Successful Aging of the Healthy Brain

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by Marian C. Diamond

I would like to begin with a general introduction before presenting the specific brain research from my laboratory at UC Berkeley that holds the promise of what I call "successful aging." In our democratic free society, the human brain has the privilege and capacity to determine its own destiny, most of the time. But no one said it was easy. It has been said that aging is not for sissies, but, in fact, life is not for sissies. I frequently use the title, "An Optimistic View of Aging," when I present my research. After all, who wants to listen to a talk called "A Pessimistic View of Aging"? Yet, recently I was asked to speak at a retirement conference and I thought to myself, the concept of "retirement" is contrary to my personal and professional values, so should I accept this invitation? I regarded it as a challenge and said yes.

Have you ever looked up the word "retirement" in the dictionary? Except for ads for retirement homes, the word definitely has negative connotations. Synonyms are: withdraw, resign, regress, recede, abdicate, depart, and on and on. There is no synonym to indicate anything upbeat or forward-thinking or optimistic. We know Robert Browning's famous: "Grow old along with me The best is yet to be The last of life for which the first was made...." What an exhilarating perspective! His words certainly do not suggest the necessity to resign, retreat, regress, recede or withdraw from life.

In light of the profound social changes and medical advances that have taken place in American society, why has it taken so long for us to challenge the meaning of the word retirement, a period in life which now amounts to almost one-fourth of our potential lifetime? I asked people all over the country to come up with a substitute word for retirement, a single, acceptable, positive word to describe this segment of our lives. I found one that, for my present purposes, fills the need: The word is REDIRECT. Think about it: Isn't redirection what most of us actually focus on when we leave the work force or change our style of living after some 60 years? I'm told that AARP has concerns about the "R" letter, also. To drop it altogether would make them the Association of People, and that would not be properly descriptive, but what about the American Association of Redirected People? Redirect suggests moving in a different direction but continuing to surround ourselves with a rich amount of stimuli to fulfill a useful life where successful aging can mean living a full one hundred years.

My scientific research for the past many years has been focused on the effects of the environment on the brain--the external environment we are sharing here today and the internal environment unique to each of us. Let me list a few factors that we know from laboratory experiments to exert a powerful influence on the well-being of the brain. Did you know, for example, that the brain has the capacity to redirect its own destiny? Isn't that amazing? That three-pound mass, which I can hold in one hand, has the capacity to conceive of a universe that is a billion or more light-years across. Just think of it.

The brain is truly a phenomenal structure, and keeping it healthy for our entire existence on this earth is a goal we can and should all aspire to. I am going to touch upon just five basic factors. And you are going to say there's nothing new about them. Perhaps so, but we now have important scientific validation we did not always have.

- **Number one, and in my mind the most important, is DIET. What we feed this brain is a significant factor in its well-being.**
- **Two, is daily EXERCISE, and that applies to the brain as well as the body. Exercising the total body serves to maintain a healthy brain.**
- **Three, we must CHALLENGE the brain. It gets bored; we know that well.**
- **Four, we need NEWNESS, new pursuits, new ideas, new activities in our life.**
- **And five, last but definitely not least, we must nurture ourselves and each other: call it sharing basic HUMAN LOVE.**

When studying human physiology generally and the brain in particular, it is essential to keep in mind that development and aging are a continuum. From the moment you are born, you begin to age. So, too, your brain does not simply "develop" in the first part of your life and "age" in the last part of your life. While your brain was forming in the embryo, it was developing nerve cells at the rate of about 50,000 per second. Think of that explosive development,--50,000 per second. But before you were born did you know that you had already lost at least 50% percent of those cells? Most are concerned about losing nerve cells at the other end of the life cycle when, in reality, you lost more nerve cells before you entered the world.

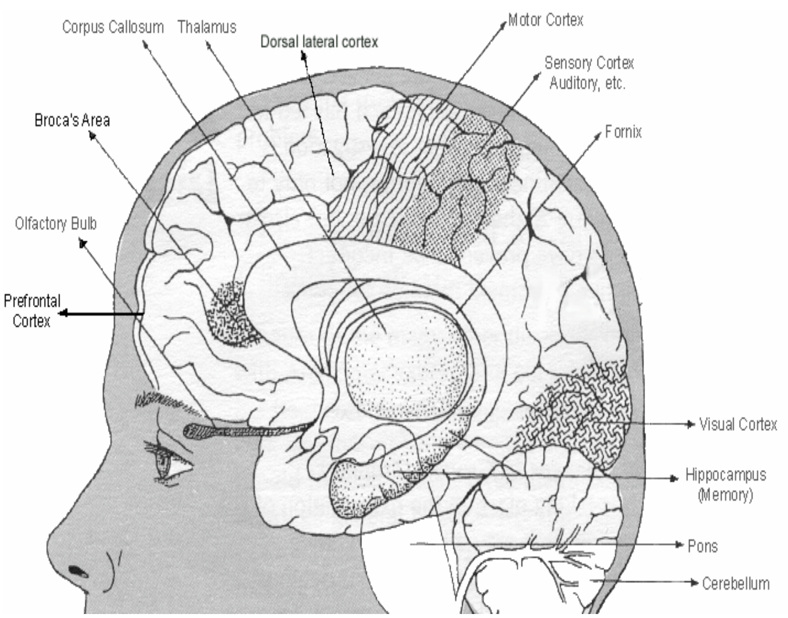
A Look at the Brain

That is an example of development, aging and loss occurring simultaneously in the very early part of your life. What I would like to do now is go through a series of slides that allow me to describe some of the research that we've done in my laboratory over the years. But first, let us take a good look at our human brain, this "three-pound universe" as it's been called, that weighs roughly 2% percent of our total body weight yet receives a fourth of the body's cardiac output. Have you ever seen your heart on an echocardiogram? I saw mine just the other day. I could see the valves opening and closing. My scientific knowledge of exactly how it works-- took second place to the sheer thrill of observing it in action.

Equally wondrous is that no two human brains are alike. No two of you will be listening to this lecture in the same way. No two of you will walk away with exactly the same ideas and information I am about to give you about the dynamics of our brains and about the importance of keeping them dynamic for a lifetime.

As a species, we think we are unique in our ability to reflect on ourselves. I say "our" ability. That ability resides in the brain How does your brain feel about studying itself? As an organ, the brain has no feeling, per se: You can cut the brain and it does not feel the injury itself. Sensory receptors in other tissues are responsible for initiating the impulses that bring pain sensations to the brain for analysis.

Let us look at a diagram of the brain.



Here are some of the key structures: dorsal lateral cortex, Broca's area, auditory cortex, visual cortex, motor cortex, prefrontal cortex, hippocampus. For me to be talking to you now, the Broca's area of my brain is firing. It's termed "the center of articulate speech." Recent technological advances have allowed us to recognize that motor speech is not always limited to the classical Broca's area, as once was thought. Although Broca's area is generally in the inferior frontal area, we now know that some people activate motor speech a little further in front of Broca's area or above it.

For you to be looking at this diagram, your visual cortex is firing. When you get hit on the back of the head, you see stars because you have jarred your visual cortex. For you to be listening to me, the auditory cortex in your superior temporal lobe is being activated. Perhaps you have noticed that the area of the cerebral cortex responsible for hearing is very small in comparison with that devoted to seeing. Is vision then more important to our survival than hearing? For me to be moving my pointer, the motor cortex is firing. There is a very large representation in the motor cortex for hand and mouth.

The highest cognitive processing is going on here in the prefrontal cortex, just behind your forehead. The prefrontal cortex is responsible for such abstract functions as taking initiative, using judgment, applying memory, planning ahead, sequencing events, and so forth. Each part of the cerebral cortex has a general function, but it has very specific functions as well.

Diet and Brain Growth

That slide presentation gives you an overview of the brain and its essential functions as they operate in the daily lives of each one of us. Let us now return to the five factors that I regard as essential for keeping our brains healthy and active throughout our life span. The first, is DIET. Yes, diet is vital to the brain just as it is to our body as a whole. For the brain to grow healthily from infancy, it certainly needs protein to maintain and develop its nerve cells and their branches through out life. In the outer layers of your brain you have millions of nerve cells and, stemming from them, as you can see, are what we refer to as branches or "processes," specifically they are called "dendrites."

Dendrites receive information from other nerve cells within the brain and from other parts of the body. These processes are critical, as I will elaborate below. In fact Science Magazine, this past year, published a major issue featuring dendrites. Books devoted to dendrites are already appearing and I would suggest it is only a matter of time before someone launches a journal devoted to dendrites.

Dendrites do not simply receive information that comes into the nerve cell. Once the information has been processed, then it stimulates an electrical impulse that travels down to the nerve cell body. The impulse leaves the nerve cell body in a process called the axon, which carries the impulse to a target tissue. When teaching children I like to use my arms and hands to demonstrate how the impulse travels down the axon to the tips of the axon (or fingers in this demonstration). The tips of the axon are not directly continuous with the receptive dendrites on the next nerve cell, represented by the fingers on my other hand adjacent to the terminals on the axon. There is a gap between the axon and the dendrites. When the impulse reaches the axon terminal, a chemical is liberated which crosses the gap known as the synaptic gap and stimulates the receptors on the adjacent dendrites. This chemical is called a neurotransmitter.

When we first started working in the field over 50 years ago, there were, perhaps, five or six known neurotransmitters. The other day I called one of the major researchers in the field, Floyd Bloom, the former editor of Science magazine who works at the Salk Institute in San Diego. I asked him how many neurotransmitters are known today. He said at least a hundred. So you get a glimpse of the magnitude of all these chemical reactions occurring at the millions of synaptic junctions in our brains. It is a wonder that any two people think alike or understand each other with such a dynamic nervous system that must keep all these transmitters in proper balance.

Another component of nerve cell branches I would like to mention here is the "covering" on the axon. It is called myelin. Myelin is a white fatty covering on the axon that serves to speed up the conduction of electrical impulses. The diameter of the axon is directly proportional to the amount of myelin surrounding it. Myelin is extremely important for the well-being of the nervous system. You have heard of diseases such as ALS, amyotrophic lateral sclerosis, commonly known as Lou Gehrig's disease, and MS, multiple sclerosis. These are called demyelinating diseases, because that is the essential feature: the person loses this insulating covering on the nerve fiber, the myelin.

At the present time, some investigators are concerned about indications that children are showing a reduction in myelin, a clinical finding they attribute to society's current emphasis on fat-free diets. Obviously, we do not live in an either/or world; even ardent health advocates do not advocate a completely fat-free diet. It is assumed that Plato's wisdom-- moderation in all things--will prevail in our quest for a healthful dietary regime.

I am spending time on dendrites and axons because, whenever we talk about the growth of the brain during development, a major consideration is the growth of dendrites and axons and the connections they make with other cells and target tissues. In some cases, one nerve cell can receive input from as many as 20,000 other nerve cells. (But most cells don't have that much input.) There can be a tremendous amount of computation for a single cell and we have more than a hundred billion nerve cells in the brain.

Now let's take a minute to look at how dendrites develop. Here you can see a sample of nerve cells from the frontal lobe of a newborn human's cerebral cortex, just behind the forehead. You'll notice that there are very few dendritic branches on the nerve cells in the newborn; however, by the age of the two years, an enormous amount of branching will have occurred. Not all of those dendrites will have made appropriate connections yet. And that probably explains why two-year-olds are sometimes difficult to deal with!

As some of you will remember after this long but important digression, the issue at hand is the critical role that diet plays in the health of the brain, whether during pre- and postnatal development or throughout that long period of "postnatal" life that constitutes the rest of our journey on earth. When you have a rudimentary understanding of the key role of dendrites and axons and neurotransmitters, you can better appreciate how important it is that protein be a major component of the diet, particularly for the fetus in utero and in the early stages of infancy when these cells and their branches are actively developing.

If I can now introduce a relevant experience when teaching in Africa in 1988, my husband, Dr. Arnold Scheibel, and I found that in Nairobi, Kenya, pregnant women would not eat protein because it meant they would have to deliver a large baby. It was much easier, in their view, to reduce their protein intake as a way of assuring a smaller baby and an easier delivery. My immediate question, as you might have guessed, was: "What effect does this reduced protein intake have on the infant brain?" That became the subject of a series of experiments in my laboratory as soon as we returned. One of my graduate students, Arianna Carughi, fed half the pregnant rats a normal, high-protein diet and the other half a low-protein diet. When the babies were born, first of all, the body weight of babies whose mothers were fed the reduced-protein diet was found to be 50 percent less than those babies whose mothers had been given a normal protein diet. And the brains?

The dendrites in baby rats whose mothers had reduced protein did not develop fully. When we placed the protein-deprived babies in enriched living conditions with lots of objects to explore, their dendrites did not increase significantly, as they did in babies whose mothers had a normal protein diet and enriched living conditions. It was clear that a protein-rich diet is vital to grow healthy nerve cells which can respond positively to enriched living conditions.

In a follow-up experiment, we placed the low-protein-diet mothers on a high-protein diet after delivery, and put their babies on high-protein diets after they were weaned. So when we put these babies in enriched environments, their brains benefited from the stimulating input and their dendrites grew almost as much as those from babies whose mothers had high protein through out pregnancy and beyond.

Generally speaking, these experiments and my ongoing studies give me cause to worry about well-intentioned and often costly programs that focus on children aged 3, 4, or 5 years of age. If there were enough money and programs to satisfy all the needs of all our children, I wouldn't be as disturbed, but until there is, I believe that considerable money should be directed toward good prenatal care. You can be certain that well-developed embryonic and fetal brains are far more able to benefit later from Head Start and other enrichment programs.

Returning to dietary components that are key to developing and maintaining a healthy brain, it has been well validated that choline is extremely important in the diet. Choline is necessary to form an important neurotransmitter, acetylcholine. Choline also forms enzymes that are associated with acetylcholine, ensuring that it functions appropriately. So important is acetylcholine that, according to Richard Wurtman at the Massachusetts Institute of Technology (MIT), nerve cells that do not get sufficient choline will cannibalize their own membrane to make acetylcholine.

By now, surely you want to know some of the dietary sources of choline! (1) Soybeans and their soy products. These days you will find an increasing number of soy-based products on the shelves. We tofu advocates have it with marmalade for breakfast. (2) Egg yolks. Yes, the cholesterol content is high, but those who do not have elevated cholesterol levels can have egg yolks and be assured of getting choline. (3) Peanuts. They are somewhat high in fat and sodium, but use them moderately along with other source foods. (My father always had a big bowl of peanuts for us when we came home from school.) (4) Liver. There are those who enjoy liver! I am one.

I mentioned only one neurotransmitter, acetylcholine, but, remember, you have about one hundred different neurotransmitters serving your body's chemical needs. Other important ones are dopamine, serotonin, and glutamate which, for sources, you can look up in your spare time.

We have known for years that B vitamins are essential for the well-being of the nervous system. Let us just take one B vitamin, vitamin B6. B6 is important in the metabolism of amino acids, which are the building blocks of proteins. And B6 is vital for the creation of neurotransmitters. Like nearly everything in life, however, this vitamin needs something else to help it function efficiently. In the case of B6, it is zinc.

Practically speaking, a vitamin B6 deficiency can have multiple effects, none of them pleasant. It can cause memory impairment which diminishes the ability to register, retain and retrieve things from the memory bank (actually, memory is laced in and out of the brain, so I should say memory banks) A shortage of B6 also can lead to nerve damage in the hands and feet.

In what foods do we find B6? A few vitamin B6 sources are: potatoes, bananas, chicken breast, beef top round steak, turkey white meat, rice bran, carrot juice, rainbow trout. That represents a quick selection from the literature; one need not struggle too much to find dietary sources of vitamin B6.

Antioxidants are other important substances in the care and feeding of the brains. Most are well aware of the major antioxidants, vitamin C and vitamin E and their food sources. Recently, however, there has been much publicity given to blueberries and strawberries, touted by the venerable American Chemical Society as rich sources of antioxidants.

Next, it is important to discuss calcium and, in particular, the interaction of calcium and the parathyroid gland. Many are familiar with their thyroid gland in the neck, but did you know that the parathyroids are right there too? Usually four of them. They regulate the amount of calcium in your blood. If you have low blood calcium, hormones from the parathyroid glands have no trepidation about going to your bones to extract the calcium needed to raise its levels in the blood. Furthermore, everybody knows that calcium is important for bone structure and muscle contraction, among other roles, but did you know that calcium is also important for nerve impulse conduction?

Exercise

Now let us turn to our second key factor in maintaining a healthy brain: EXERCISE. We know that exercise improves skeletal muscle tone and function and that it helps the venous return in our legs, a good reason to keep our legs active. In fact, the value of regular exercise cannot be overrated. Among the long list of routine health conditions ameliorated by exercise, we hear today from many corners that lack of exercise is responsible for or contributes to the increased incidence of sugar diabetes, cardiovascular problems, obesity, and depression. Very important about exercise is that it is essential for bringing oxygen to all parts of the body, and, as I will explore now, especially to the brain. One particular brain structure is most vulnerable to a lack of oxygen, and that is the hippocampus. Early anatomists thought that the hippocampus resembled a seahorse.

The hippocampus deals with the processing of recent memory and visual spatial processing. As we age and our blood vessels become less efficient, it is very important to get the oxygen through the vascular system up to the hippocampus, as well as to the rest of the brain and body.

As a good exercise, I agree with those who emphasize swimming. Yes, walking is a wonderful form of exercise that uses our lower extremities, but total body swimming exercises both upper and lower extremities. Many are well aware of feeling depressed after having been indoors for several hours. I certainly do. Exercise is a trustworthy antidote to depression. I am focusing on older adults now, but there is increasing concern that children are spending too much time sitting in front of their computers and video games, and not getting the exercise they need. (Interestingly, exercise has also been shown to benefit children with hyperactivity problems.)

Suffice it to say that everyone, from the toddler to the frail elderly should have some appropriate daily exercise routine that is as implanted in your day as brushing your teeth, getting dressed, and eating your breakfast. I advise a minimum of an hour a day, but you can work up to it. Five minutes is better than no minutes, and, for those who have never been exercise enthusiasts. Don't be surprised to find that it will cease being a "have-to" and become something you look forward to.

Challenging the Brain

I have come to CHALLENGE, a third vital component of brain health. What I am about to say has been validated by my years of laboratory research, which I will soon discuss. In terms of "successful aging," it is not enough to continue activities in the same groove, year after year, with the same expenditure of mental and physical energy. Remember Alice in Wonderland who discovered that on the other side of the looking glass a person had to move very fast to stay in the same place? The underlying laws of physics Lewis Carroll was playing with when he wrote for his beloved niece have their correlate in neurophysiology: the brain needs new challenges if it is to remain a healthy, functioning organ. Translated, if you have been enjoying working on the same kind of crossword puzzles year after year, it is time to advance to more complicated puzzles or to introduce a new game that will challenge different skills that are lying dormant.

As some of you know, my research has had to do with studying the brain of rats. The laboratory rat is an excellent model for brain research. The rat brain has the same basic pattern of brain structures as humans, but the rat brain is the size of a pecan whereas the brain of humans is the size of a cantaloupe. For my research, I divide the animals into experimental groups: two experimental groups of rats living in conditions I describe as "enriched" and "impoverished.". An enriched environment is one in which 12 rats live together in a large cage, filled with a variety of play objects, objects that present some challenge. In contrast, the impoverished environment houses one rat. The animal lives by itself and there are no objects in the cage and a control group which consists of so-called normal housing conditions of three animals to a small cage that is devoid of any objects.

Examining and comparing brain tissue from each of the three groups yields a wealth of information. The outer layers of the cerebral hemispheres are called the cerebral cortex. Cortex means "bark." The cortex is a dynamic structure. Parts of the human cortex have sent humans to the moon. The thickness of the cortex is one of the first measurements we make because it is simple and let's us know if changes are occurring in the constituents of the cortex, namely, neuron number and size, dendrite growth, synaptic growth, etc. (All of these variables we have measured previously to determine meaning of cortical thickness.)

Examining cortical tissue from 24 pairs of enriched and impoverished male rats from two successive experiments, we found that in the first experiment rats living in enriched environments showed an increase in cortical thickness in the frontal area, but no significant changes in the general sensory area. By contrast, when we compared the visual cortex of enriched and impoverished animals, we found dramatic changes--a seven percent difference in thickness between those living in enriched and those living in impoverished environments. The same pattern was observed in animals from the second experiment. In other words, we have 24 pairs of rats that show the same pattern: very definite changes in the frontal cortex, no significant changes in the general sensory cortex, and a 7% difference in the visual cortex.

As in most of the work now done with laboratory animals, we wanted to determine whether female rats would respond in the same way. Examining 23 pairs of non-pregnant female rats that had lived in enriched and impoverished environments, we saw, in the first experiment, significant changes in the frontal area AND in the general sensory cortex, but only a 4 percent difference in the visual cortex in contrast to the 7% we observed in the male animal. A replication experiment confirmed these findings.

My students suggested that we further challenge the females in the enriched conditions to see whether that would bring the changes in the visual cortex up to the level of the males. And so how did we "challenge" them further? We placed obstacles in front of their food cups! In other words, whenever they wanted to eat, they had to climb over a number of obstacles to get to the food. We were all gratified to see that the additional challenge did accomplish our goal: the visual cortex of the female rats increased to the level of their male counterparts. If you have been following the details of these experiments, you might ask whether we then tried to bring the general sensory cortex of the male up to that of the female? No, that's an experiment we saved for future students to embark upon.

By now you might have trouble understanding why thicker is better. Psychologists have tested the rats living in enriched or impoverished conditions and found the enriched rats ran maze tests faster than did the impoverished. Evidently more dendrites, hence, thicker cortices, indicate a greater ability to solve problems.

If we extrapolate these findings to our species, we begin to recognize that the value behaviorists and sports psychologists have long placed on "personal best," on going one step beyond what you think you can, is validated by neurophysiological findings. We all know the temptation to take the simple route--the difficulty of pushing ourselves beyond and taking on more, although countless stories show us what individuals can do when challenged by unusual, or difficult, or seemingly impossible circumstances.

There are obviously different kinds of challenges. Here is another experiment from my rat world. Pretend there were no barriers in this box. We put a rat in one corner of a large box and food in the opposite corner. The rat ran straight to the food. The next day we put a barrier in the box. The rat had to run around the barrier to find his food. Each day we added another barrier until we had 19 barriers. As you can guess, based on our previous findings, we wanted to find out what changes might take place in the brain when animals are sequentially challenged with a relatively simple task.

The only change we found was a 6% difference in the visual cortex in both hemispheres of the rats in the box with barriers versus the box with no barriers. The difference was statistically significant, but despite the addition of a barrier a day, it represented a single challenge only to the visual cortex.

The point to take away today is that multisensory inputs effect changes in many cortical areas, whereas a single challenge gets a response from only one area of the cortex.

So when children, or anyone, sit in front of TV sets or computers for hours a day, their brains are being fed a specific type of input. Were they to be exposed to a more enriched environment, in addition to exercise and to problem-solving challenges, many areas of the cortex would be affected.

I haven't spoken about the sociability factor built into our experiments. Are there differences in the brain tissues of rats maintained under so-called normal housing conditions of three to a cage versus the "impoverished" condition where a rat is alone, versus the "enriched" condition where 12 rats are caged together? And can we distinguish the effects of the sociability factor apart from the presence in the cage of toys and obstacles?

When an experiment was conducted with 12 rats in an enrichment cage with no toys, an increase in cortical thickness was found, but not to the extent observed in animals housed 12 to a cage with toys. And what about the lone rat? When toys were added to his cage, what do you think happened? Not much! The cortical changes found were considerably less than those recorded in rats who lived with toys and 12 other rats. So both sociability and challenge are important.

Another condition we wanted to investigate besides the thickness of cortical tissue in these experimental groups was the impact of enriched and impoverished environments on a substance called "lipofuscin." Lipofuscin is an "aging pigment" that accumulates in our brains as we age. It doesn't sound good, does it? Well, it is not. It is thought to interfere with the normal function of the nerve cells. Earlier you saw what the nerve cell body looks like, and learned that it is normally hard at work producing proteins to supply the many functions of these cells. You do not want that nerve cell body filled with an aging pigment. We found that rats maintained in enriched environments produced less of this aging pigment in their brains. You can almost picture that one, can't you? Doesn't that make a grand case for keeping challenge and activity in your life always?

Brain Challenges and the Immune System

Our most recent research focuses on human beings. A secrete passion of mine was to find a relationship between the cerebral cortex and the immune system. The immune system, once the nearly exclusive interest of the scientific community, is discussed everywhere these days, and the words are bandied about freely by the pharmaceutical industry and health food stores alike. Well, the immune system, of course, is extremely important to our health at all ages, and certainly it is critical to successful aging. Naturally, the experiments we had been working on over many years led us eventually to looking at what effects challenges to the brain might have on the immune system.

In 1980, French investigators, working with female mice, had stripped off most of the cerebral cortex in their animals and found that this procedure affected the number of circulating T cells in the blood. That was the key I had been looking for. It told me that the cerebral cortex was involved specifically with immune function. The task was to find out which part of the large cortex specifically affected the immune system.

Let me quickly summarize years of work in this area. We spent a great deal of time lesioning the cortex trying unsuccessfully to find an area specifically related to the immune system before we decided to measure the cortical thickness from the front to the back of the whole mouse cortex In doing so, we found an area on both the right and left cortices that was thinner in the immune-deficient female mice compared to normal mice cortices. Immune-deficient mice have no thymus gland. It is congenitally lacking. A graduate student decided to transplant the thymus into the immune-deficient animal, and found the cortical thinness deficiencies were reversed. In other words, no significant difference was found in the thickness of the cortex after a thymus transplant between the immune deficient animal and the control. We then knew we had established an area, the dorsal lateral frontal part of the cerebral cortex, that is related to the immune system.

I am telescoping this work drastically, but I hope you can appreciate that finding this area of the cerebral cortex was the culmination of a dream for me. Why? Because it indicates that the cerebral cortex, part of which is under voluntary control, has a specific area related to immune system functions. An immediate question is: Can we voluntarily stimulate this cortical area to alter immune function?

For that, let me take you to some experiments carried out by investigators in the late 1980s. Schizophrenic patients were given what is called the Wisconsin Card Sorting Test,a reliable test for clinically measuring certain psychological factors. While the patients were undergoing this card-sorting test, they were given a PET scan, which showed that during the test, the dorsolateral frontal area of the cortex was activated.

For our part, I felt that most people haven't heard of the Wisconsin Card-Sorting Test, so I set about finding a game everybody has heard of and decided on the card game of "bridge". Playing bridge calls for working memory, planning ahead, sequencing, initiative, and judgment--all functions associated with the dorsolateral frontal part of the cortex.

We invited 12 women to come to the lab to play bridge with one another. Before they started playing, we took blood samples from them to measure the initial level of their T cells. Then we took blood from them after they had been playing for an hour and a half. The before and after data were exciting to us because we found a significant increase in their CD4-positive T lymphocytes. We did not find such a T cell increase in the blood samples of the control women who did not play bridge, but sat listening to quiet music during the time the others were playing bridge.

We were terribly thrilled with these results. Clearly, the cerebral cortex has a role in controlling the immune system, and our present task is to find ways to "educate" the critical dorsolateral cortex and keep our immune systems healthy.

Although this is just a preliminary study that must be replicated and followed through, for me these results provided a very exciting moment. Here is another set of experiments that yielded important findings in the late 1980s. We wanted to know what happens in our experimental animals if their brains were damaged. If you lesion the left motor cortex in a young, sexually mature rat, it will lose the function of its right forepaw. The left motor cortex controls right paw movement. After a number of rats were lesioned, half were placed in the enriched environments and half in control environments. When the brains of rats living in the control conditions were later measured, those dendrites did not grow very much at all, either around the lesion, on in the opposite hemisphere or back in the sensory area of the cortex. But the dendrites in animals maintained in the enriched environment had grown significantly. They grew around the lesion. They grew in the opposite side of the cortex, and they even grew back in the somatosensory cortex. From these findings we can only conclude that, even when brain damage is present, animals living in a stimulating environment are able to compensate for the damage. Look at the promise that holds for our species who receive some degree of brain injury.

Newness versus Overstimulation

Is it possible, you might ask, to overstimulate or overenrich the brain? In fact, my conversation with a pediatrician, concerned that children are being constantly bombarded with new experiences, inspired the following experiments. You will recall that in the experiments we have reported here, our practice was to change the toys in the enrichment cage two or three times a week or in some experiments every day. Because "newness" is an important aspect of challenge, we had to change the toys frequently; otherwise, the brain at first responds to the enriched conditions but decreases its growth activity when the newness wears off. In our new experiment, instead of changing toys two or three times a week, we decided to change the toys at 7 seven o'clock at night, 8 eight o'clock at night, 9 nine o'clock at night, for four nights a week for four weeks. In short, we bombarded our rats with stimulation and wondered whether we were now going to see huge brains in these super-enriched animals. (Oh, the fun of research!) It seems that the significantly different results we had recorded between the enriched and non-enriched animals under our original experimental conditions did not take the leap we thought they might when we stepped up the frequency of changing their toys. In fact, the enrichment effect in these animals was less than with the enriched conditions originally established. And that also tells us something of great importance: Too much stimulation can constitute a stress that is sufficient to militate against the enriching effect of "just right" conditions. Obviously, with humans "just right" varies, no? good stress/bad stress? variability of interests, passions, competences?

What chemical stress factor can be involved? The corticosteroids. Corticosteroids come from the adrenals and they have been shown responsible for reducing cortical thickening. Do you know where your adrenals are? The word tells you: ad-renal, adherent to the renal or kidney. When we take out the adrenals, the cortex grows significantly, indicating that in the absence of corticosteroids, cortical growth is enhanced.

The lesson for humans? Too much stress decreases the dimensions of the cortex and is detrimental to our well-being at any age. The lesson for parents and teachers? Children need enriched learning environments but not to the degree that they are stressed. What is problematic in our species is that what is stress to one is not to another, and this variability needs to be reckoned with if we are to maximize everyone's opportunities for successful "aging" from childhood on.

Love and Nurturing

And our last subject, then, oddly enough, is LOVE. To appreciate how this concept entered the ivy-covered walls of academia and the sterility of its laboratories, you need a little background on our ongoing experiments. We had started our experiments using young rats, which are readily available and easy to work with. When we found that our enriched conditions accelerated the growth of dendrites (you recall how important dendrites are) we wanted to see whether older rats would do as well. We began to do our experiments with 600-day-old rats, an age that is possibly equivalent to 60 years -old in humans. Again, placing half of them in enriched conditions and half of them in non-enriched conditions, we found significant increases in dendritic branching in the cerebral cortex in the animals maintained in enriched conditions.

We were pleased with these results, but were disturbed that we were beginning to lose one or two of the animals at 600 days. Following the publication of these findings, I was invited by the German Academy of Sciences to report on this work, of great interest at the time because, to date, no one had shown that these effects could be realized in the older brain. While there, I was struck by the comment of a German scientist that German rats lived to be 800 days old.

I returned to my laboratory determined to see how we might get our rats to live longer. Was there something missing in our experimental design? I began to reflect on conversations and observations I had had with groups of older folks around the country. It was clear to me that many were not getting enough attention, enough "TLC," enough "random acts of kindness." Sure, they had their television sets, they had adequate food, but where was the nurturing, the love? That I didn't see. I mentioned to my technician that we were going to add an ingredient to our experiments: love.

Instead of putting the rats immediately in their control cages after they were cleaned, we held them against our lab coats and petted them. The rats in this group survived to 766 days at which time we placed half of them in the enriched environment and half back in the control environment. At 904 days, possibly equivalent of 90 years old in people, we were still finding thicker cortical tissue among those rats maintained in enriched conditions.

In other words, we first got the rats to live longer and then we got cortical growth to continue into old age. How can we not conclude that stimulating the brain works its magic right up until the end, and may even advance when we call it "the end"? We used to believe, as scientists, that the loss of dendrites was an inevitable correlate of the aging process. It was simply our fate. Yes, it takes concerted attention to stave off the "inevitabilities" we have accepted for so long, but is the price really that high? Is it too much work to follow a healthy diet, enjoy plenty of exercise, seek out new challenges and get lots of love? My own life and work have been enriched immeasurably by two fortuitous statements I absorbed many years ago: a family crest that states:"Love conquers all" and the words of my Swiss grandmother: "In spite of all difficulties, upwards and onwards." A good combination.

About the Author:

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