process, but in most cases this large influx of free radicals is caused either by environmental stresses or from being near various industrial processes. It is a great concern of researchers today that there are more free radicals being released into the environment by industrialactivities and other forms of pollution. These free radicals are easily bound to various food products that are produced by humans and have a detrimental health effect on both animals and humans. If more free radicals are present in the environment than in past historical records, there is a high risk of ingesting enough oxidants to produce an imbalance of free radicals that could lead to the ADS system not being able to handle the extra oxidant load. This would then result in a large epidemic of environmentally caused free radical damage and disease.

Degradation and the Effects on Brain Function

Due to the importance of the brain function to the body, it can be seen why it is imperative that the brain be kept in good working order so to speak. If the brain is allowed to degrade to the point that motor functions and memory is affected, then there could be long term health effects that can cause more problems than just brain functioning. If the brain is allowed to degrade to a point at which everyday muscular functions and other physiological functions begin to become harder to perform then there is a possibility that other more serious side effects could be on the horizon. Certain diseases are caused by brain degradation or are causation factors in brain aging and degradation itself. One such disease is Alzheimer’s Disease.

Alzheimer’s disease is a brain disorder that has many symptoms and causes the loss of memory, the ability to learn, and the ability to carry out everyday

activities. Towards the end of the disease progression, Alzheimer’s can cause personality changes and even cause hallucinations and paranoia (Alzheimer’s Association, 2005, 2). Alzheimer’s is a form of dementia: a category of diseases that cause the systematic destruction of brain cells and lead to a decline in brain function and quality (Alzheimer’s Association, 2005, 2). It has many stages and eventually leads to the complete breakdown of the brain to the point of death (Alzheimer’s Association, 2005, 2). A person who has a dementia disease will eventually need full-time care because of the loss of a large portion of the brain function (Alzheimer’s Association, 2005, 2). While Alzheimer’s and dementia are not the only neural disorders that have a progressive effect on brain function, they are two of the main problems that are faced in countries such as the United States and England. Researchers have not yet identified a known cause of Alzheimer’s disease, however the field has progressed great strides in the past few years. As of right now, the disease is linked to a genetic predisposition to the disease and generally bad aging habits (Alzheimer’s Association, 2005, 2). But there is still some value to the school of thought adopted by a few doctors that believe that diseases like Alzheimer’s, dementia, and Parkinson’s disease are all due to not only genetic factors but also to environmental stresses which would include the introduction of free radicals into the body. Free radicals can cause great disruption in the brain function mainly because the neurotransmitters and neurons that are present in the brain are very delicate and can be destroyed easily. The free radicals can bind to the various proteins that are used to transmit messages and perform repairs in the brain tissues, preventing them from performing their duties and causing a weakened brain state. Proteins are themselves very specific concerning

binding properties and will only function correctly if they bind with the correct substrate (Staines et al, 1993, 130). Therefore, if the active site of the protein is disrupted by a free radical, then that protein is completely changed and will not perform as it was intended.

Brain Aging: An uphill battle

Many diseases are linked to free radicals and other types of oxidants, however another factor of brain function needs to be examined to get the entire picture concerning brain functions and memory. This factor is, of course, brain aging. It is what some call an unfortunate fact of life, but we all grow older. From the time of our birth all the way to our death, our body is in a constant state of degradation and repair (Ebbing and Gammon, 2002, 809). This is true for every part of the body including the brain and carries great consequences for overall brain function and health. The brain is a delicate organ that stores the information that runs the rest of the body's functions. If it is allowed to age past a certain point and it is not in good health, then it is possible for bodily functions and memory to be detrimentally affected. As the brain ages, it becomes slightly more sluggish and tends to lose its edge so to speak. Because of the complexity of the brain itself, aging tends to have a harsh effect on its ability to function correctly. A major factor in the development of diseases such as dementia and other neural system diseases is often the aging of the brain. The older the brain is, the less it functions correctly. As of now, there is not a particular treatment or cure for dementia. The best that we can do is to simply make the patient comfortable and to try to make their lives as easy as possible when dealing with everyday life functions. It is the hope of researchers of brain aging that by forging new

paths in the field of neural aging, that a cure will be found for such diseases as dementia and Alzheimer’s.

For years it has been common practice to believe that brain and neural diseases were caused either by environmental stresses or from brain aging. Today, however the tide is swaying more towards the middle than to either extreme. Researchers are starting to realize that the environment as well as brain aging could be factors in the development of certain diseases and disorders. Not only can both environmental factors and the age of the brain itself work together to cause stress on the brain, but some environmental factors can actually cause the brain to age prematurely as well. This premature aging is actually a worse form of aging than the actual aging process of the human body itself. Premature aging means that the brain is aging faster than it would naturally; in other words a brain that is supposed to only be five years old would look and function as if it were ten years old or older. The implications of this type of aging process are obvious. As the brain ages, neurons and neurotransmitters die and do not function as well as when the brain was younger, leading to memory loss and slower reaction time.

Brain aging is caused by many factors including environmental factors, industrial processes, and of course the passage of time. Two of these factors can be regulated: environmental factors and industrial processes. By regulating certain chemicals and industrial processes, it is possible to cut down on the amount of premature aging that occurs in the brain (Sharon, 1998, 167). Certain industrial processes such as the metallurgic processes used in alloy formation as well as welding are known causes of brain degradation and causation factors in such diseases as Parkinson’s and

manganism (Landis and Yu, 1999, 213-217). Certain chemicals that are present in these various processes are able to penetrate through the blood brain barrier and contact the brain tissue directly. This can lead to tumours and neuron death that then causes cognitive problems as well as body function problems. The only good way to prevent such contamination is to completely negate contact with these chemicals at all. Researchers know this and that is why environmental laws are being put into place that allow for the prevention of release of these chemicals.

Aging of the brain occurs whether or not there are external environmental stressors present in the person’s surroundings. It occurs throughout the entire lifespan of the organism. Earlier in history it was believed that the aging of the brain caused the degradation of neurons no matter the circumstances, however it is the common belief today that as long as a few guidelines concerning lifestyle choices are followed, it is possible for the neurons of the brain to stay completely healthy and fully functional all the way until death. Brain aging is defined as the breakdown of the brain itself. The grooves in the brain tissue will grow wider and the actual weight of the brain material will decrease dramatically. New studies are showing that the plaques and neural tangles that were previously believed to have been the culprits of Alzheimer’s disease may actually not be the main disease causing factors after all (Brady et al, 2000, 864). It is a growing school of thought that the actual cause of dementia type diseases is actually result of complex chemical reactions in the brain (Brady et al, 2000, 864). This information is very important to neural researchers because it can completely change the

focus of their research and hopefully eventually lead to a cure for dementia and other diseases of this type.

Conclusions

It is apparent that the aging of the brain is a major concern, especially to researchers studying the effects of specific kinds of neural diseases. It is believed that these diseases could have a myriad of causes, but brain aging may be a contributing factor in several or all of them. The overall aging of the brain is coming to the forefront of modern medicine because not much is known about it. It is becoming evident that what was thought to be facts concerning brain aging before was little more than just educated guesses. Now however, the technology is available that will allow the actual study of the brain and its functions to try to give a better picture of the breakdown of the organ. Once a specific timeline is established that shows the breakdown of a healthy brain, it will be possible to quantitatively measure the degradation of a diseased brain. While this may not seem very important, it is actually very useful information. This information can be used to explain to patients what they should expect to experience at specific time periods of their disease and could help prepare them for what is to come.

Brain aging information can also be of use to the doctors that are administering treatment, in as much that it would allow the doctor to determine at what stage the aging was in, and therefore what type of treatment to administer.

Oxidative brain stress is a completely different matter than brain aging as far as research is concerned. While it is true that more is known about free

radicals and their effects on the brain than the aging process, it is important to understand why research of this kind needs to be continued. The world is constantly changing and the chemicals and different kinds of pollutants that are released are in a continuous state of advancement. Because of this it is necessary to continually be studying the physiological and biological effects of each new chemical that is developed and put onto the market. By performing this kind of research early on in the development process, it is possible to determine if there are any harmful effects of using the new chemicals. The early research performed as a preliminary study could lead to less disease and fewer health problems later on.

Overall, oxidative stress along with brain aging is newly emerging field that has the job of trying to answer age old questions that are concerned with brain and neural health. It is important to continue research in both of these areas so that advancements in modern medicine can be pursued. Society owes a great debt to the researchers who have and will spend their entire lives studying the effects of brain aging and oxidative stress on the functioning of the brain. Hopefully in the near future there will be great advancements made in the field of neural medicine to allow for better and more effective treatment of certain nervous system diseases.