

# Changes in Medicine

The Way Forward

Kenneth M. Heilman

 Springer

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*Dedicated to Dr. Melvin Greer, who was the Chair of the Department of Neurology at the University of Florida. In addition to being a wonderful clinician and teacher, he was a great mentor, helping to develop my and many other physicians' careers.*

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# Introduction

# 1

It is now more than one half of a century since I started my medical internship (post-graduate year one). Since I am still working, many people have asked me, “Why haven’t you retired?” When they ask me this question I ask them, “Why I should retire?” They often respond, “When you retire, you can do all the things you wanted to do.” I tell them, “I am doing what I always wanted to do.”

I am a neurologist who takes care of patients with diseases of their brain, spinal cord, nerves and muscles. I am not sure how much longer I will remain being a clinician, teacher and investigator, but I have always felt that being able to perform these activities has been a great blessing. However, over the five decades that I have been performing these activities, many things have changed, and one of the most important to me are the new treatments for neurological diseases.

There have also been many changes for the physicians working at health centers. Some are good and some have been troublesome. Most of these changes have to do with economics. For example, when I was a neurology resident at the Harvard Neurology Division at Boston City Hospital, Dr. Maxwell Finland who was the director of Boston City Hospital, was also an internal medicine-infectious disease expert. He wrote more than 800 journal articles and was also editor of the *New England Journal of Medicine*. Dr. Finland died in 1987 and it is estimated that between the money he gave to Harvard Medical School and the money he influenced companies to give to Harvard, was about six million dollars. Now many executives-directors-officers and presidents at academic medical centers have yearly salaries that are about one million dollars. In addition, they make additional money by being paid for lectures, writing books, and other activities. Unfortunately, there are only a small number of executives who return any of this money to their universities, for education and research. However, we will discuss economics later in this book.

When I was taking my internal medicine residency at Cornell-Bellevue, many of my attending physicians would ask me, “Ken, what branch of internal medicine are you thinking about specializing in?” I told them that I really like all the branches of internal medicine. I liked cardiology, but there were several heart sounds that sick



hearts make that I could never hear, so that eliminated cardiology. I also thought that infectious disease was also interesting, but I thought with all the antibiotics they were inventing, in a few years this would be a dead specialty. However, this was a bad diagnosis that I made. The infectious bugs have stayed way ahead of us. I enjoyed seeing patients with endocrine disorders, but in practice almost all had the same disease, diabetes. There were many other subspecialties that were of interest, but neurology had the greatest appeal to me.

Medical specialization, for the most part, is based on the organ that is sick, e.g., cardiology, gastroenterology, dermatology, endocrinology, etc. Whereas all these specialties deal with a variety of diseases of an organ that might be difficult to diagnosis, treat and manage, the organ that is the most complex is the brain.

During my medical residency, when my mentors and colleagues at Bellevue Hospital asked me about specialization, and I told them, that I was interested in neurology, they would often say something like, “Well, neurology is interesting, but there are so few things you can do for these patients.” I usually responded, “Yes, and that is one of the reasons I am thinking about specializing in Neurology.”

At the time of my medical residency at Cornell-Bellevue (1963–1965), the comments that there was so little that could be done for patients with neurological diseases, was true. Back then we could treat meningitis with antibiotics, treat some people with a seizure disorder with phenytoin (Dilantin) or phenobarbital, but that was about it. There was little that could be done with patients suffering with some of the most common neurological diseases, such as Parkinson’s disease, multiple sclerosis, muscular dystrophy, stroke, brain tumors, Alzheimer’s disease and amyotrophic lateral sclerosis (Lou Gehrig’s disease). However, since I was a medical resident in the mid-1960s, there has been many dramatic changes in the practice of neurology. For example, when I was a medical resident, little could be done for patients with diseases such Parkinson’s disease. Although there were some medicines used to treat the Parkinsonian tremor, in most patients this is a resting tremor that goes away with action and thus this tremor was not often disabling. In addition, some of these patient’s medication, may have impaired memory. In my first year of neurology residency, we saw patients with Parkinson’s disease who could not even get out of bed without help. We often helped them by getting them out of bed and then having them push the chart rack when we were making rounds. Parkinson patients have what is called, akinesia paradoxa. They have trouble self-initiating actions; however, they can perform activities in response to suggestion or invitations. This exercise helped them, but when these patients went home, they very often again became akinetic. They needed to be helped. The following year, in the second year of my neurology residency, Cotzias [1] reported that treatment with a medication called levodopa could help patients with Parkinson’s disease. When my patients were given this medication, there were miraculous changes in their behavior. These patients were then able to get out of bed by themselves as well as care for themselves. However, although these medications provided symptomatic relief and reduced disability, they do not stop the progression of this disease.

One of the most disabling neurological diseases to impair young adults is multiple sclerosis. In 1868 the famous father of neurology, Jean-Martin Charcot,

lectured on the features of multiple sclerosis and gave this disorder its name. Throughout the 1800s and 1900s, many forms of therapy were tried, but without success. Then, in 1951, cortisone was used to treat multiple sclerosis. It was found that this medication could reduce the severity of the relapse and to shorten its duration. During my neurology residency we used steroids to treat patients with this disease. Unfortunately, this treatment had little or no long-term effects on the disability caused by this disease. Fortunately, we currently have many medications that are approved for the treatment of multiple sclerosis.

Stroke has been and still is one of the major causes of disability and death. We now have medications that reduce the bad cholesterol and treat high blood pressure. These treatments often help to prevent strokes. In addition, if a patient who has a stroke comes to the hospital soon enough, they can now be treated with medications that help to break up the blood clot that caused their stroke. In addition, if this blood clot is in a large vessel such as the carotid artery or the middle cerebral artery, these blood clots can often be removed. These treatments can often reduce the chance of death as well as reducing the size of the stroke and the severity of the disability.

Unfortunately, there are still many terrible neurological diseases that have no successful treatment. Some of these diseases are common, such Alzheimer's disease, Lewy Body Dementia and amyotrophic lateral sclerosis (ALS). Although there are no cures or good treatments for these diseases, there is still much that can be done to help reduce these patient's disability and suffering, and this is still one of the jobs of clinical neurologists.

Although there have been many great advances in medicine, and these advances have helped to prolong life, reduce disability and suffering, there still much that needs to be done. Unfortunately, there are many factors that are interfering with progress in medical research and patient care. This book discusses several of the major problems that are hindering the advance of medicine and the goal of this book is to make people aware of these problems.

Khalil Gibran, the American Lebanese author wrote, "For life goes not backward nor tarries with yesterday. You are the bows from which your children as living arrows are sent forth. Let your bending in the archer's hand be for gladness." I hope the bending of this archer's hand will help to promote changes that will improve our ability to bring about a reduction of disease and suffering.

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## Reference

1. Cotzias GC. L-Dopa for Parkinsonism. *N Engl J Med.* 1968;278(11):630.



One of the major reasons that medical research has always been an important part of my life is that when I was a young boy, I noticed that in my left antecubital fossa (where the elbow bends), I had a scar. I asked my mother why I had this scar. She told me that when I was a six-month-old, I developed a high fever, a stiff neck and became less responsive. I also might have also had a rash. My pediatrician, who came to our apartment in Brooklyn to examine me, told my mother that I had meningitis and that when babies get meningitis, many of them die, but he hoped that I would not be one of them.

Unfortunately, I cannot recall the name of my pediatrician, but he was on the clinical faculty at Columbia University, in New York City. The year was 1939 and the first antibiotic, penicillin was not yet available. My pediatrician, however, learned that at Columbia University Hospital they were studying a new medication called “sulfonamides” or “sulfa” drugs. These investigators found that this medication could help cure some infections. My pediatrician went to the laboratory where they were working on one of these drugs and was able to get some of this medicine. He then came to our apartment in Brooklyn to treat me with this medication. He had to put this medicine directly into my blood. He had trouble finding a vein that was big enough to inject this medicine into me and to get access to my vein he did what is called a “cut down.” When performing a cut down, the doctor cuts the skin and then searches for a large vein. After the vein is surgically exposed, he inserts a tube (cannula) into the vein and gives the medicine along with other fluids. It worked! He found the vein, was able to give me this sulfa drug and I am alive. This scar at my elbow has always been a reminder of how both medical research and a courageous doctor saved my life.

From the time I was a boy, I have been aware about the terrible suffering that many people undergo. Growing up during World War II, I was aware about how many of our soldiers were injured and died during this terrible war. After this war was over, I learned what the Germans did to the Jews, and to even young Jewish boys living in Europe. However, I also learned that after the German’s were defeated, how America worked to repair the damages done by the Nazis and this war.

During World War II, they developed another great medicine that could treat infections, including meningitis, called penicillin. However, I was still aware of how much suffering was caused by diseases and I wanted to do medical research. For our high school yearbook, we were asked state what we wanted to do with our lives. Next to my name and picture they wrote, "Ken wants to do medical research."

When I was in college at the University of Virginia, I majored in chemistry. I majored in chemistry, because I thought that understanding protein chemistry would allow me to learn the cause and treatment for many diseases. In my third year I took a graduate school course in advanced organic chemistry. Our professor was giving lectures about quantum mechanics and topology. I did not understand these lectures and became sad because I realized I reached a glass ceiling and could never be a theoretical chemist and study proteins. As I was walking back to my apartment, I passes by the medical school. Even though I was not premed, and a third-year undergraduate, I decided to apply to medical school at the University of Virginia. I walked into the dean's office and asked the secretary for an application form. She asked me, "Are you applying for admission this fall?" I told her that I was only a third-year student, and I would have to wait a year and take biology, which was an admission requirement. She told me that this year the medical school is trying something new. They will be admitting two college students after the third year of college, and they did not need a bachelor's degree. I, therefore, filled out the application and returned it to her. She then asked me to step out of the office so that she could call the office of the dean of the College and obtain my grades. After, she received these grades she said, "Let me set up two interviews with members of our faculty." I had two interviews that I think went well because when I returned in a week, she told me that I had been admitted. I told her, "...but wait I have not taken my National Medical and Dental College Admission Test and I never had a biology class. She told me that next semester I should take a biology class and I should take the National Medical and Dental College Admission Test, which I did.

When I was a medical student at UVa, our inpatient service, like many other hospitals had large rooms (wards) that contained about 16 beds. Next to each bed there was a nightstand and a curtain that could be pulled around the bed to allow the patient to have some privacy when needed. When I was on the neurology service, I was walking on one of these wards, to see my patient, who had trouble keeping his eyes open because he had a disorder called myasthenia gravis. On the way to my patient's bed a man who was not my patient call out to me, "Hey Doc, can you come over here?"

I walked over to his bed. He was sitting up in bed and was eating his lunch. He looked up and asked me, "Doc, what kind of place is this?" I responded, "This is a hospital." He said, "I know, but why do they only serve vegetables?"

I looked down at his plate and noticed that he had eaten all the vegetables on the right side of his plate but had not eaten any of the roast beef on the left side of the plate. I turned his plate around one hundred and eighty degrees. He now saw the meat and said, "Thanks doc." I thought he probably did not see the left side of his plate because he lost his vision on the left side. This can occur if you have a stroke of the right occipital lobe. I, therefore, asked if I could test his vision. I tested his

vision by holding my left hand on the right side of his head and my right hand on the left side of his head. I told him, "When I wiggle my hand, tell me you can see it moving and which hand is moving." I was surprised to learn that he was able to see my right hand move in his left visual field, and I could not understand why he could not see his food.

The next day I was walking down the ward and this same man called me. "Doc, can you come over here again?"

I walked over to his bed and asked, "How can I help you?"

He picked up his left hand, which appeared to be paralyzed by his stroke and asked me, "Can you get this person out of my bed?" He then attempted to throw his left arm out his bed. However, when patients have weakness from a cerebral stroke, they often have increased tone in the muscles of that limb, and it acts like a spring. Therefore, after he threw it out, it came back and hit him. He looked up at me and said, "See when I try and get rid of him, he comes back and hits me."

I walked over to the left side of his bed to hold his left arm and he asked me, "Doc, where are you?"

I, therefore, walked back over to his right side and reached for his left arm and tried to show him how his hand was connected to the forearm, how his forearm was connected to arm and how his arm was attached to his body, but I never convinced him. I explained to him, "You had a stroke, and your arm is weak from this stroke." He said, "No, I did not have a stroke." I was surprised by his answer, but later learned that this disorder of not recognizing one's own illness is called anosognosia (a = without, noso = disease, and gnosis = knowledge) and often occurs with right hemispheric strokes.

I then asked him, "Why do you think you are in the hospital?" He replied, "I do not know. My daughter brought me here."

I had been interested in conscious awareness for many years and in college I took courses in philosophy and psychology to learn more about conscious awareness, but I still did not understand the basis of the mental process that allows conscious awareness.

I asked the attending neurologist who was taking care of this patient, to explain to me why this stroke might have produced this clinical picture. He told me, this patient has a disorder called the "neglect syndrome" and that he could not fully explain why these patients revealed these signs and symptoms. He did suggest that I read the work of Dr. Denny-Brown, who wrote a paper about the possible mechanisms accounting for this neglect syndrome. The title of his paper was "Amorphosynthesis."

I went to the library, as soon as I could, got a copy of this paper, read it over many times, but did not fully understand the mechanisms that Dr. Denny-Brown wrote about in this paper. However, I still want to understand the mechanisms of this phenomena called the neglect syndrome.

After graduating from medical school and taking two years of internal medicine training at Cornell-Bellevue, during the war in Viet Nam, I joined the Air Force and was Chief of Medicine at the NATO hospital in Izmir Turkey. Although, while I was in the Airforce, I very much enjoyed practicing internal medicine, I still wanted to

understand the neglect syndrome, as well as other neurological disorders and hopefully find treatments for these diseases. Therefore, while living and working in Turkey, I wrote to Dr. Denny-Brown and applied for a residency in neurology. Several weeks after I send him all of the information he needed, he wrote me a letter accepting me as a resident in his training program at the Harvard Neurological Unit, which then was in Boston City Hospital.

Unfortunately, before I got discharged from the Air Force and started my residency, Dr. Denny-Brown had a heart attack and decided to retire. Although, another neurologist, Dr. S Locke took over as Acting Chief, because Dr. Denny-Brown accepted me and the other residents into his program, he did come to the Harvard Neurologic Unit almost every Saturday, to make Grand Rounds. He also continued to perform his research with animals.

While I was a resident, we admitted a patient who had some of the signs of this neglect syndrome and thus I thought that this was an opportunity to have Dr. Denny-Brown explain the brain mechanisms that might account for this disorder. I, therefore, asked Dr. Locke if I could present this patient to Dr. Denny-Brown. Dr. Locke did give me permission to present this patient and I was very excited about the possibility that I would now understand this disorder of conscious awareness. Before presenting this patient to Dr. Denny-Brown, one of our residents, Louis Caplan, another resident, who was one year ahead of me, told me, "Ken, Denny-Brown is very impatient and gets angry very easily. He had a Dupuytren's contracture and surgery did not correct it, so he had his ring finger amputated. When he gets agitated, the stump of that finger starts to tingle, and he will rub it against his other hand. This is a sign he ready to explode."

When presenting this patient to Dr. Denny-Brown, as well as to the other residents and faculty in the audience, I said, "The motor strength on the right side of his body was normal, but he does not move his left arm."

Before, I could tell him more about this arm, Dr. Denny-Brown said, "Dr. Heilman, did he have a hemiparesis?"

I replied, "I did not see him use his arm and when I tried to test his strength, he did not move his arm."

Dr. Denny-Brown started to rub that stump in one hand against his other hand, and said, "Heilman, do you know what a hemiparesis is?"

I said "Yes, it is weakness on one side of the body, usually caused by injury of the motor cortex or the corticospinal tract."

He kept rubbing his hand and said, "Good! Did he have a hemiparesis?"

He appeared so irritated that I did not want to go into detail about why I had previously said that he did not move him arm and so I said, "Yes, I guess."

The patient did show many signs of neglect and Dr. Denny-Brown did explain that he thought that this patient's neglect was caused by a cerebral infarction and that most likely this cerebral infarction injured his parietal lobe. When Dr. Denny-Brown discussed amorphosynthesis, he explained that the inferior parietal lobe, receives information from visual association cortex, auditory association cortex and somesthetic (touch) association cortex and that the synthesis of this information allows the parietal lobe to development of representation of contralateral space.

With damage to the parietal lobe there is a loss of this representation (knowledge) of this contralateral (opposite) side of space and that this loss of knowledge produces the signs and symptoms of neglect.

Although I liked Dr. Denny-Brown's theory of hemispatial neglect, when patients are unaware of stimuli in their left side, if you ask them to look to that side they can see and be aware of these stimuli on the left side. When you are reading this book, you were probably unaware of how your left foot feels in your left shoe, but now you are aware of your foot, because you allocated your attention to your left foot. Therefore, unawareness can be caused by a failure to allocate attention. In many of the studies we performed and published we did obtain support for this attentional hypothesis.

When I presented this patient to Dr. Denny-Brown, in 1967, we did not have CT or MRI brain imaging and thus we could never learn the location of this patient's cerebral infarction.

Since Dr. Denny-Brown stepped down as chair of the Harvard Neurological Unit Dr. Norman Geschwind, was recruited to be the new Chair of the Harvard Neurological Unit. Dr. Geschwind was the person responsible for the development of cognitive and behavioral neurology in America, After I completed my residency, he allowed me to take a fellowship in Behavioral Neurology and during my fellowship he allowed me to work with a brilliant neuroanatomist, Deepak Pandya, who unfortunately recently died.

Dr. Pandya was performing studies on cortical connectivity. It has already been known that each primary sensory cortex, such as visual, auditory and somesthetic (touch) cortical areas send projections to each of their modality specific association areas in the cortex and that these association areas were important for sensory perception. However, Dr. Pandya revealed that all these sensory association areas send projections to the monkey's inferior parietal and posterior superior temporal lobe. All three of these areas get their sensory information from the opposite side of space and the convergence of these three sensory systems would be important in the development of a representation of contralateral space. To test Denny-Brown's sensory synthesis hypothesis and to understand the mechanisms of unilateral neglect, we demonstrated in animals, that ablation of this sensory converge area, including the inferior parietal lobule and both banks of the caudal portion of the superior temporal sulcus did produce contralateral spatial neglect.

During my fellowship, Dr. Geschwind would often ask me to cover the consult service when they were overwhelmed. One day I was asked to see a patient on Harvard Medical Service at Boston City Hospital, who on examination revealed the signs of neglect and that were similar to patient I presented to Dr. Denny-Brown. I explained to the interns and residents on our service that this patient had the left sided neglect syndrome, that this syndrome has been shown to be caused by injury to the inferior parietal lobe and therefore his stroke injured his right parietal lobe.

In 1969 there was a new procedure that could help physicians localize a stroke. In this procedure a radioactive isotope is injected into a vein of the patient and this isotope is carried by blood vessels to different parts of the body, including the brain. Since in the area of the brain that is damaged by the stroke, the blood vessels are



damaged, this radioisotope leaks out and by measuring the radioactivity coming through the skull, the localization of the brain lesion can be determined.

The resident who was taking care of this patient asked me if they should obtain this radioisotope imaging for this patient. I responded by saying, "No. I told you he had a stroke, and this stroke damaged the parietal lobe of his right hemisphere. Do not waste money and expose him to radiation."

The resident nodded and I left to see another patient.

A few days later, I saw this resident walking down a hallway with a large envelope used to carry X-rays. He called out, "Ken, let me show you something." He opened this envelope and took out a radioisotope scan of the patient that I diagnosed as having a right parietal lesion. I held the scan up to the light and this imaging revealed a right frontal stroke, not a parietal stroke. I told the resident, "I am sorry, but I never heard of neglect being caused by a frontal lesion. It still looks like a stroke, and I would still treat him as we discussed."

When I searched the literature, I found that frontal lobe strokes in humans had not been reported to produce the neglect syndrome. Therefore, Ed Valenstein and I reported this patient as well as others who had strokes of their frontal lobes that induced neglect [1].

After I completed my Cognitive and Behavioral Neurology fellowship (1970), I took a position as an Assistant Professor at the University of Florida. Although I wanted to continue my research on the neglect syndrome, I did not want to continue to perform research with monkeys.

When I came to Gainesville, there was a resident, whose name was Robert T. Watson. Bob was just starting his residency, but he had heard me speak about the neglect syndrome and some of the research in humans and monkeys that we had performed. He came to speak to me and told me that this research fascinated him, and he wanted to perform further research with monkeys on the neglect syndrome. I told him, that we did not have a laboratory, we did not have monkeys and being a resident, he would not have time to do this research.

I made a bad diagnosis. Bob was so highly regarded by Fred King, the Chair of the Neuroscience Department, that Bob was able to get a laboratory and monkeys from Fred King. Bob and I discussed the patient who had I presented to Dr. Denny-Brown during my training in Boston. We discussed the possibility that the reason patients with the neglect syndrome fail to respond to stimuli on the side opposite to their brain injury, is that they are inattentive-unaware of these stimuli.

As mentioned, the human brain is continuously flooded with incoming stimuli and cannot fully process all these stimuli. Therefore, it triages this information, so that the most important information to that person is more fully processed and one of the first steps in this processing is being aware of these stimuli. Similarly, we can perform many possible actions, but there is a limit on the number of actions we can simultaneously perform. Therefore, we must decide if we want to or do not want to initiate an action. If we decide an action is needed, we need to decide what action is needed and when it is needed. Another possible reason for the patient who I presented to Dr. Denny-Brown to not move his left arm is that with the neglect syndrome, even in the absence of weakness, he might be impaired at being able to



initiate an action. Thus, the man I presented to Dr. Denny-Brown may have not had had a hemiparesis, but rather he may have had an action-intention deficit, an inability to activate the portion of the motor system that moved his left arm (motor neglect).

We, therefore, want to learn if a frontal lesion does induce an action-intentional deficit (motor neglect). Bob Watson, Ed Valenstein and I developed a relatively simple testing paradigm that would allow us to determine if a patient had hemispatial neglect from unawareness (sensory inattention) of one side of space or would not perform actions in one side of space. Bob, and Barbara Haws, our laboratory director, trained monkeys to respond with the arm on the side that was opposite the side that was stimulated. Thus, when stimulated on the left side they would be trained to move their right arm and when stimulated on their right side they would be trained to use their left arm. After being trained on this task Bob and Ed ablated an area, one side of the prefrontal lobe. This area was in front of the primary motor cortex, they did not injure the motor area. After they ablated the right lateral prefrontal lobe, the monkeys appeared to have left sensory neglect because they would not respond to left side sensory stimuli. However, if these monkeys had sensory neglect. then these monkeys would fail to respond to left sided stimuli, by moving their right arm. We found that following the right prefrontal lobe ablation, when the monkeys were touched on their left side, they did respond with their right arm in right hemispace. In contrast, these monkeys did not respond with their left arm to right sided stimuli. Therefore, these animals did not have sensory-attentional neglect, but instead had motor-intentional neglect. Motor neglect was not known to clinicians. However, differentiating these two types of neglect could be important, since they require different forms of rehabilitation.

To further test monkeys and to study of humans, to learn more about this terribly disabling disorder, was expensive. Unfortunately, Dr. King could no longer support our studies. We, therefore, decided to submit a grant to the National Institutes of Health (NIH) to learn if they would help support our research.

The research proposal submitted to NIH was complex. Since we were all clinicians and educators, as well as having families, we were very time poor, but we were able to submit a complex proposal for funding.

After several months, we learned that our proposal would not be funded. The reviewers of our proposal had several negative comments. Overall, they thought that we would not obtain interesting or important results. One of their final comments was, "If these neurologists find anything of interest it would have to be serendipitous."

We were finally able to get funding for this project. These funds were provided by the Veterans Affairs Research Service who thankfully had people on the review committee who were aware of the importance of this disorder. We have now been the authors of more than 170 peer reviewed journal articles about the neglect syndrome.

The review that NIH sent us, when we first submitted this proposal has always troubled me. Yes, I was disappointed that we were not funded, but there were two things that troubled me. Although it was clear that they did not like our research

proposal, they did not provide any suggestions for improvement. Most troubling is that they invited us to stop doing research. One of the most important activities for academic physicians to invite rather than discourage research.

The goal of clinicians and investigators is to prolong life and reduce suffering. When reviewing a paper or research proposal, even when it is not accepted or not funded, when possible, it is an opportunity to help the investigator. Therefore, a reviewer who is critical of a research proposal should not only reject this proposal for funding but, when possible, should also provide suggestions for improvement.”

We have noted that many patients who initially revealed evidence of neglect, after a period of several weeks to months these patients perform normally on many of the tests we use to assess for spatial neglect. For example, three of the most used tests used to assess patients for spatial neglect are line bisection, cancellation and drawing tests (both copying and spontaneous). In the line bisection test the patient is shown a line that is usually about 24 cm in length and about 2 mm thick. Each line is drawn on a sheet of paper and the line is placed so that it is parallel to the patient’s body (horizontal). This line is presented below eyes level, usually on a desk. The patient is asked to place a mark in the middle of the line. Patients with neglect will often deviate to the side of their stroke because they are inattentive or unaware of the portion of the line that is opposite to their brain lesion. When performing the cancellation test the patients are presented with a sheet of paper that has many target marks randomly distributed over this sheet of paper and they are asked to cancel–mark out all the target marks. Patient with neglect from a right hemisphere stroke will often fail to cancel targets that are on their left side of their body and page. When copying a drawing they will often fail to draw the portions of the picture that are on the side of space that is opposite to their brain injury. Some patients with neglect when asked to draw a picture, rather than copying a picture, will also fail to draw the left side, suggesting that they have imagery neglect. These patients with spatial neglect often remain more severely disabled than almost all the other forms of deficits caused by strokes.

Rubens [2] reported that cold water caloric stimulation of the left ear will improve patients’ left hemispatial neglect. The reason why cold water injected into the left ear improves left sided sensory inattention is not entirely known. Some have posited that cold-water stimulation increases arousal of the right injured hemisphere and this increased arousal allows patients to detect contralesional sensory stimuli.

Cold water injected into an ear also activates the vestibular system inducing nystagmus and a feeling of body rotation. In patients with left sided neglect, moving objects toward the right side of a patient’s body can improve detection of stimuli in that were neglected in the contralesional hemispace and cold-water caloric stimulation might alter egocentric perceptual systems in a similar manner.

Although it has been posited that cold-water stimulation increases arousal of the brain and this increased arousal allows patients to detect contralesional sensory stimuli, cold water injected into an ear also activates the vestibular system inducing nystagmus and a feeling of body rotation. In patients with left sided neglect moving objects toward the right can improve detection and cold-water caloric stimulation

might alter egocentric perceptual systems in a similar manner. When cold water is injected into the left ear, this person will reveal nystagmus of their eyes. Nystagmus of the eye has two parts. With left ear caloric stimulation there is an initial fast horizontal movement toward the right, and a slow movement back to the left. This movement to the left helps might help patients with neglect be aware of their left hemispace. Inducing optokinetic nystagmus may help patients with spatial neglect. There are now many other treatments that may be used, such as mirror therapy, transcranial magnetic stimulation, smooth pursuit eye movement training, saccadic eye movement therapy, direct current stimulation, eye patching therapy, and prism adaptation treatment.

Fortunately, there are now medications that can help to prevent strokes or reduce their severity. These medications help by treating hypertension, high levels of cholesterol, and reduce the possibility of blood clotting. In addition, if patients come to the hospital shortly after the onset of their symptoms, they can be given a medicine that helps break up clots and this can be followed up with a procedure that removes the clot. In addition, when people have strokes there are now treatments that can reduce the disability caused by strokes. For example, patients with neglect have been successfully treated with prism glasses. In patients with left sided unilateral spatial neglect, these glasses move the objects they are viewing toward their right side. Therefore, when they attempt to reach for a target they deviate their arm-hand to the right of this object. These patients are then trained to direct their hand to the target when they are still wearing these prism glasses. However, after practicing reaching. when these glasses are taken off, many of these patients no longer show the signs of neglect. Unfortunately, the effects of this treatment might only last for several days or weeks. In addition, many patients with this neurobehavioral disorder cannot obtain this treatment, and therefore additional research about how to prevent and treat these disorders is still needed.

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## Funding

In the mid-1980s, several Chairs of Departments of Neurology noted that there was a dramatic drop in the percent of neurologists being funded by grants from NIH. There were and are two leading neurological organizations, the American Academy of Neurology (AAN), and the American Neurological Association (ANA). When the officers of the AAN were informed about this drop, they wanted to form a committee to meet and learn what might be the cause of this reduction and how it might be remedied.

The AAN asked me to be their representative. Dr. Donald Silberberg who was Chair at the Department of Neurology at the University of Pennsylvania represented the ANA and Dr. William Landau Chair of Neurology at Washington University, represented the Society of Neurology University Professors. We met and decided that we need to better understand the possible reasons why there was this dramatic decrease in physician funding. We arranged a meeting with the Director of NINCDS

(the neurological diseases portion of the National Institute of Health) and other members of this division of NIH.

During our discussions, it was mentioned that there has been a reduction of the number of proposals submitted by physicians and the reason for this reduction appeared to be related to several factors. However, one of the members of our committee, stated that he thought one of the problems might be that when investigators are submitting proposals, unless they have preliminary data, it was unlikely for this proposal to be funded.

Hearing this made me somewhat angry, because almost all physicians in academic medical centers are time poor and in the absence of funding, their administrators will fill up their schedule seeing patients. Thus, it is rare that without research funding they would be able to get sufficient time to perform this preliminary research. Based on this problem, we suggested to the Chair of the NINCDS to develop a means whereby investigators can apply for one to two years of funding, to support their efforts to obtain preliminary data.

We were delighted to learn that the leaders at NIH did develop an “R21” for this purpose. Unfortunately, more recently, when one of my former Cognitive and Behavioral Neurology Fellows applied for an R21, it was not funded because this fellow did not provide preliminary data. Clearly the universities, and health centers should develop the means of being able to support “preliminary studies.” It is critical that we support young investigators and their new ideas.”

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## Peer Review

Several decades ago, I got a letter asking me to become a member of a study section at NIH. I was probably asked to do this because I recently had a grant proposal funded by NIH. As a clinician, who had several clinics each week and was the attending on our in-patient and consult services for several months each year, I barely had enough time to perform research. Despite having three children at home, I was working more than 60 hours per week. Fortunately, my wife was and is a great mother. But I was still time poor and therefore wanted to write back that I would be unable to be a member of this study section. However, there were not many behavioral neurologists or neuropsychologists on NIH study sections and people doing neuropsychological and behavioral neurology research had a difficult time obtaining research funding. Therefore, I felt that I had an obligation to join this study section and I agreed to serve on this study section.

This study section met three times a year and each meeting took two days. The administrator who was in charge of this study section, sent me about 14 research proposals to be either the primary or secondary reviewer. There was a neuropsychologist who was also on this same study section. Her name was Susan Corkin, and she was a Professor at MIT. She was the primary reviewer for all the proposals where I was the secondary reviewer and vice versa. I had not done anything to help train Susan Corkin or played any role in the selection of this woman, but she was one of the most brilliant neuropsychologists in the world. The remainder of the

members of the study section, came from two other specialties, neuropharmacology and neuropathology. There was a total of about 10 reviewers at this meeting and we all sat around a long table, with the chairperson at the head of the table. The chairperson of our study section told us that we would go around the table and each one of us would present one of the proposals where we are the primary reviewer, and this would be followed up by the review by the secondary reviewer.

The first reviewer would present their review. After they presented their review, other members of the committee were able to ask questions and make comments. The Chair would then ask the second reviewer to present their critique and again following this the other member of the committee could ask questions and make comments. After both reviewers answered these comments, the Chair asked the primary and secondary reviewer to make suggestions about how to rate this proposal using a Likert Scale where one was the highest score and ten was the lowest score.

I was pleased that Susan Corkin and I, for the most part, had similar evaluations. We suggested that four of the proposals we reviewed were excellent and should be given high scores. Five were good but needed some further work and the last five were poor and needed much work. After we discussed each of the proposals, all the members of the study section were then given a card to write down their vote, then to fold their card and to give it to the Chair. These scores were then averaged and based on these scores these proposals were given a percentile score. When I was on the study section, they were funding about the top 20 to 25% of these proposals.

About 3 or 4 months later I was again sent about 12 new proposals to review. In about one half of these proposals, I was the primary reviewer and the other half the secondary reviewer. At one of our American Academy of Neurology meetings, I listened to several Behavioral Neurologists discussing how difficult it is to get NIH funding. Therefore, when it was my turn to do my first review, before starting my review I said to the Chair, "Before I start my current reviews, I would like to learn the mean scores of the proposals I reviewed for our last meeting and which ones got funded."

The Chair said, "Ken, we do not do that."

I said, "Before presenting my reviews I would like to know this information."

The Chair replied, "No! We will not do that."

I said, "If you do not let us see the mean scores of those proposals that were funded and those that will not be funded, I will not present my reviews."

The Chair with a raised voice exclaimed, "Ken, you cannot do that!"

"Well, you can watch me walk out and take a taxi to the airport."

The Chair said, "Let's take a ten-minute break. Let me see if I can get the scores of the proposals where you were the primary or secondary reviewer."

The Chair came back in about 10 minutes and handed me a paper with the scores of all the proposals that I reviewed. None of the proposals that Susan Corkin and I reviewed were in the funded range. I was both disappointed and angry. After looking over the mean scores of these proposals, I decided to speak with members of the study section. I explained, "Dr. Corkin and I reviewed 14 proposals. We both felt that there were four excellent proposals that we recommended be given high scores, so they could be funded. When I just reviewed the scores, none of these were

scored in the fundable range. That means that despite the strongly positive comments about these proposals, many of you gave these proposals a low score, but I do not recall anyone expressing any concerns about the proposals that we thought were of high quality. I think we need to all agree that if you are going to score a proposal more than one point lower than recommended by the primary and secondary reviewers, the person who is going to score it lower should explain their concerns about this proposal.”

The Chair asked if anyone wanted to discuss this further, but no one raised their hand, and all voted in favor of this scoring method. After this vote, I did discuss the current proposals I reviewed. After my discussion of each proposal, I provided the score I was planning to give this proposal and asked if other members of our study section wanted to discuss the proposal or disagreed with my or Dr. Corkin’s proposed scores.

The next meeting of our study section, the Chair gave me a copy of the scores for our last meeting, and for the most part these scores were in concert with our recommendations. Several years after I completed my service on the study section, I learned that NIH formally adopted a similar procedure for all study sections.

Although I was happy to learn this news, based on other proposals we and our colleagues sent to either NIH or the Veterans Affairs Research Service, we became aware of another major problem, peer review. As mentioned, I am a behavioral neurologist and I have been fortunate to be funded for my research for more than 40 years. Recently, we sent in a proposal for funding. However, this proposal did not get funded. When we looked at the reviews, we found that there were three reviewers, but none of them were a Cognitive and Behavioral Neurologist or a Neuropsychologist. The reason we looked this up was because the reviewers repeatedly wrote that the research projects that we are proposing was not new and had been previously performed. However, they provided no examples, and before we resubmitted this proposal, we carefully searched Pubmed and Google Scholar to learn if these studies had been performed. We found no evidence that these studies had been previously performed. There were no comments about our a-priori hypotheses, the means and methods by which these hypotheses would be tested, and the means by which this data would be analyzed. It was clear that these reviewers were not familiar with the type of research we proposed.

I suspect that in many study sections, when a member of this study section is asked to review a proposal, even if they are not truly a peer with expertise in this proposal’s domain, they will still agree to review this proposal. When a reviewer of an article submitted to a journal, or a proposal submitted to NIH or the VA, does not have expertise in this domain, but likes what they read and accepts an article or provides a high grade for the proposal, and it turns out that this work is not original or of good quality, that reviewer will be strongly criticized. However, if this person rejects a new and highly creative proposal, it is rare that this reviewer will be criticized. Thus, for a person who is not an authentic peer, rejection is safer than acceptance. Therefore, the Chair of study sections should, by some means, determine if the reviewers they select are truly peers. There are several means by which this might be done. For example, if the principal investigator (PI) is a neurologist, a

board-certified neurologist should be a reviewer. In addition, there are now many subspecialties in neurology, and the reviewer probably should have completed a fellowship in the same specialty as the investigators who wrote this proposal. Furthermore, there are specialty boards and being certified in the same specialty as the authors of the proposal may be a requirement. Finally, it should be determined if this reviewer has written and published papers in this domain, because only true peers should perform peer review.

There may be additional problem, for example, the reviewer's personality. I know some excellent clinicians and investigators who by nature are very critical, not only of other people's work, but even their own. Thus, these reviewers, when even reviewing excellent proposals may be hypercritical and give lower scores than other reviewers might give. I do not know how to correct this problem. Perhaps, the scores they have suggested could be averaged and then if the average is significantly below the scores recommend by other reviewers a correction can be made to their scores.

## Whispers of Nature

Throughout our lives we see many new things. In medicine, seeing something new may provide a clue to something very important. Some of the great research discoveries in medicine were made as a result of a highly creative person developing a hypothesis, and then testing this hypothesis. However, the discovery of penicillin, the first antibiotic and one of the most important advances in medicine, was made by Alexander Fleming, who was a Scottish physician, and microbiologist. Fleming did not cover some dishes that were growing bacteria, and also left the windows in his lab open. While he was not in his lab some mold flew in through the open window, landed on a plate with the bacteria and killed the bacterial in the area that it landed. It was Fleming's prepared mind that allowed him to detect this whisper of nature and understand its great importance.

The many diseases that I see as neurologist were first reported by physicians who saw a whisper of nature. For example, patients with strokes of their left hemisphere often develop a language disorder. Franz Josef Gall (1758–1828) was a neuroanatomist, physiologist, who made some important theories of the localization of mental functions in the brain. Although, he is primarily known for the pseudoscience of phrenology, he made two important hypotheses, that different areas of the brain have different functions and that the better developed this anatomic area, the better will be the performance that depends on that area. Gall believed that speech was mediated by the frontal lobes. There was strong opposition to his localization and magnitudes hypotheses. For example, the Roman Catholic Church considered his theory as contrary to religion. In 1825 Bouillard published a paper where he wrote that clinical evidence supports Gall's frontal speech hypothesis, namely that articulate language is mediated by human's frontal lobes. Earnest Auburtin who was Bouillaud's student also promoted the concept that the frontal lobes were the organ of articulation. Auburtin offered a cash award to any person who could demonstrate a person with the loss of speech from a brain injury who did not have damage to



their frontal lobe. However, it was Paul Broca, with a case report about Leborgne that appeared to support Gall's hypothesis. Leborgne was a patient admitted to Broca's service because he had a gangrenous infection in his right lower extremity. He had lost his ability to produce fluent speech 21 years prior to be Broca's patient. Because "tan" was the only word he could speak, Leborgne was often called "Tan." About 10 years after he lost his speech he developed right arm weakness, and then several years later right leg weakness. Whereas Leborne's speech was non-fluent, he was able to comprehend other people's speech. Broca, who had heard Auburtin speak in 1861 about Gall and Bouillaud's hypothesis of the frontal lobes' role in speech production, invited Auburtin to the hospital to see Leborgne. After seeing this patient with Broca, Auburtin stated that this patient's loss of speech must have been caused by damage to one of his frontal lobes. Leborgne died from the gangrenous cellulitis of the right leg. Leborgne's brain was removed and revealed a lesion that included the anterior portion of the left temporal lobe, the anterior portion of the parietal lobe, as well as the inferior portion of the frontal lobe. Paul Broca thought that the center of the lesion, in the left inferior frontal lobe, including the pars opercularis and pars triangularis, was site that caused his aphasia and he published this case report. This paper was a major advance in neurology. It was the first report attempting to understand the biological basis of aphasia. Broca's second major report was about eight patients who had aphasia and all 8 of these patients had left hemisphere lesions, which Broca noted would have been unlikely to have occurred by chance. Broca's papers supported Gall's postulate of modularity.

One of Gall's postulates was in the brain, that bigger is better. According to portions of the left Broca's area are larger than the homologous region on the right. This observation appears to support the postulate of Gall...that bigger is better.

In my neurology clinic one of the most common disorders, I see are patients with Alzheimer's disease. This disorder was first described Alois Alzheimer in 1906. He evaluated a woman named Auguste D. This patient had severe memory loss, was suspicious about activities performed by members of her family and had other evidence of progressive cognitive decline. Auguste D died, and Alzheimer examined her brain. He found that her brain had dramatic shrinkage (atrophy) and he also found that there were abnormal deposits in the brain around nerve cells (amyloid) and the neurons had what appeared to be fibrillary tangles.

There are many other examples of the discovery of diseases and treatments based on a clinical evaluation. I even had the opportunity to describe a new disease and several new disorders. For example, I saw a man in clinic who liked to play golf. However, whenever he stood still, his legs started to rapidly shake. If he started walking this shaking would go away and this shaking was also not there when he was sitting. The main reason it bothered him, is than when he was ready to swing at the golf ball this shaking came on and at times, he felt like he would lose his balance. Then in a couple of weeks I saw two other patients who had a similar problem. Fortunately, I also found a medication that reduced the severity of these symptoms. I wrote a paper about this disorder and sent it to Archives of Neurology. I called this disorder "orthostatic tremor" and this now a well-recognized neurological disorder.



Unfortunately, the cause is not entirely known and although there are treatments, there is yet no cure.

While case reports have made a huge contribution to neurology, as well as other medical specialties, there are now several factors that might reduce this important source of information. Several years ago, one of the editors of the major neurology journal wrote an editorial that his journal would no longer accept case reports and reports had to be population studies. This neurologist is no longer the editor of this journal, and now this journal will occasionally publish case reports. However, in general, currently only a few case reports are published in the major journals. Fortunately, there are now journals, like Neurocase that do publishing case reports, but the number of people who read these journals is small.

There is another important reason for a reduction of case reports, and it is relative value units or RVUs. Typically, now even in academic medical centers, the administrators set limits for the time allowed for a physician to evaluate a patient. Although the time allotted is most often adequate to complete a history, physical examination, a brief conversation with the patients and writing notes, the time allotted is often not sufficient for fully discussing these patients with the residents and students, and often this time limit does not allow a detailed evaluation of these patient's disorder. For example, we saw a patient whose major complaint was difficulty with writing. When performing a neurological examination, part of the standard examination is examining mental status. A loss of the ability to write is called "agraphia" and agraphia is often associated with aphasia, a disorder of speech and language. When obtaining a history, the physician can tell if the patient has a severe aphasic (language-speech) deficit with problems understanding the physician's questions or telling the physician why he or she came to see the doctor. Although this patient did not appear to have any major problem with understanding speech or speaking, there are patients with aphasia who have problems with repetition and/or naming. To test repetition, we just ask patients to repeat, "No ifs ands or buts" and having them repeat this sentence is a good test for repetition. This patient repeated this sentence well. To test naming, we often ask patients to name many objects and therefore, we give them the Boston Naming Test. There is now a shorter version of this test but when we gave this test to this patient there were 60 different pictures that patients are asked to name. This patient was able name well and thus did not appear to have an aphasic language deficit. Patients with agraphia often have trouble with reading, alexia. When we tested his reading, he again did well. The next step was to have him spell words that are regular, where the phonemes (letter sounds) that make up the spoken words match the spelling (e.g., dog) and irregular words where the phonemes in the spoken word do not match the letters in written word (e.g., yacht). He also did well on these two tasks. When we had him write, we saw that the letters he was making were not made properly, and he appeared to not know the movements needed to make letters. A loss of the ability to make correct movements is called "apraxia," and when this apraxia interferes with writing, the medical term is "apraxic agraphia." Patients with apraxic agraphia often have problems with correctly programming other movements such as those needed to use certain tool and instruments. The most sensitive test is asking these patients to pantomime the use of tools

such as scissors to cut paper or a knife to slice turkey. He did all these correctly. Therefore, it appeared that his apraxia agraphia was just for writing. To test this hypothesis, we got a typewriter and asked him to type out several words and he did this flawlessly. We, therefore, not only diagnosed him as having an apraxia agraphia but also let him discover a means by which he could write. We later found he had a small stroke in his left parietal lobe. This testing was done by a behavioral neurology fellow and me. Therefore, during this testing there were also discussions about why we were doing this testing and what the result meant.

Examining this patient allowed us to hear a whisper of nature, telling us that when we learn to write we learn to spatial sequence of movements needed to make letters and how to program our hand and arms to make these movements. We also found out where in the brain these programs are likely to be stored and this stored knowledge is independent of knowing how to speak, understand speech, read, and use our hands and arms to perform other skilled activities.

I was taught to perform this type of analyses by my two major mentors Drs. Norman Geschwind and Denny-Brown. Although both leaders were wonderful teachers, in almost all academic programs residents were taught to use this method of patient evaluation. Thus, in many respects, each patient's evaluation is a research project.

When I was a resident and even when I first joined the faculty at the University of Florida there a limited number of tests that could be performed to learn the location of brain damage and the cause of this damage. EEG was available and would help us diagnose seizures as well as where in the brain these seizures were coming from. With injury to the brain there is often slowing in the area injured. However, other information about location and cause of other diseases was limited. Then several years after I moved to Gainesville, computer tomography (CT) became available, and several years later magnetic resonance imaging (MRI). The residents often felt that this imaging was the critical diagnostic test. Therefore, these imaging methods reduced our resident's and student's need to carefully investigate their patient's deficits to determine the location of their brain injury as well as the cause of the brain injury. Thus, many neurologists now think that there is less of a need to carefully investigate patients and to use deductive reasoning to determine the localization and cause of neurological diseases. Although these new tests have clearly improved patient care, we now are often not teaching our trainees methods of inductive and deductive reasoning.

When I was applying for an internship, I applied to some of the programs at Boston City Hospital. The Boston City Hospital also called BCH in the 1960s was one of the leading hospitals for patient care, training and research. I joined the residents and attending physician while they were making rounds on the newly admitted patients. After one of the medicine interns presented a patient who was admitted for being in a semi-comatose state, the attending asked the intern the disorders that he thought might be causing this patient's decreased level of consciousness. The intern listed several diseases including hypothyroidism, and uremic encephalopathy. The attending asked, "Did you rule out a mass lesion?" The intern said, "The best we could. We got skull x-rays. He has a calcified pineal and it was in the middle of his brain." The attending said, "That's good. The pineal is in the center of the

brain and if there was a tumor or blood clot, it would likely to be shifted.” The intern also said, “He also did not have a dilated pupil” and the attending said, “Good! His brain is not herniating.”

The attending then said, please tell me what tests you have had ordered and why you ordered them. In addition to naming tests such as blood urea nitrogen, for uremia caused by kidney failure, the intern mentioned, bicarbonate. The attending asked, “Why did you order bicarbonate?” The intern looked puzzled and said, “My resident asked me to get this test.” The attending physician turned to the resident and asked, “Why.”

The resident said, “Well, this man, had breasts that we could feel. His palms were very red (palmar erythema), and his chest had spider angiomas. I therefore, wanted to rule out hepatic encephalopathy.” The attending smiled and said, “Many patients with liver cirrhosis, who develop hepatic coma, do not have elevated liver enzymes, but they do have a low bicarbonate because they are hyperventilating. Good job! But there is something important sign you did not tell me about.” The resident looked up to the ceiling then looked at the attending and said, “Oh yes, he did have a large spleen, but we did not see any myoclonus.” The attending said, “Great job! Did you order other blood tests to test this possible diagnosis? The intern said, “Yes, his albumin is low and prothrombin time elevated.” “Yes!” the attending said, “He clearly has hepatic encephalopathy.”

As a student I was pleased to attend these rounds, because it was a great example of how physicians should think about what is causing the patients disease, positing the possible diseases that may cause these signs and symptoms and getting the tests that can either confirm or disconfirm the presence of their patient’s disease.

Unfortunately, today many of our residents are not being taught to perform these detailed types of analyses. There are several possible reasons. One of the reasons may be the use of relative value units (RVUs). To perform such an analysis, the physician needs to perform a very complete history of present illness, and past medical history. In addition, a very detailed general physical and neurological examination needs to be performed. All these processes take time, and now administrators limit clinicians time, so they can make more money for the institution, and administrators.

The are other reasons that there have been many advances made in diagnostic tests. Before the introduction of imaging methods, such as computer tomography and magnetic resonance imaging, the localization of a brain injury and the disease causing this damage was almost entirely dependent upon the patient’s history, the findings on the general physical and neurological examination and then the consolidation of all this this information. For example, if we saw a patient who had trouble speaking, we would learn if this trouble came on suddenly or slowly and what other problems were associated with this trouble speaking. For example, was there weakness of the face or limb, trouble seeing, numbness, etc. When we performed a mental status examination, we would examine the patient’s speech fluency (fluent versus non-fluent) and listen for errors, such as using incorrect words and incorrect sounds (phonemes) in words, speech comprehension, repeating words and sentences, naming objects and actions, as well as testing reading and writing. For example, if the patient was fluent but made phonological errors when saying words, could comprehend speech, but had trouble repeating and naming,

he would have a syndrome called “conduction aphasia.” This disorder is most often caused by injury to the dominant hemisphere’s inferior parietal lobe. This area of the brain is far away from the motor cortex and therefore, the absence of weakness on one side of the body would provide further evidence to this localization. In addition, the presence of reading and writing disorders would provide additional evidence for the location of this lesion. Very often lesions in this region of the brain also cause trouble performing arithmetic (e.g., adding, subtracting, multiplying and dividing), being able to name fingers, and knowing right from left. The testing for these disorders would also be important and the presence of these disorders will provide even greater evidence for localization to the dominant inferior parietal area. This disorder can be caused by several disorders, including a stroke and a form of Alzheimer’s disease. If the history provided by the patient and their family informed the clinicians that this disorder came on suddenly, the cause, most likely, would be a stroke; however, if it was slowly progressive this disorder can be a form of Alzheimer’s disease and is called logopenic primary progressive aphasia. In contrast to this detailed evaluation, now all the neurology residents would have to do is order an MRI of the brain, and the report would most often tell this resident the localization and the likely cause. Therefore, now with these advances in diagnostic procedures, a less detailed examination has to be done, and less thinking has to be performed by our residents who are in training. However, the development of creativity ability is heavily dependent on learning how to think about problems.

Even with excellent brain imaging technology, almost every week when I am the attending on our inpatient service, I disagree with the radiologist’s report. For example, we evaluated a patient who had on examination an impairment in naming and comprehending some words. The imaging was read as showing “atrophy compatible with aging.” This patient disorder was progressive, and this combination of symptoms-signs suggested a disorder called “semantic dementia.” Typically, patients with this disorder have left anterior temporal lobe atrophy. When I viewed this patient’s magnetic resonance imaging it was clear that there was left anterior temporal lobe atrophy.

These experiences brought up several thoughts. The first is that whereas computer tomography and magnetic resonance imaging have been a great contribution to the care of patients with neurological diseases, a detailed neurological examination and knowledge about localization helps with the interpretation of imaging (e.g., knowing what to look for and where to look. During their training to be neuroradiologists these trainees do not spend any time on the neurology or neurosurgery services. Their interpretation of images may be greatly improved if neuro-radiologists, during their training spent some time on the clinical neurology and neurosurgery services.

## **Institutional Review Board (IRB)**

There are many stories of about how medical research was performed in a manner that was sinful. Like many of the other stories about NAZI Germany, there were several German physicians who performed terrible unethical research, even using children

as subjects. And even in the United States there were also several studies where physicians engaged in unethical research. For example, there is this well-known story about the United States Public Health Service and the Centers for Disease Control and Prevention wanting to learn the natural history of untreated syphilis. The study was carried out primarily at Tuskegee University which was a historically black college in Alabama. The subjects of the study were about 600 poor African American sharecroppers. The men who participated in this study were promised free medical care. About two thirds of the men enrolled in this study had syphilis, and about one third were not infected. Despite untreated syphilis being a terribly disabling disease (e.g., dementia, blindness, deafness, a loss of the ability to walk and death), as well as being contagious, the men who had syphilis were never informed of their diagnosis. Furthermore, at the time this study was being performed, it had been shown that antibiotics such as penicillin could cure this infection. However, these men, who were infected with syphilis, did not receive treatment. Many of these men died. In addition, 40 wives of these men became infected and there were 19 children who suffered with congenital syphilis. The study continued until 1972, when a leak to the press finally resulted in this study being stopped. After knowledge of this study became public, the United States Department of Health and Human Services, Office for Human Research Protections was established, and regulations were developed that require institutions that perform research to have institutional review boards (IRBs) for the protection of human subjects.

Now before research can be performed with participants at medical centers, a protocol has to be submitted to the institution review board. This protocol must provide the hypothesis being tested, the participants who will be studied, the criteria for inclusion in the study as an experimental or a control participant, how they will be recruited for the study and how they will be studied, including the procedures they will undergo and the measurements taken, how many experimental and control participants will be included, the possible positive results as well as the possible negative results and risks.

Although protecting research participants is very important, there are some problems with IRBs. For example, we had a post-doctoral neurology fellow who came from another country and wanted to do research with us. Within the first few weeks that he was here, along with members of our faculty, he developed a wonderful research protocol, that had no serious risks to the participants. The IRB returned his protocol a couple of times, for corrections and explanations. He remained here for a year and did become involved in some other research projects. However, his protocol was finally approved by the IRB two weeks before leaving America to return home.

Sometimes, there are minor clerical errors such as a consent form not being dated, or missing the investigator's signature, and although the participant and investigator have spent time and energy on this experimental testing, the IRB often requires that investigators not include these participants. Is this throwing out the baby with the bathwater.

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In 1963 when I graduated from medical school there were very few neurological diseases that could be treated and many of my teachers asked, “Why do you want to specialize in neurology? You cannot help many people with neurological diseases.” Although I usually responded by saying, “Neurology really interests me,” in medical school I learned that in order to help people who are sick, we first need to learn to diagnose why they are sick and know how treat and manage people with this illness. That is why for more than 50 years I have been and still am an academic neurologist, who does research, as well as patient care and teaches.

Studied hundreds of older adults, who early in life had been highly creative. They found that those people, who are at a younger age were “intellectually gifted” had less favorable psychological well-being at the age eighty. It has been noted that with aging even Charles Darwin became depressed about his failure to continue his creativity.

Bronowski (1972) in his book “The Ascent of Man” defined creativity as “the ability to find unity in what appears to be diversity” (e.g., “finding the thread that unites.”) In creative works of art, music and literature, there is often a great diversity of elements; however, these elements are joined together and unified. Great scientists also develop theories that unite. Perhaps the most famous is Einstein’s uniting matter and energy ( $E = MC^2$ ). I have therefore defined creativity as “the new discovery or understanding, development, and expression of orderly relationships [1].” Simonton [2] wrote that whereas major discoveries steadily increase when people are in their twenties and thirties, it then declines.

Creativity is a stepwise cognitive process organized in stages. Preparation is the first stage. This is the stage where a person learns the knowledge and skills needed to be creative. This preparation stage depends on several major factors, including being educated and the brain’s ability to store, process, and use this knowledge (intelligence).

According to Helmholtz and Wallas, the next stage is when a person subconsciously searches for an answer to a problem. They called this stage “incubation.”

This stage is followed by “illumination.” This is the stage when person discovers the answer (“ah-ha” or “Eureka”).

Not all great creative discoveries, however, require incubation. Many great discoveries are made by viewing a whisper of nature. For example, Fleming’s observation that a mold that flew through his open window, on to a bacterial culture, killed these bacteria. Thus, we [3] proposed combining the incubation and illumination stages into a stage we call the “innovation” stage.

The last step in the creative process is the production of this creative work.

The information that can be stored in the human brain is almost infinite. The different forms of information and knowledge stored in the brain, are often stored in different sections of the brain. This is called modularity. Many of our brain’s modules are interconnect. For example, when we see an object, the inferior portions of the posterior temporal and occipital lobes that store the images of objects and faces allows us to recognize these objects. This visual object knowledge module has connections with the left perisylvian cortex. This perisylvian cortex contains the modules that allow us to know the sequence of phonemes that compose words and their meaning, as well as other modules that allow us to program our speech apparatus to produce words.

Our brains are divided into a and right hemisphere with the corpus callosum connecting these two hemispheres. Each hemisphere has four major lobes, the frontal, parietal, temporal and occipital. The temporal, parietal and occipital lobes receive sensory information. The auditory information coming to temporal lobes, the visual information to the occipital lobes and touch to the front portion of the parietal lobes. Each of these primary sensory areas process incoming information, such as shape, color and location and then sends this information to other adjacent areas of the brain called sensory association areas. These specific sensory association areas store sensory information. For example, what a dog looks like, how its barking sounds and what the dog’s fur feels like. All of these sensory association areas project to multimodal association areas, such as the inferior parietal lobe, where the knowledge from these sensory association areas is combined, to develop semantic knowledge.

Intelligence is often defined as the ability to acquire, store and use knowledge. The Miriam-Webster dictionary defines “genius” as “a person endowed with extraordinary mental superiority; especially a person with a very high IQ.” In a famous study, Lewis Terman, a psychologist at Stanford University, had children’s IQ tested and followed those children who had exceptional performance on this IQs test. He found that whereas some of these “geniuses” were successful, most of his geniuses turned out to be no more creative than those with average IQs. None of these “geniuses” were awarded a Nobel Prize. However, two people not included in Terman’s IQ genius group, because their IQ scores were too low, were William Shockley, who went on to invent the transistor and Luis Walter Alvarez who was responsible for inventing three important radar systems. Barron and Harrington [4], as well as other investigators, found that people need to be sufficiently intelligent to gain the knowledge needed to be creative, but once this threshold is reached, intelligence and creativity are not directly related.



The intelligence test contains two types of questions, one that tests knowledge and the other that requires thinking. For example, providing definitions of words is a test of knowledge and what two words have in common (e.g., How are a tree and a rose similar?) is a test of thinking. Cattell [5] posited that “fluid intelligence,” our ability to solve problems, is more related to the innovation portion of creativity.

When in 1970 I first joined the Division of Neurology, in the Department of Medicine, at the University of Florida, Melvin Greer MD was our division Chairperson. When I was interviewed, he told me that I would be asked to perform clinical services for one half of the year and research the other half. Back then, promotion and tenure were primarily based on research productivity. I was fortunate that I was given all this time, because after three years I was promoted to an Associate Professor and two years later to a full Professor. In addition, before you can obtain a research grant you must show research productivity, and this enabled me to obtain research funding.

In 1976 at the University of Florida I started a Behavior and Cognitive Neurology Post-Residency Fellowship program. We have had about 80 fellows and research associates, who were trained in our program. Most of these fellows, when they completed their training became academic physicians at academic medical centers. Most of these former fellows, in addition to being clinicians and teachers, perform research. We are still training fellows, however, most recently although our fellows have been offered positions at major universities, these neurology departments want them to perform one hundred percent, clinical activity if they did not have research grant funding. In a paper, noted that whereas in 98% of programs they measured clinical activity; however, in only 61% of neurology programs did they measure research productivity. I suspect if they now repeated this study, they would find that even fewer programs use research productivity and when they do, the most important factor is usually how much grant money are they able to bring into their department.

In our society, the most important reward to many people is making money. Unfortunately, in many forms of creativity, the person who pursues creativity does not do financially as well as full time clinicians. Although there are some creative people who do become wealthy, in general in literature, music, visual arts and even in science and medicine, creative work leads to less monetary rewards than other pursuits. Although my family and I are very comfortable, how much wealthier would I be if instead of seeing patients with neurological diseases, and performing neurological research, I instead removed cataracts from peoples' eyes.

There are many creative people, especially in the ‘arts’ such as composer-musicians, authors, and fine artists, who abuse drugs such as cocaine. Eisenman et al. [6] performed a study that compared the creativity of students who had used drugs with those that had not used drugs. They found that the students who used drugs tended to be more creative. Although one might conclude from this study that drugs enhance creativity, it appears that taking these drugs does not enhance creativity [7]. One the most famous movie directors, Cecil B. DeMille said, “Creativity is a drug I cannot live without.” I believe he was suggesting that the same brain

mechanisms that produce a “high” with drug use, might also be responsible for the feeling of delight and the sense of joyful bliss during the “Eureka” experience.

Olds and Milner [8], wanted to learn about the brain mechanism that might account for this “Eureka” experience. They inserted electrodes in rats, deep into the lower middle region of the frontal lobes, near the nucleus accumbens. When these rats pressed a lever, these electrodes activated this region of the brain and this stimulation was so rewarding to the rats that they continued to press this lever and not eat or drink, until they were exhausted.

Our brain normally stimulates this nucleus accumbens by giving off a chemical neurotransmitter called levodopa. This neurotransmitter is sent up to the nucleus accumbens from nerve cells that have their body in the brain stem. Functional imaging studies have shown that this system becomes activated when people receive a reward. Novel stimuli also activate this system [9]. These observations suggest that like drugs, creativity can excite this reward network and that performing research could be considered a positive form of addiction. Now in many medical schools the students are given time to participate in research, but this often comes at a time early in medical school, before they take their clinical rotations and therefore, rather than develop their own a priori hypothesis, they join a team of investigators who are already working on a project.

Originality is a critical element of creativity. Therefore, after preparation one of the first steps in the creative-innovative process is disengagement. Before a person can develop new ideas, theories, concepts and products, they must first disengage from previously and current theories, concepts, and beliefs. They must produce products that are different from those previously produced. Thus, almost every important creative act is initiated with disengagement. Disengagement is a form of rejection, breaking off, separation or renunciation. There are some forms of disengagement that can be socially harmful. One of the best examples, is the story of Galileo. In 1543, Nicolaus Copernicus published a model where instead of the Earth being in center of the universe, it was the sun and the planets including Earth that rotated around a motionless sun. Whereas Copernicus could not test his hypothesis, Galileo, who invented the telescope, was able to provide support for sun-centered hypothesis. Although this was a great scientific advance, Galileo was accused of heresy by the Catholic Church and was forced to recant his findings and to spend the remainder of his life under arrest. Finally, in 1992, Pope John Paul II, acknowledged that what the church did to Galileo was an error. Some teachers in medical school, when discussing a patient or giving a lecture, do not provide students with an opportunity to discuss alternative hypotheses. This is unfortunate because allowing and encouraging students and residents to provide alternate hypothesis is an important lesson in developing a creative physician.

There is a test called the Stroop Test where participants are presented with the printed names of different colors. The ink with which these words are printed, however, are often a different color than the printed word. These participants are asked to rapidly as possible to name the color of the ink of each word and not read the word. People with damage to their frontal lobes often read the color words rather than naming the color of the print, a disorder of disengagement. Like many other

functions performed by the brain, growth is related to practice and to educate future physicians, they should be taught to disengage and develop new hypothesis.

Of all the portions of the human cortex, the frontal lobes appear to receive the most connections from other parts of the brain that perform different functions. Overall, the frontal lobes are thought to primarily mediate executive functions. Before an executive can make good decisions and take appropriate actions, the executive must also receive a variety of important information. Executives know that when an action that is being performed by their company is not successful, they must stop this activity and disengage. This is an important function of our frontal lobes. Therefore, medical students and residents should be encouraged to use disengagement.

After disengagement, the next step in the creative process is divergent thinking. For example, after Copernicus disengaged from the hypothesis that the Earth is the center of the universe, he probably asked himself, "What is in the center of the Universe? Could it be Mars or Venus, or other planets or perhaps the sun?" Thinking of alternative solutions is called "divergent thinking" and like disengagement, divergent thinking is a critical element of creativity and is also important when considering differential diagnoses of a patient.

William James [10] suggested that creativity requires an "... unheard of combination of elements. Suggested that creative ideas result from the combination of two or more ideas that have been previously isolated or as mentioned, creativity is "finding the thread that unites."

As mentioned, different portions of the brain store different forms of information than do other portions of the brain. In addition, different areas of the brain perform different forms of cognitive processing. Creativity often requires that there be communications between these modules. One of the best examples of this is a study by Lewis [11]. In almost all right-handed people, it is the left hemisphere that performs the processing of language, and the right hemisphere is dominant for performing visuospatial tasks. Lewis [11] administered the Ink Blot (Rorschach) test to eight patients with epilepsy. They were asked to look at these inkblots and to provide a creative name for each. These patients were going to have their corpus callosum cut (cerebral commissurotomy) to stop the spread of their epileptic seizures from one hemisphere to the other. After they had their corpus callosum cut, they were again tested using the same method and Lewis found that there was a reduction in their creativity, most likely because this commissurotomy cut the thread (cable) that unites left hemisphere mediated language and global-visuospatial perception.

Even within each hemisphere, there are multiple area of the brain that store different information and perform different cognitive processes and the interactions between these cognitive networks is often important in creative innovation. Connectivity of brain networks can in part be assessed by examining electroencephalography (EEG). When there is coherence in electrical activity between different areas of the brain, it suggests that these different networks are interacting. Study of normal participants when performing creative thinking revealed an increase of

anatomically distributed coherence of EEG oscillations suggesting that during creative thinking these participants' brains are "finding the thread that unites."

In the mid-nineteenth century, it was known that the chemical benzene had six carbon atoms; however, the structure of benzene was not known. August Kekulé was one of leading theoretic chemists in Europe. He wanted to learn the structure of benzene. On a bus ride home, he had a daydream of a snake chasing its tail, making a ring and this daydream provided Kekulé with the idea that benzene has a ring-like structure.

Raymon y Cajal, a Nobel Prize winner, who developed the nerve theory in 1897, wrote a wonderful book named "Advice for a Young Investigator." In this book, he wrote, "If a solution fails to appear after all of this, and yet we feel success is just around the corner, try resting for a while. Several weeks of relaxation and quiet in the countryside brings calmness and clarity of the mind. Like the early morning frost, this intellectual refreshment withers the parasitic and nasty vegetation that smothers the good seed. Bursting forth at last is the flower of truth, whose calyx usually opens after a long and profound sleep at dawn-in those placid hours of the morning that Goethe and so many others consider especially favorable for discovery."

In accordance with Raymon y Cajal's theory, several of the greatest creative scientific advances came about while these scientists were in a restful psychological state. For example, Einstein's theory of relativity came when he was alone in his office during the evening. Mendel's hereditary theory was developed while working in his garden., Darwin's was on a cruise when he developed his theory of evolution. Newton's development of calculus and his theory of gravity came when he left Cambridge University, because of the plague, and went to his mother's farm and sat under the apple tree. All these great advances occurred during the times these creative people were in a relaxed state.

There are several different physiologic states of the brain during sleep. Drago and her colleagues wanted to learn the relationship between sleep and creativity. Sleep has several different stages, including rapid eye movement sleep, and non-rapid eye movement sleep or slow wave sleep. Non-rapid eye movement sleep has been divided into four states, based on the degree of slowing of the participant's electroencephalogram (EEG) slow-wave activity. Drago and coworkers studied healthy young adults by performing electroencephalogram recording on three consecutive nights. These participants were then assessed with a test that measured their creativity. They found that creativity positively correlated with several stages of the non-rapid eye movement sleep and negatively correlated with the extent of rapid eye movement sleep. Whereas the entire reasons that non-rapid eye movement sleep is associated with higher levels of creativity are not fully known. One possibility is that non-rapid eye movement sleep is associated with low levels of cortical arousal, and low cortical arousal may enhance the ability of people to access more remote associations and find new associations, a critical factor for creativity.

It is not fully known why being in a relaxed state enhances creativity. Fear, anxiety and stress are associated with increased arousal of our brains and during high levels of arousal we primarily focus our attention on external stimuli rather than internal stimuli, such as trying to solve a problem. Creativity often requires "going

inside our own mind,” and in addition, creativity often requires global rather than focal attention.

Norepinephrine has an important role in modulating our brain’s arousal and therefore, finding the “the thread that unites” while resting or relaxing might be related to alterations in the level of brain norepinephrine. Mednick [12] developed The Remote Associates Test. This test assesses people’s ability to find the thread that unites three words. For example, the participant being tested is given a series of three common words, such as “American, blue, and goat.” These words at first appear to be unrelated, however the participant is asked name a fourth word that is related to these three words (e.g., cheese). Martindale & Greenough [13] reported that when under stress during this test, peoples’ performance deteriorates. One reason for this change is that stress increases brain norepinephrine and brain norepinephrine reduce the brain’s intrinsic activity, such as thinking, imagining and reasoning as well as increasing the processing of external stimuli. Evidence to support this hypothesis, comes from a study by Beversdorf and his coworkers [14] who gave healthy people anagrams (words with the letters in different positions). We then asked these participants to find the word that these letters could spell if their positions-locations were changed. When we gave these people propranolol, a medicine that blocks the effects of norepinephrine on the brain, these participants performed much better at finding the word. This result suggests that the propranolol blocked norepinephrine, thereby allowing the brain to have better connectivity and find the word that unites these letters.

Unfortunately, many of our medical students, residents and fellows are often under stress, and are often rushed to see more patients. The more patients they see, the better is their evaluation by their supervisors. In some respects, evaluation of a patient is like performing an experiment. Stress might not only reduce creativity, but also the ability to reason about patients who have complicated disorders.

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Several years ago, I received a copy of a very disturbing email, which was probably sent to me by error. Our department was trying to recruit a new neurologist to join our faculty. I perform research on dementia and cognitive disorders. A wonderful woman, who lost her husband from a dementing disease, gave a contribution to our university for me to have an endowed chair and be able to do more research in dementia and other cognitive disorders. This email was sent by a neurologist in our department who was trying to recruit a new neurologist to join our department. The email said that since I was in my late seventies, this endowed chair would soon be available for them. I think that the person they were trying to recruit with this offer knows me and declined this offer. However, shortly after I saw this email, I received a letter from the Dean of our medical school (who thankfully is now gone). The letter stated that my position would be terminated.

The IRB monitors reviewed hundreds of our participant's letters of agreement to do research and they found a few errors such as the person doing the testing forgot to sign this agreement and one patient scored one point below the threshold for acceptance. After several months we were able to satisfy the IRB. I wrote back to the dean, and I told him that all these problems have been successfully addressed. He wrote me back that he has not changed his mind. Fortunately, I had a part time position at our Veteran's Medical Center. I wrote again to this dean that our research has continued to be very productive and that along with my colleagues, we have written more research papers than almost any other person in our medical school. I also explained that we would probably have a new research grant funded by the National Institutes of Health. This research is to learn how we might be able to slow or even reverse the memory loss associated with dementia. I also bragged about my clinical and educational evaluations. This dean wrote back to me that all this information about my accomplishments did not change his mind. It appeared that his decision was based on something about which he never told me about. After terminating my active faculty appointment at the University of Florida, they did appoint me as a Distinguished Professor Emeritus.

My endowed chair was provided by a woman who lost her husband who had dementia. Even though this woman made this donation to support research in dementia, but after my removal from the active faculty, our department gave this endowed chair to a wonderful clinician, whose major interest is not in memory and cognitive disorders. When I called to learn why this was done, I was told that when she donated this money, she did not write that this money was to be used for a faculty member who does research with patients who have memory loss or dementia.

As mentioned, fortunately, I have a position at the North Florida/South Georgia Veterans Affairs Health Center, and despite being 84 years old, I continue to do research. If our former dean and vice president for health affairs searched Pubmed by typing in my name, they would have seen that I am continuing to author and co-author many research papers in peer reviewed journals and probably more than most members of our department. I am also still seeing patients and teaching medical students, resident physicians and fellows. I am also planning to continue these activities, if I can. If they search Google Scholar, which cites the number of times a research paper is cited, they will notice that since the age of 50 there has been no major decline. If they searched the history of artists, writers, and composers they would find at there have been and are many people who remain creative into late age.

With aging, there is a growth of knowledge, and this enables many aging people to continue and perhaps improve their ability to ask questions and to find answers to these questions. With aging people should continue to engage in creative activities. If not in one domain, try another. Not only will it bring joy and health to the creator, but also may bring joy and health to others. Creators should not only create products, but also invite, train, and encourage creativity of others, including our students, residents, fellows and members of our faculty.





Relative value units (RVUs) are a payment formula for physicians. This was developed by the government to determine the fees paid to physicians who are seeing patients who are insured by Medicare. Now this system is also used by many different agencies including insurance companies. The service provided by a physician is coded and there are about 7000 different services that physicians can provide that are listed. The payment to the physician depends on the code.

Discussing all the problems with this payment method would be a very lengthy report and thus I want to focus on some of the main problems.

In the late 1950s and early 1960s, automobiles made in American were of terrible quality and this is one of the reasons that foreign made autos were able to capture a good part of the American automobile market. There were many reasons for this drop in the quality of American cars. I had heard that one of the reasons for the loss of quality is that the plant managers attempted to increase productivity by paying many of their workers based on how much they accomplished during their working period. Unfortunately, this means of payment had many of the workers sacrifice quality for quantity. In many health centers, the salary they pay their physicians is dependent on their RVUs, rather than the quality of care they provide for their patients. Even when physicians want to provide high quality of care, administrators are often unhappy because they are sacrificing RVUs.

Let me give a personal example. I was an attending physician who had a memory disorder clinic at the University of Florida. The patients I saw in this clinic were for the most part referred by other neurologists, who wanted a second opinion, most often because there was something very unusual about their signs and symptoms or laboratory tests. In addition, often attending this clinic with me were one or two behavioral neurology fellows, who had completed their training in neurology, but wanted to specialize in Cognitive and Behavioral Neurology. In addition, there was often a neurology resident and medical students. One of the critical functions of medical schools is education, and much of my time, I was teaching.

Most of the patients seen in my clinic already have had a neurological and neuropsychological evaluations. Most have already had blood tests and brain imaging.

Some patients even had other special tests such as a lumbar puncture with analysis of the spinal fluid and some had electroencephalograms. All this material needed to be reviewed by me. When I and many other neurologists see patients in their clinics, we ask the patient and their family to bring their brain imaging. We examine these images as well as read the reports about these images.

Many of the patients I saw in our clinic at the University of Florida, were first evaluated by one of our fellows or a neurology resident. Therefore, before going into room and speaking with this patient, her/his family or caregiver and examining this patient, I listened to our resident or fellow present of this patient, including the patient's chief complaint, the history of present illness, their past medical history, the tests that were performed and the results of these test. The resident or fellow then reported their findings on examination, including the patient's general physical examination. This is important because many disorders of the nervous system are caused by a disease of tone of the major organs, such as the heart, lungs, kidneys and liver. This is followed by an examination of this patient's mental status, cranial nerves, the motor system including the cerebellum, the sensory system and reflexes as well as gait (walking) and balance. As mentioned above, examining the mental status can take a few minutes if normal but hours if there are abnormalities and many of the patients we were seeing had been referred because they were having impairments of their cognitive functions.

After the resident or fellow presents this patient's history and finding on their examination, the resident or fellow is first asked to try and localize where in the nervous system their patient's dysfunction is occurring and then to discuss the possible diseases that could be causing this dysfunction. Following this discussion of diagnosis, the residents or fellows are asked to discuss the tests that may be able to confirm their diagnosis or provide information about other possible diagnoses.

After this discussion with the resident or fellow, I go into the patient's clinic room and also obtain a detailed history from both the patient and family or caregiver, as well as attempt to perform portions of a general physical examination, a complete neurological examination, including an examination of cognitive functions, including, evaluation of episodic and working memory, language (speech production, repetition, naming and comprehension) as well as their ability to read and write, frontal-executive functions, and visuospatial functions.

The fellow or resident and I discuss the evaluation of this patient, the possible localization in the brain of this dysfunction, the differential diagnosis of diseases that can cause this dysfunction, possible further testing and possible treatments. In addition, a very important part of the clinic visit is after our evaluation of this patient, to speak with the patient and the patient's family members, who have accompanied this patient, explaining the possible diagnosis, possible future tests, possible treatments, the possible benefits and complications of treatments, the prognosis and management. I then ask the patient, family and or caregiver if they have any questions and attempt to answer these questions.

All these clinical and education activities take much time. Several weeks after the Dean's office selected a new Chair of our Neurology Department, our new Chair selected a new Administrative Executive. This Executive, wrote me an email, where

he stated, that he learned that I come to my afternoon clinic about 12:30 PM and often do not leave until after 6:30 PM, but he did not understand why I only saw three or four patients. His message was clear, see patients more rapidly and you can make more money for our department. When I mentioned this story to my colleagues from other health centers, they almost all had similar stories of being pushed to increase their RVUs.

In an article in Medscape Medical News, August 2, 2019, the author Kerry Dooley Young wrote an article titled, “Docs Get Tiny Raises While Nonprofit Healthcare CEOs Get > \$10M.” Not only are the doctors getting small or no raises, but also the nurses and other hospital personal are also not getting substantial raises,

Many of the new diagnostic and therapeutic procedures have revolutionized medicine. Many of these procedures have allowed us to live longer and healthier lives, as well as having reduced pain and suffering. However, almost all diagnostic and therapeutic procedures are expensive and are another major source of income to health centers and especially to executives and administrators. Since there has been a decrease in the time allowed for taking a history and performing an examination, patients’ clinical evaluations are often incomplete, and thus patients’ evaluation are more heavily dependent on diagnostic procedures. According to Verghese [1] there are some physicians who bypass the traditional bedside evaluation and therefore rely solely on laboratory evaluations.

In some respects, medicine, like many American industries are reverting to an economic system of medieval Europe, where there are Lords now called CEOs and serfs who are called clinicians. Physicians and nurses currently make more money than did the serfs, but like the serfs, we have masters who remind us to plow more fields and to do it more rapidly so that they can enjoy a royal life.

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# Patient-Physician Relationships and Interactions

# 6

## Obtaining Patients' History

Shortly after joining the faculty at the University of Florida, I was seeing a patient with a first-year resident. The patient was a young woman who told us she developed weakness of her right arm and leg. After we got her medical history, we wanted to examine her and asked a nurse to help her change into a gown and to lay down on the examining table while we stepped outside. When I stepped outside of the examining room and walked into a physician's meeting room, I told the resident, that I suspected that this woman had a psychological conversion disorder, often called hysteria. The resident asked me why I thought this was a functional disorder and he wanted to know if it was her age? I told the resident, that it was not her age. Even young woman can have a brain hemorrhage, from an aneurysm or an AV malformation in their brain or even brain tumors. In addition, if they have certain forms of cardiac disease or a blood clotting disorder, they can have a blood clot in the one of the vessels that feed the brain.

I also told this resident, that when we were speaking with her and she told us that she awoke with this complete right-sided paralysis, I did not see that her face had any expression of fear or sadness. I did explain that some patients with right hemisphere stroke are not aware of their weakness and some that are aware of their weakness are impaired at expressing emotions with facial expression and changes in their tone of voice-prosody. However, this patient's weakness was on the right side of her body and movements of the right side of their body are most likely to have an injury to their left hemisphere. I also mentioned to him that with a large stroke of the left hemisphere many patients are aphasic, but her speech was normal. Finally, I told him, she also did not appear to have any lower right sided facial weakness, but this is not always seen.

When we returned to the room, in addition to performing a general physical examination, including listening to her heart for abnormal rhythms and murmurs as well as listening to her carotid arteries for sounds suggesting there was abnormal flow (bruit), we performed a neurological examination. As part of my motor

examination, I examined her for a Hoover's sign and a reverse Hoover's sign. While she was lying on her back, I put my open right hand under the heel of her left foot and my left open hand under the heel of her right foot. I then asked her to try and press her right leg against my hand and she applied no pressure. When I asked her to do this with her left leg, she was able to apply pressure on my hand. I then asked her to try, as hard as she could, to lift her right foot off my hand. She did not lift this foot off my hand. Normally, when people try to lift one leg off the bed they have to press down with the other leg. Her left leg was able to apply this pressure when I asked her to press down with her left leg; however, when attempting to raise her right foot and leg she did not put any pressure on my hand that was under her left foot. This finding suggests that she was not really trying to lift her right leg. I then asked her to try and press her right foot against my hand and she applied no pressure. However, when I asked her to lift her left foot off the bed, she pressed her right foot against my hand. These positive Hoover's signs indicated that she did not have a neurological disease that caused weakness of her right lower extremity.

After we completed our evaluation and walked out of the room the resident said to me, "You were correct. How could tell this from just looking at her face."

I explained that one of the major symptoms-signs of a conversion disorder is called "la belle indifference." This is when the patient appears to be unconcerned about their disability. Whereas some patients with right hemisphere damage, may be unaware or unconcerned about their impairment, most often when people have left hemisphere damage, they can have a catastrophic reaction, and appear depressed and anxious about their impairments. This patient, however, showed no expression of concern.

Computers and computerized medical records have helped to improve medical care. Previously when a patient, who we were evaluating for the first time, who has a chronic disease, we needed to obtain a history from the patient and those who accompanied this patient, since often we could not see their prior medical records. These records often contained details about this patient's prior history and results of prior physical examinations, tests and treatments. Now with computerized medical records, we can obtain prior results of clinical evaluations, test results, diagnoses, the types of treatments, as well as the results of these treatments. Unfortunately, now with electronic records, when many physicians are taking a history from a patient, instead of looking at the patient's face while they are speaking, the physician is looking at the computer monitor while they are typing the patient's history.

Observing a patient, is perhaps one of the most important functions performed by physicians. One the founders of modern medicine, William Osler in 1901 wrote that, "the whole art of medicine is in observation." However, according to Block and co-authors [1], medical residents now spend 40% of their time looking at computer screens, but only about 12% observing and interacting with the patient. Salvatore Mangione and co-authors wrote, "...that meticulous observation is fundamental to the practice of medicine. That learning the art of observation requires both method and practice and that today's medical education provides little of either...".

Not only are physicians, who are looking at their computer monitor, miss seeing non-verbal expressions provided by the patient, but the patient does not have the

opportunity to fully observe the physician's face and body. Viewing the physician often allows the patient to know that their physician is empathetic and therefore concerned about their health. This knowledge will often encourage the patient to provide information that might be important to the physician's evaluation. In addition, even in the absence of a medication or surgery, communicating with an empathetic physician often has important therapeutic effects. However, communicating with a patient, face to face and then writing this patient's current symptoms and history would take more time. Thus, properly interviewing a patient and then writing this patient's history would reduce the RVUs a physician could acquire each day, and this would not make many administrators very happy.

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## The Physical Examination and Laboratory Tests

When I was a neurology resident there were fewer diagnostic tests than there are now, and the availability of new diagnostic tests have really helped to provide patients with better care. For example, when I was a neurology resident, there was no computer tomography (CT) or magnetic resonance imaging (MRI). If we wanted to image the brain, to learn of there were anatomic changes in the brain caused by a neurological disease, the best method was a procedure called pneumoencephalography.

When performing this procedure, a lumbar puncture was required, and some spinal fluid was removed. After the fluid was removed air was injected into the subarachnoid space and since the patient was at first sitting up in a special chair, this air traveled to the ventricles deep in the brain, as well as to the subarachnoid space on the outside of the brain. To make certain this air was distributed over the entire brain, the patient was strapped into this chair and this chair then vertically rotated (heals over the head) for 360°. All this was terribly unpleasant or even painful for the patient and while it did allow us to see the outline shape of the brain and occasionally did provide some important information, this procedure did not allow us to view the actual brain such as the MRI allows us to do, and therefore, the information provided by this procedure was very limited. In addition, if the patients had a tumor or swelling of their brain, this procedure could cause brain herniation, where the hemispheres push down on the brain stem and this herniation can cause death. Thus, MRI imaging can provide important anatomic information, allowing us to diagnose the cause of many neurological diseases, such as a stroke or a brain tumor.

As the population ages we are seeing more patients with degenerative diseases that cause dementia. The most common cause of dementia is Alzheimer's disease. At one time in addition to a history of a cognitive decline and cognitive disabilities, the diagnosis was based on detailed mental status-cognitive testing. Now patients are most often given brief tests such as the Mini-Mental Status Test (MMSE) or the Montreal Cognitive Assessment (MoCA). These tests assess patients for an episodic memory impairment (e.g., knowing the month, day of the week, year and location), being able to recall several words immediately and after a delay, naming three animals, drawing a clock, a cube or pentagons, drawing a trail thought targets,

repeating a series of numbers, performing subtractions, naming words that begin with the letter “P” and determining how two words are similar.

In these tests, if a patient scores below a certain score, they are diagnosed with dementia and these tests are sensitive and valid. However, the overall score on these tests do not provide the clinician with all the knowledge they should know about their patient’s disabilities and there are many cognitive deficits that are not assessed, that might be important to assess. For example, these tests do not fully examine frontal lobe functions, such as disengagement, that tests like the Stroop can evaluate. In the Stroop there are the printed words used to communicate the color of an object. In addition, many of these words are printed such that the color of the letters is different than the name of the color denoted by the word. For example, the word “red” can be written with letters that have a blue color. The patient is asked not to read the word, but to name the color of the font used to print each of these words and to do this as rapidly as possible. Patients with frontal-executive dysfunction, have trouble, naming the colors rather than reading the words and this is because they are impaired in disengagement.

Now neurological diagnoses are often made by performing an imaging test, such as an anatomic MRI. If the patient has atrophy of their entorhinal cortices and/or medial temporal lobes, they would be likely to be diagnosed as having amnesic mild cognitive impairment or Alzheimer’s disease. Brain scanning for the abnormal presence of amyloid, or the accumulation of tau could help to confirm the diagnosis of Alzheimer’s disease. Similarly, seeing frontal lobe atrophy may lead to the diagnosis of a frontal lobe dementia. There is now even a blood test that may help diagnose Alzheimer’s disease. However, the best means of diagnosing a patient’s form of dementia, is still the clinical evaluation.

The increased quality of diagnostic tests has improved our diagnostic ability. One of the best examples is the MRI, which has allowed us to better learn about the location of the cerebral injury, and help us learn about the cause of an injury. What I have noticed, however, is that with increases in diagnostic ability of laboratory tests, there has been a reduction in the quality of the neurological examination. Seeing a lesion on an MRI does not fully tell the clinician the disabilities with which the patient is suffering. Furthermore, there are many neurological diseases where there are no major changes in brain structure.

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## Cognitive Evaluation

Although patients with a stroke, head trauma or dementia often have cognitive deficits, almost every disease that affects the central nervous system can cause cognitive deficits. There are so many different cognitive tests that for a clinician to perform all these tests it would probably take several days of testing.

Whereas the patient’s history, as well as information from family and caregivers, can provide important information about cognitive deficits, patients and family are often unaware of many cognitive deficits. Therefore, an examination of cognitive functions is a very important part of the examination.



While speaking with the patient the clinician often becomes aware of any major problems with speech and language; however, during a conversation with the patient mild naming and repetition disorders can be missed, if not specifically assessed. For example, there are disorders, such as a form of Alzheimer's disease called logopenic primary progressive aphasia, where patients' main problems are naming and repeating, and this disorder can be missed if naming and repetition tests are not formally assessed. In addition, there many other functions that family will often fail to detect, such as acalculia, agraphia, alexia, and finger agnosia. During conversation with the patient, and without formal testing, disorders of frontal executive dysfunction may not be detected.

As mentioned, many neurologists when evaluating patients with cognitive disorders use a screening examination, such as the Mini-Mental Status (MMSE) or the Montreal Cognitive Assessment (MoCA). When patients have a serious cognitive deficit, these tests will be able to confirm a cognitive disorder. However, these test results might lead the clinician to not being aware of other important signs of cognitive dysfunction.

Several famous neurologists, such as Drs. Denny-Brown and Normal Geschwind taught that viewing and analyzing the patient's means of performance will often provide important information about the patient's disorder, rather than pass or fail score. For example, the MoCA has a subtest where the patient is asked to draw a clock with all the numbers and then have the hands of the clock show the time as ten minutes after eleven. When performing this test, the patient might fail to perform correctly, and therefore get a low score on this test; however, the type of errors that patient's makes on this test might be important in learning more about these patients' cognitive disorder, and the localization of their brain dysfunction. This information may help the clinician learn the cause of their patient's disability. For example, when a patient is putting the numbers on the clock face and they put all the numbers on the left side of the clock (right side of the patient's body), they probably have hemispacial neglect, suggesting that this patient has right parietal or right frontal dysfunction. Or if they leave too much space between each of the earlier numbers (e.g., 1-9), then toward the end of their number placements, they will have little space between the last number that they have written and the number 12. Therefore, they may have to place the numbers 10, 11 and 12 very close together. This is often a sign of poor planning and patients with frontal lobe dysfunction may reveal, this type of error.

There many other functions associated with brain injury or degeneration that are almost never tested. Spatial and body neglect are one of the major causes of disability associated with stroke. Neglect can also be seen with other diseases. Although the clock drawing test can detect unilateral neglect, it is not very sensitive. The most commonly used tests to detect neglect are the line bisection test, the cancellation test, drawing and copying figures. Although spatial neglect is one of the most disabling disorders, these tests, are not part of the Mini-Mental Status Examination or part of the Montreal Cognitive Assessment. In addition, there are several other right hemisphere mediated functions that are not tested by these batteries including, recognition of faces, the recognition of people's voices, both the comprehension and



expression of emotional faces, and both the comprehension and expression of emotional speech prosody.

It was Paul Broca who first reported that language and speech disorders are most often associated with left hemisphere injury. There are, however, other forms of verbal communication, including emotional prosody. There are two forms of prosody, one that is used grammatically, such as raising the tone of voice upward when asking a question. The other form is the communication of emotions (e.g., It is not what you said, but how you said it.) Studies of patients with stroke revealed that emotional prosody is processed in the right hemisphere with posterior lesions causing impaired comprehension of prosody and more anterior lesions causing expressive aprosodia [2] Defects in the expression and comprehension of prosody have also been described with degenerative diseases. Disorders of prosody can impair all forms of relationships. However, these disorders were not described until near the end of the twentieth century and in the early twenty first century. Unfortunately, I do not know of any test battery for dementia that examines for these emotional prosody disorders.

In addition to the disorders of the comprehension and expression of emotional prosody, patients with right hemisphere dysfunction from lesion, or forms of degenerative disease, can have impairments of facially expressing emotions as well as recognizing facial emotional studies [3]. Whereas these disorders were first described in patients with right hemisphere strokes, these disorders can also be seen with degenerative diseases. However, like disorders of emotional prosody, I do not know of any test battery that examines for these facial emotional communication disorders.

The Mini Mental Status Examination (MMSE) is often used to assess patients for cognitive disorders. This testing battery assesses episodic memory (e.g., orientation and recalling three objects), working memory and math, naming objects, repeating a sentence, following verbal commands, speaking, reading, writing and copying a picture (intersecting pentagons). However, the Mini Mental Status Examination, does not appear to have any tests that assesses patients for frontal executive dysfunction. There are, however, several bedside tests that can assess frontal-executive function, such as letter-word fluency (e.g., in one minute, please give me all the words that begin with the letter f, but please do not include names and numbers). In addition, other than drawing there are no tests that assess many of the right hemisphere's functions mentioned above.

It is a clear that there is need for a more complete battery of neurobehavioral tests. This battery of tests should allow the physician or psychologist to examine almost all types of cognitive disorders. For example, one of the most disabling disorders is spatial neglect, and if a patient with neglect is given the MMSE, neglect might not be detected. Each test should have what scores are normal or abnormal for each of the cognitive functions being tested. Like the MMSE or MoCA, these tests can have a summary score, but other than diagnosing a cognitive impairment these summary scores do not help inform the clinician what is impaired. These tests should be easy to administer, take a short period of time to administer and there should be no special equipment that is necessary. The training needed to perform these tests should also be brief.

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When I was in medical school, during my residency and even for many years after I came down to be on the faculty at the University of Florida, we had weekly grand rounds. These rounds were attended by students, residents, fellows, and almost all the faculty in our department.

Typically, at these grand rounds, one of the neurology residents or faculty would speak to the chief resident about an interesting or difficult case that they saw on the neurology service or as a consult. After the chief resident selected the patient that they wanted to present at grand rounds, they would request that the patient come to grand rounds. It was explained to the patient that although grand rounds is primarily an educational activity, the physician who will be examining them and discussing their case often has valuable advice. Almost all patients who were invited agree to attend. The chief resident would also ask one of the faculty who was very knowledgeable about this patient's possible disorder, to be the discussant. However, the discussant was not usually the attending who was primarily responsible for this patient's care.

At the time these grand rounds were held, the resident who was taking care of this patient would present this patient's medical history and the results of their neurological examination. After this presentation, the resident would introduce the patient to the discussant and the audience. The discussant would then often thank the patient for coming and ask the patient some questions about matters that the discussant thinks may be important but were not presented by the resident. Following this, the discussant would perform a neurological examination. During this examination, the discussant would often show the audience many of the abnormal signs exhibited by the patient, and this would enable people in the audience to learn how to elicit these signs and their significance. In addition, the discussant would often perform tests that were not mentioned by the resident and sometime these signs would be very helpful in making the correct diagnosis.

For example, many years ago the resident at grand rounds presented a patient to me who complained about the sudden onset of weakness of their left upper limb, which after a few minutes got better. However, he was still having problem with

performing certain actions such as buttoning his shirt. When the resident presented this patient, he told the audience that he could not find any weakness in this patient's left upper limb, and that position sense and touch sense were both normal. He thought that he may have had a slight increase in his triceps reflex, but no other neurological signs.

The motor cortex of each hemisphere controls the movements of the contralateral arm, hand and fingers. This motor cortex sends down long cables through the hemisphere, through the brain stem and into the spinal cord. In the spinal cord these cables connect with the motor nerves that go down to the muscles. Paul Bucy (1948), a neurosurgeon, had a patient with hemiballismus who had trouble sleeping and performing many other activities because her arm was violently jumping. He and the patient agreed that it would be better to have a paretic left arm than hemiballismus. Therefore, Bucy decided to cut the portion of the corticospinal track that controls this arm. Immediately after surgery, this patient could not move this arm, forearm, hand or fingers and her hemiballismus was no longer present. However, after several week she regained strength in this arm, but she could not perform, independent, but coordinated precise finger movements. H. G. Kuypers [1] also showed this in moneys who had their corticospinal track sectioned in their medulla.

Therefore, I gave this patient a nickel and asked this patient to rotate the nickel between his thumb, index finger and middle fingers. He rotated the coin well with his right hand but had trouble doing this with his left hand and repeatedly dropped the nickel on the table. I told the audience that this was evidence that this patient did injury either his motor cortex or corticospinal track.

One of the best things about these former grand rounds was that many members of our faculty attended and very often made terrific suggestions about the patient's examination, as well as lesion localization, pathology, diagnostic tests and treatment.

A member of our faculty raised their hand, and said, "Ken, in addition to examining the patient's arm for spasticity, increased deep tendon reflexes, an extensor plantar response, all of which you did, there is another test for corticospinal injury. You should know this since you gave the Wartenberg lecture at the American Academy of Neurology meeting."

I replied, "Oh yes, the Wartenberg's sign." There are actually two Wartenberg signs, one is when patients who have damage to the ulnar nerve have their small finger making a V with their ring finger when their hand is just resting on their lap. But the other one, is a test for damage to the corticospinal system. The patient is asked to place the tips of their fingers on the tips of the examiner's fingers and then to pull back his hand. When normal people do this, they extend their thumb, but with injury to the corticospinal system patients move (flex) their thumb toward their palm.

When I tested this patient for the Wartenberg's thumb sign, the patient did demonstrate this abnormal posture. I then looked at the faculty member who mentioned this and said, "Thanks for reminding me of this. More evidenced for a corticospinal lesion."

I then mentioned that most likely this patient's disorder was caused by a small cerebral infarction deep in the hemisphere and that this was probably caused by a

thrombosis of a small artery branching off from the middle cerebral artery, but other causes such as an embolus from the heart needed to be ruled out. I then discussed possible treatments.

Another member of our faculty raised their hand and asked, “If this patient had an injury of his corticospinal track, why was he not weak.” Following this question, a discussion among several faculty ensued, about other motor networks that might be important in limb movement.

The resident then presented the results of the patient’s laboratory evaluation, which was very complete. He then showed the results of the brain imaging, revealing that this patient had a small subcortical infarction.

Another member of the faculty then raised their hand and asked, what type of rehabilitation is best for this disorder. Fortunately, there was an occupational therapist in the audience who explained the different types of exercises they have patients perform.

For several years, patients have no longer been presented at our grand rounds and now almost every week we get a lecture at grand rounds. Many of these lectures are terrific and provide important knowledge. I know that we are not alone in having made this change since I have been asked to visit several schools and give grand round lectures. Although I believe many of these lectures are very valuable and should be continued to be given, the loss of patient presentations has reduced some of the important educational value of grand rounds, including the best means of taking a history and performing a clinical neurological examination, the thinking and reasoning about localization and causation as well as discussions about pathophysiology, diagnostic testing and treatment.

These are the actions neurologists perform when seeing patients and there are still no better means of teaching students, residents and even trained neurologists how to perform all these important skills.

We need to find a means of bringing patient presentations and discussions back to grand rounds.

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When I decided to become a neurologist in 1967, there was not a great demand for neurologists. Therefore, there were fewer neurology training programs than there are today, and there were only a small number of residents in each program. For example, when I took my training at the Harvard Neurological Unit, I think we had a total of six residents. When I joined the faculty at the University of Florida, we had two or three residents for each of the three-year residency. Also, after I joined the faculty at the University of Florida (UF) in 1970, we had only three neurologists (Melvin Greer, Fred Vroom and me) at the Shands Teaching Hospital at the University of Florida. Our Veteran's Affairs Medical Center, which is right across the street from the University of Florida's Shands Teaching Hospital, and is part of our academic program, had two neurologists (BJ Wilder and Ed Gonyea).

When I joined the faculty at the University of Florida College of Medicine, Neurology was not a department, but rather a division of the Department of Medicine. Back then, as now, physicians made more money when performing procedures than when seeing patients, and performing a full evaluation, including taking a patient's history and performing both a general physical and neurological examination.

We very much wanted to have our own neurology department, but back then even though there were only a few diseases that we could treat, we performed many procedures. Computer tomography was not yet available and thus when we wanted to see if a patient had hydrocephalus or a brain tumor, we performed a pneumoencephalogram. As mentioned, in this procedure the patient sat in a chair, and we performed a spinal tap by inserting a needle in the patient's lumbar area. We would then remove some spinal fluid and inject air into the patient's spinal canal. This air would float up to the patient's brain. However, to get the air into all the spaces where there was spinal fluid, we strapped the patient into this chair and rotated the chair vertically 360° so that for a short period of time the patient would be upside down. After we did this, we could get X-rays of the patient's head and see the outline of the brain, as well as the ventricles. If a patient had hydrocephalus, they revealed very large ventricles with little air over the cerebral cortex. If a patient had a tumor

there would be less air over the part of the cerebral cortex where the tumor was located and the ventricle under the tumor would often be compressed.

There have been great advances in brain imaging. For example, before magnetic resonance imaging (MRI), if a patient had a stroke or transient ischemic attack, to see a patient's brain vessels we would inject dye directly into the carotid arteries that feeds blood to much of the brain. Now we can see blood vessels that go to the brain by performing arterial magnetic resonance imaging or a computer tomography angiogram. Back then if we needed to see if there was a tumor of the spine cord, we would perform a myelogram, where we again did a spinal tap and inserted a dye that would surround the spinal cord in the subarachnoid space. We are now rarely performed these tests because of magnetic resonance imaging and computer tomography. We also performed electromyograms (EMGs) and nerve conduction tests to diagnose neuropathy, diseases of muscles and disorders in the connection between the nerve and muscle. We still continue to perform electromyograms and nerve conduction studies. We also performed and continue to perform electroencephalograms (EEGs) to diagnose epilepsy and other electrophysiological disturbances of the brain.

In the early 1970s when we were performing these procedures, the other specialties in the Internal Medicine Department had very few procedures. The cardiologists could do EKGs, and the gastroenterologist could examine the stool of their patients for blood and could perform colonoscopy. The endocrinologists and infectious disease specialists had no procedures, except for drawing blood from their patients and sending it to the lab. However, since neurology had so many procedures it brought in much money into the Department of Medicine, and if Neurology left the Department of Medicine, the Department of Medicine would likely to have financial difficulty.

During this time our Division of Neurology was able to recruit great residents. For example, when I first joined the faculty at the University of Florida, one of the first residents with whom I worked, was Dr. Robert T. Watson. From his colleagues, I learned that Bob graduated first in his class from college at the University of Florida, as well as being first in his medical school class at the University of Florida. During the time he was a first-year resident, after reading some of research about unilateral neglect that my coinvestigators and I performed, he wanted to also do research to better understand the neglect syndrome. During my fellowship at the Harvard Neurological Unit, I had done research with monkeys, but did not have a primate laboratory here at the University of Florida. Bob Watson was, however, able to obtain both a laboratory and monkeys. He was, therefore, able to perform further research on unilateral neglect. For example, in one study he found that unilateral ablation of the mesencephalic reticular formation, important in hemispheric arousal, induced severe unilateral neglect. There were also many other brilliant and hard-working residents that were here at the same time as Bob.

After the introduction of computer tomography and magnetic resonance imaging. Many of the procedures performed by neurologists, such as the pneumoencephalogram, were no longer performed. In addition, other medical specialties, such as cardiology and gastroenterology, developed many new procedures. Therefore,

the relative income of neurologists dropped compared to other medical specialties. The average specialist in internal medicine, now makes about \$372,000 a year, but the average neurologist makes about \$267,000. Although this is an excellent yearly salary, with the huge debt acquired during both college and medical school, many graduating medical students look for specialties where they can make more money. Thus, currently although we still get several brilliant students as residents, because these students have a strong interest in neurological diseases, we now do have to accept many more graduates from foreign medical schools, as well as students who were not outstanding in their medical school. In addition, our department has grown. We now take about seven to nine residents a year and we now have about 40 physicians on our neurology faculty.

Dr. Denny-Brown performed research in many different domains of neurology. For example, in 1935, he and Mary Walker learned that myasthenia gravis could be treated with anticholinesterase inhibitors. This was not only important to patients with myasthenia gravis, because it reduced patients' disability, but it was the first example of how alterations in a neurotransmitter can cause disease. In 1938, he helped to develop electromyography, which is still used to diagnosis neuropathies and myopathies. In 1951, he introduced British anti-Lewisite as the first treatment for the copper overload disorder called Wilson's disease, a terribly disabling disease that causes abnormal movement, and dementia.

I wanted to train with Dr. Denny-Brown, because I was drawn into neurology after seeing a patient with unilateral neglect. I had always been interested in conscious awareness. When I was in medical school, I saw a patient who was unaware of objects that were on the left side of his body. He was also unaware that he had any neurological defects (anosognosia) and I wanted to learn why this injury to the right parietal lobe could cause this disorder. When I asked our attending neurologist about this, he said that I needed to read the papers written by Dr. Denny-Brown, since he was the person who most recently wrote papers about this disorder. Thus, Denny-Brown, performed research of patients with neuromuscular diseases and cognitive behavioral neurology. His clinical and research interests were clearly not in a single domain of neurology. However, things have changed.

When I was in high school taking physics, I learned that the pressure, that makes alterations, equals force over area. However, this law applies to many domains other than physics. Physicians have worked and do work very hard for many hours each week. Many even work up to 80 hours each week. How then can they increase their pressure (making greater alterations in people's health). One of the means we can increase our pressure is by reducing area. Whereas at one time almost all neurologists were seeing patients with almost all types of neurological diseases, and the only major division was pediatric versus adult neurology. Then departments started to have their neurologists specialize in domains, such as cognitive-behavioral diseases, neuromuscular diseases, neoplastic diseases, autoimmune diseases, etc. This specialization continued and now there is sub-specialties in neurology departments that are based on specific diseases. For example, when I first came to the University of Florida in 1970, I did general neurology and cognitive behavioral neurology. Almost all diseases of the central nervous system can be associated with cognitive



disorders. Patients with strokes, movement disorders, seizures, degenerative disorders, head trauma, and many other disorders can have a variety of different forms of a cognitive-behavioral disorder (amnesia, aphasia, apraxia, agnosia, acalculia, right-left confusion, inattention-unilateral neglect, constructional apraxia, apathy, imper-sistence, perseveration, defective response inhibition, prosopagnosia and many other disabling deficits) and a cognitive-behavioral neurologist would most often test for many of these disorders. However, recently the only patients we see have some form of degenerative dementia such as Alzheimer's disease, Picks disease and other forms of frontotemporal dementia as well as patients with vascular dementia.

There are some neurobehavioral disorders that can be treated with medication, and others with speech, and occupational therapy. However, those patients who do not fully respond to these therapies and their family or caregivers can be informed about the nature of these disorders, what limitations these patients might have and how to best manage their disabilities. Currently, for the most part, we only see patients with degenerative dementia. Since almost all disorders of the central nervous system can impair cognition and emotion, we are not sure how these changes in the practice of behavioral neurology may influence the well-being of patients who have neurocognitive disorders from causes other than degenerative disease.



A case report is a detailed report of a patient that describes this patient's symptoms, signs, and test results. Case reports often include pathology, imaging, and treatment. Most case reports are submitted to journals for several reasons, including describing a new disease or new signs of a known disease and new diagnostic tests of a disease that have not been previously reported, as well as a possible new treatment.

In neurology, almost every neurological disease was originally described by a case report. For example, in 1906, Alzheimer presented the first case of the disease that was named after him by Emil Kraepelin, an important German psychiatrist who worked in the late 19th and the early twentieth century. The publication about this first case was a relatively short communication. Subsequently, in 1911, Alzheimer published a more comprehensive paper, where he discussed details about this second patient.

Another example of a case report introducing a previously unreported disease was Okazaki, Lipkin, and Aronson's [1] paper (Diffuse Intracytoplasmic Ganglionic Inclusions (Lewy Type) Associated with Progressive Dementia and Quadripareisis in Flexion) that was one of the first case reports of Lewy Body Dementia.

A list of all the important case reports would fill up this book, but for some reason, it appeared to me that case reports in major journals are almost extinct. For example, I searched the current issues of some of most read and highly rated journals, including *Neurology*, *Brain*, *JAMA Neurology*, *Annals of Neurology* and the *Journal of Neurology, Neurosurgery and Psychiatry*. This month, I did not find any case reports in these major neurology journals. In a prior journal article, several years ago, I wrote a paper [2] titled, "Case reports and case studies: an endangered species." The following discussion is, for the most part, discussing the same issues as this prior report, as much has not changed. Therefore, much of the following discussion is similar to this prior article (self-plagiarism?).

In Thomas Kuhn's book, "The Structure of Scientific Revolutions," he wrote that "Discovery commences with the awareness of an anomaly." Many of the major advances in clinical neurology, and especially in Behavioral and Cognitive Neurology, have been initiated by case reports. In addition to the examples given

above the founding of Behavioral and Cognitive Neurology have been initiated with the observation of an anomaly in a specific patient. In speech and language disorders, there was Broca's 1861 report of the non-fluent patient Leborgne, whose primary utterance was "tan" and Leborgne despite being non-fluent could comprehend others speech, but not repeat sentences. Subsequently, Wernicke's in [3] described another patient who was fluent, but spoke in jargon, and could not understand or repeat. About a decade later, in 1885, Lichtheim reported a patient with poor comprehension but with intact repetition, now called transcortical sensory aphasia. He also reported a patient who was non-fluent, but unlike the non-fluent aphasia that Broca's reported, Lichtheim's patient, could repeat sentences, a disorder we now call transcortical motor aphasia). These nineteenth century case reports were not limited to speech. These nineteenth century case reports were the beginning of modern aphasiology and behavioral neurology.

There are many other case reports in other cognitive domains that have helped in the understanding of brain function and dysfunction. Perhaps one of the most important case reports was the patient H. M. Even with medications, this man had poorly controlled seizures and to treat these seizures, they removed his right and left temporal lobes, including his hippocampi. After recovering from surgery, he was found to have a profound disorder of episodic memory. There have been many important papers written about H. M. that are all case reports. One of the most famous case reports is that of Harlow [4]. He described Phineas Gage who had a severe frontal injury from the passage of an iron bar that passes through his brain. Remarkably he did not die but developed severe executive dysfunction. Gage's story is still often quoted and even a reconstruction of this Gage's skull and brain was reported in Science [5].

There are several negative aspects of case reports. The major problem is that since these reports are based on an individual patient, the people who read these case reports must be careful about generalizing. However, there are many diseases that are not very common, but to the people who have these uncommon diseases, the low prevalence of their disease is not trivial. Even when a disease is untreatable, the failure of a physician to recognize this disease may increase the patient's suffering. During the Vietnam I joined the Air Force, and I was assigned to be the Chief of Medicine at the NATO hospital in Turkey. When I was living in Turkey, I heard two men arguing and one angry man curse another by saying, "May you come down with a disease that not only has no cure but is also one that cannot be diagnosed." Therefore, one of the positive attributes of case reports is that they can reduce the failures to recognize a disease. For example, I described three patients with a new disease, which was characterized by a tremor of their lower extremities when standing but not while sitting or walking. After describing this "orthostatic tremor," unexpectedly I received many letters from people all over the world, thanking me because they or a family member had this disorder but were told it was functional.

Case reports also serves as an invitation for further studies, allowing clinicians to learn if this disorder exists in the general population, as well as learning the cause and treatment of these newly described disorders.

Another advantage of case studies is that they allow new in-depth investigations. The related disciplines of behavioral-cognitive neurology, such as speech pathology, neurolinguistics, clinical neuropsychology, and cognitive neuroscience all study the relationships between biological systems (i.e., anatomic, physiologic, pharmacologic) and behavior (i.e., cognition, conation, attention, and emotion). One of the major goals of these studies is learning the component processes that comprise complex behavioral functions. One of the best methods of analyzing complex and widely distributed networks into their major components is to study normal brain function. This has become possible by using electrophysiological (eg, evoked potentials and magnetoencephalography) and functional imaging techniques, such as positron emission tomography (PET), single photon emission computed tomography (SPECT), and functional magnetic imaging (fMRI)]. Although the use of these techniques has caused a revolution in cognitive neuroscience, it should be known that these techniques have many problems. For example, many of the imaging studies used to study brain functions, examine alterations of blood flow. However, interpreting the meaning of the changing patterns of blood flow induced by performing a complex behavior, may be difficult. For example, when seeing changes in blood flow, we cannot know if it is related to the activation of excitatory or inhibitory neurons.

From the time of Paul Broca's and Karl Wernicke's reports, studies have provided us with important information about both the organization of the brain and how brain injury, in specific areas of the brain, might lead to abnormal behavior. Although the presence of double dissociations provides strong evidence that many complex functions are often composed of multiple components and that many of these components are mediated by anatomically distinct areas. However, there is no perfect method of studying the brain, and the lesion-case study method has its limitations.

Hughlings Jackson reported that a cortical brain injury, cannot only induce a loss of a function, but the injured area might have been inhibiting other more "primitive" areas that mediate other more stereotypic and primitive functions. Therefore, with brain injury, with disinhibition, these more primitive functions might become manifest. Acute injury to a specific area of the brain can also cause dysfunction in other areas of the brain. Von Monakow called this diaschisis. Therefore, the loss or alteration of a function that a clinician sees after a brain injury might not be caused by injury to the area defined by anatomic imaging. Further, after an injury to the part of a brain that mediates a specific function, other areas of the brain might be able to take over the functions of the injured area. Therefore, the absence of deficit after a brain injury might be related to functional plasticity. Before clinician and investigators can correctly infer the function mediated by a specific brain area, they should not solely rely on the lesion method, which is often the basis of case studies. Ideally, investigators should also obtain converging evidence by using such techniques as functional imaging. In addition, there are several hundred functional imaging studies of healthy participants that report the portions of the brain that mediate specific functions. However, the results of these studies should ideally be supported by lesion studies.

Whereas cases studies still appear to be critical in advancing our discipline, in an editorial in the highly respected journal *Brain*, Professors John Newsome-Davis and John Rothwell state that this journal has an impact factor of 7.1–7.4 for the last four years.” They also note that *Brain* was ranked second of all the clinical neurology journals. The editors of *Brain*, as well as editors of other journals, think that they can increase their power rating if they limit the number of published case reports. Although I am not sure that limiting the number of case reports will increase their impact factor, I feel confident that journals that eliminate case studies will be missing many important scientific contributions.

Although case study reports appear to be an endangered and has its limitations, case studies are a valuable tool that should be protected from extinction. The published case study is a critical method for the distribution of information about anomalies, and it is the observation of anomalies that leads to the identification of both new diseases and new ideas.

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## Depression and Anxiety

Fond et al. [1] wanted to determine the prevalence of anxiety and depression in a national sample of young physicians. The study used a cross-sectional observational epidemiological study. An online anonymous questionnaire was administered to the young physicians of all French medical faculties. Anxiety and depression were assessed with the Hamilton Anxiety & Depression scale sub-scores for anxiety and depression. Psychotropic drug consumption, psychotherapy follow-up and other variables were self-declared. They had 2003 study participants. A current anxiety disorder was present in 32.3% of participants and in 8.7% a current major depressive disorder.

In addition, these investigators found that almost one third of medical students reported an anxiety disorder or major depression. In addition, less than one on five received the recommended treatment (psychotherapy or antidepressant).

These authors conclude that the prevention and treatment of psychiatric disorders should be improved in this population.

Another study by Samuel Ofei-Dodoo and co-workers [2] assessed the prevalence of loneliness, burnout, and depressive symptoms from a national sample of 401 family medicine physicians who were members of the American Academy of Family Physicians (AAFP) and AAFP National Research Network between December 7, 2019, and January 20, 2020. The participants completed an anonymous, 30-item survey measuring loneliness, burnout, symptoms of depression, and fatigue. These investigators found that the prevalence of loneliness, burnout, and depressive symptoms was 44.9% (165 of 367), 45.1% (181 of 401), and 44.3% (163 of 368) respectively.

According to the authors, these findings demonstrate that loneliness, burnout and depression are common in practicing family medicine physicians. The authors also note that future work is needed to understand these changes in order to help learn about effective interventions.

## Physician Morbidity and Mortality

Frank and co-workers [3] examined data the National Occupational Mortality Surveillance database, which is derived from deaths occurring in 28 states between 1984 and 1995. Occupation is coded according to the U.S. Bureau of the Census classification system, and cause of death is coded according to the ninth revision of the International Classification of Diseases. These investigators found, some good news for physicians. Among both U.S. white and black men, physicians were, on average, older when they died, (73.0 years for white and 68.7 for black) than were lawyers (72.3 and 62.0), all examined professionals (70.9 and 65.3), and all men (70.3 and 63.6). According to Carpenter, Swerdlow, and Fear [4], the top ten causes of death for white male physicians were essentially the same as those of the general population, although they were more likely to die from cerebrovascular disease, accidents, and suicide, and less likely to die from chronic obstructive pulmonary disease, pneumonia/influenza, or liver disease than were other professional white men.

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Fortunately, I have health insurance for my family. I usually watch the news on the television after I come home and have dinner. While watching the news, I noticed how many advertisements were about medications. I thought, “Wow, the pharmaceutical companies must be making a fortune.”

Dr. David Blumenthal wrote an essay called, “Monopoly money representing high drug costs.” In this essay he notes that after a pharmaceutical company develops a new medicine to treat a disease, then tests this medication to show it works, has minimal side effects and gets approval from the Federal Drug Administration (FDA), only this company can sell this medication for those patients who need it. This allows these drug companies to benefit from government-enforced monopolies for these new drugs and provides these pharmaceutical companies with ability to set prices. These prices are major problem for healthcare for Americans.

Current laws prevent competitors from selling the same drug for many years after this drug patent is filed. Research has revealed that most new drugs, have on average, 12–13 years of market exclusivity. This allows pharmaceutical companies to charge any price for these medications. Unfortunately, these companies often pick prices that in addition to covering the cost of development, bring in large profits to these pharmaceutical companies. These profits are greater than most other industries.

Fortunately, other companies develop different medications that have the same effect, and this competition lowers these medications’ prices. Unfortunately, many medications remain unaffordable for many patients who need these medications. In addition, many generic drugs are manufactured by only one company. Without competition, a medication can be very expensive. Therefore, the price for some older medications have risen.

Since pharmaceutical companies do have a monopoly in the United States with their new medications, in a free market there is no means by which drug prices can be reduced. However, in many other countries the government controls the cost of medications, and this reduction improves health care. Therefore, in America, unless our government controls drug prices, so that they are affordable, for many



medications, prices will remain expensive, and difficult for some patients to pay these high prices. This impairs medical care for many Americans.

The Center for Responsive Politics (CRP) was founded in 1983 by retired U.S. Senators Frank Church of Idaho, and Hugh Scott of Pennsylvania. It was CRP who reported that in 2017 there were more than 1000 lobbyists working for the pharmaceutical companies. This study [1] analyzed by publicly available data on campaign contributions and lobbying in the US from 1999 to 2018, by pharmaceutical companies. Wouters found that the pharmaceutical and health product industry spent \$4.7 billion, an average of \$233 million per year, on lobbying the US federal government as well as \$414 million on contributions to presidential and congressional electoral candidates, national party committees, and outside spending groups; and \$877 million on contributions to state candidates and committees. These contributions were given to senior legislators in Congress, who are involved in drafting health care laws and state committees that opposed or supported key referenda on drug pricing and regulation. From 1999 to 2018, the pharmaceutical and health product industry recorded \$4.7 billion—an average of \$233 million per year—in lobbying expenditures at the federal level. This was more than any other industry. Of the 20 senators and 20 representatives who received the most contributions, 39 belonged to committees with jurisdiction over health-related legislative matters, 24 of them in senior positions. The pharmaceutical industry also contributed \$877 million to candidates in state elections and in those years, there were state referenda on reforming the pricing of medications.

A comparison of brand-name drug prices between Canadian-based Internet pharmacies and major U.S. drug chain pharmacies was written by Quon, Firszt, and Eisenberg [2]. These investigators calculated the per unit and annual savings, in dollars, if an American buys one of 44 brand-name medications from a Canadian Internet pharmacy rather than online from an American chain pharmacy. They found that Americans can save an average of 24% if they purchase their medications from Canadian Internet pharmacies rather than one of the major online American chain pharmacies. They also found that only one of the 44 brand-name medications was less expensive in America. Thus, brand-name medications are often less expensive when purchased from Canadian then when purchased from an American drug chain pharmacy.

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According to Morris et al. [1], “increasing racial and ethnic diversity among health professionals...is associated with improved access to care for racial and ethnic minority patients.” However, they note that an all-inclusive health care workforce remains an aspiration. Currently, only about 12% of U.S. physicians are either Black or Hispanic. However, according to the U.S. Census, the percentages of African Americans in the U.S. population is about 18.3%. There are other racial and ethnic groups that are also underrepresented, including Native American, Alaska Natives, Native Hawaiians and other Pacific Islanders. Therefore, achieving the goal of a truly representative health care workforce will require a change in the racial and ethnic composition of the student body in our national medical schools.

The percentage of women enrolled in medical school, in the last few decades has doubled, and now women are majority of medical students. However, the percentages of Black, Hispanic, and other racial and ethnic groups, enrolled in medical schools remain well below the national census percentages of these groups. The increase in the percentage of women over the study period coincided with a marked decrease in the percentage of White men, from 61.2% to 25.7%. However, the percentage of Asian men increased from 2.1% to 10.7%. Unfortunately, with African Americans men there was a decrease (from 3.1% to 2.9%). In addition, Hispanic men’s net change from 1982 to 2019 was minimal. Finally, the men and women who identified as American Indian, Alaska Native, Native Hawaiian or Pacific Islander composed less than 1% of the total enrollee population.

Morris et al. [1] also found that the diversity trends in the national medical student body were similar in public and private medical schools. Similar conclusions held for the four geographic regions in the study.

According to Morris et al. [1], these observations suggest that there is a persistent failure to substantially improve the racial and ethnic diversity of health care workers such as physicians. Racial and ethnic diversity is an important goal.

The reason this is an important goal is that when many people search for a doctor, they often look for a physician who is the same race or from the same culture. Public health officials have known for many years that non-white people have a higher rate of illness and death. These illnesses include a wide variety of health disorders, such as diabetes, hypertension, obesity, asthma, and heart disease. These difference in health care are, in part, the result of social-cultural, racial and economic injustice.

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There are always problems trying to predict the future, but the following are some of the changes we are seeing and some changes we might see in the future.

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## Robot Surgery

Dr. Albert B. Lowenfels wrote a paper called, “A Closer Look at Robotic Surgery Cost, Use, and Trends” where the use of robotic surgery at the University of California was examined and reviewed over ten years (2005–2015), when they had a total of 3203 robotic procedures. performed by 45 different staff surgeons. During this decade they had a fourfold increase in robotic surgery.

This increased use of robotic surgery was associated with a reduction of 1.8 days for the patient’s length of stay. However, there was an increase in costs. In addition, they found that after 2009, their readmission rates for the robotic procedures were 15%, compared to 23% for open procedures and these were significantly different.

During the 10-year period from 2002 to 2012, the authors of a single-center report [1] found that long-term survival based on the surgical approach to lobectomy for clinical stage I non-small cell lung cancer: comparison of robotic, video-assisted thoracic surgery, and thoracotomy lobectomy for managing early lung cancer. When these patients were matched by propensity score (i.e., age, sex, smoking, clinical stage, etc.), postoperative mortality and complication rates were similar. However, the robotic surgery yielded significantly more lymph nodes and a shorter length of stay. With follow-up, survival rates for robotic, video-assisted, and open surgery, were not significantly different.

## Video-Medicine

During the COVID-19 pandemic several things have changed in the practice of medicine. In my clinics, I see patients with neurological disease. Since I mostly see older patients, almost all my patients have been vaccinated and when they come into our hospital, they are given masks and asked to wear these masks all the time. Thus, both the patient and I are masked during their clinic visit and there is a very small risk of being infected with COVID-19. However, many of my patients do not want to come to clinic and want to use video communication. Some other patients and their families want us to just use the telephone.

Many people are promoting video medicine and there appears to be increasing interest in video-communication medicine as a primary means of patient care. Some states are mandating coverage of virtual video visits with the same reimbursement as an office visit. The companies that want doctors to buy their apparatus in order to provide medical video patient care, make statements such as, “Medicare has made substantial progress toward enhanced telehealth reimbursement” and “Telehealth can help your practice stay competitive in a more consumer-oriented healthcare market.”

The problem with using video, and especially the telephone, is that we cannot do a complete examination. In addition to obtaining a history of the patient’s current disorder, we can get a past medical history, a family history, and a review of symptoms. However, regarding the examination with video communication or telephone, we cannot do a full general physical and neurological examination. We can test some elements of a patient’s mental status, including tests of speech-language, working and episodic memory, and some executive functions (“name in one minute, all the words you can that start with the letter “f” but do not use numbers or names”). When examining the cranial nerves, if we use video, we can examine eye movements, facial, and tongue movements, but not assess a patient’s visual fields and facial sensation. In regard to motor examination, we can see if a patient can move their limbs but cannot test for mild weakness. We can learn if they can make accurate movements or have abnormal movements or poor coordination of their limbs. However, we cannot examine these patient’s resistance to passive joint movements, their deep tendon reflexes, and the presence of abnormal reflexes such as Babinski’s sign. We can ask the patient if they have any numbness, but we cannot test important sensory functions such as proprioception of the big toe position.

Traditionally, after a physician, such as a neurologist, finishes taking the patient’s history, and performing a complete examination, the physician speaks with the patient and the patient’s family in the office, explaining what he thinks is causing this patient’s problem, the possible tests this physician wants performed, the possible treatments and the prognosis. These things can be performed by means of video, but when you are actually in the same room with the patient, this conversation appear to be more meaningful to the patient and their family.

Therefore, a telephone-clinic is almost useless, and video medicine, while better than the telephone, still leads to an incomplete evaluation and should not be promoted, unless it would be dangerous for the patient and the physician to meet, in person.

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## Funding

Since the 1940s when penicillin was first introduced until now, there have been many wonderful advances in medicine and these advances has made important contributions to reduce the suffering of people and prolong the length of their life. Many of these advances were made possible because of funding from the National Institute of Health (NIH). Currently, however, only about 18% of the proposals submitted to NIH receive funding.

Research funding in many countries derives from a government's research bodies and private organizations. This money is used for equipment, salaries, and other research expenses.

The National Science Foundation reported in 2015 that in America federal agencies provided only 44% of the \$86 billion spent on basic research. The National Institutes of Health contributed \$26.4 billion and pharmaceutical companies collectively contributed \$27 billion. However, both contributions are less than 30% of the money spent on this research. Other contributors include biotechnology companies (19%) and medical device companies (10%). From 1995 to 2010, NIH support for biomedical research increased from 11 to 27 billion dollars. However, even with this large increase in federal spending, the number of citations of publications remained unchanged. Since 1980 the share of biomedical research funding from industry sources has grown from 32% to 62%. In part, this has resulted in the development of numerous medical advances. The relationship between industry and government-funded research in the US has seen great movement over the years.

The National Institutes of Health, state on their instruction page, "Initial preparation. We advise you to allow two months or more of dedicated time to prepare for a simple R01." Two months for a physician is very expensive. As discussed below, the average family physician, who is one of the lowest paid physicians, makes on average \$231,000, or about \$20,000 each month. Considering that this physician would have only about an 18 percent chance of being funded, it would seem to be an unwise decision to write and submit a grant proposal. As mentioned, when I was on a study section, I learned that many excellent proposals were not funded. Therefore, I always wondered, "What have we missed?" Fortunately, there is a simple cure for this problem. Allocate more money for research funding.

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## Tenure

Academic freedom is essential in teaching and research. There are several definitions of tenure. My favorite is the following, "the right to keep a job, such as being a professor at a college or university for as long as you want." Tenure systems are

currently used in almost every university in the United States. The current concept of tenure in America was initiated by the American Association of University Professors in 1940. The development of tenure was formulated and endorsed by the Association of American Colleges and Universities. Currently, the concept of tenure is endorsed by over 250 colleges and universities. Academic tenure in the United States is a contractual right that grants a teacher or professor a permanent position of employment at an academic institution such as a university or college. Historically, tenure has served to protect teachers, and investigators from dismissal without just cause, and allowed development of thoughts or ideas considered unpopular or controversial among the community.

One of the best examples of how tenure might protect investigator who disagree with the leadership of a country and/or its religious leader is the story of Galileo. Galileo di Vincenzo Bonaiuti de' Galilei was an Italian astronomer who used the telescope for scientific observations of celestial objects. Using his telescope, he reported his observations of the four largest satellites of Jupiter, observations of Saturn's rings, and he performed an analysis of sunspots. However, Galileo's greatest and most important observation was providing support for the Copernican theory of heliocentrism (e.g., instead of the sun rotating around earth, the earth was rotating around the sun). His findings were opposed by the Catholic Church in 1615 and were investigated by the Roman Inquisition. They concluded that heliocentrism was not only incorrect but was also heretical since it contradicted the Bible. Galileo was found "vehemently suspect of heresy." He was required to reverse his findings about heliocentrism. In addition, he was sentenced to formal imprisonment. On the following day, he was sentenced to house arrest, and remained under which he remained for the rest of his life. His writing was banned; and any publication of any of his work was forbidden. In 1992, Pope John Paul II acknowledged that the Catholic Church had erred in condemning Galileo for providing evidence that the Earth revolves around the Sun ("heliocentrism").

Many academicians think that tenure is essential in academics because it protects academic freedom. Tenure at many universities, however, depends primarily on research publications and funded research grants. After a teacher-professor earns academic tenure, they do not have to worry about losing their job except in the two possible circumstances. One such situation is considered "termination for cause," or the dismissal of an educator for a specific reason. Although rare, tenured professors have been asked to forfeit employment for several reasons, such as immoral behavior, incompetence, violation of their universities policies and rules. However, the majority of clinicians at medical schools, primarily see patients and teach. Some also perform clinical research. It has, therefore, never been clear to me why physicians and surgeons at universities would need tenure.

In 1994, a study published in *The Chronicle of Higher Education* found that "about 50 tenured professors in the United States are dismissed each year for cause [2]. In addition, although tenure does protect the occupant of an academic position, unfortunately, it does not protect against the university eliminating that position.

In 1985 the United States Supreme Court's decision in the case of the Cleveland Board of Education versus Loudermill, the court ruled that a tenured professor-teacher cannot be dismissed without an explanation of the employer's decision. The professor-teacher must also be given an opportunity for a hearing.

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## Training

In order to become a practicing physician in the United States of America, a person usually must go to college, medical school and then take an internship and residency. College often takes four years to complete. Medical school also usually takes four years to complete, the internship one year and residency about three or four years. Thus, for example, to become an ophthalmologist who removes cataracts, it takes about 12–14 years after graduating from high school to be a board-certified ophthalmologist. Removal of a lens takes knowledge about how to perform this procedure. The first reported removal of a cataract from the eye occurred in Paris in 1748. The early techniques involved removing the entire opaque lens in one piece using an incision that went halfway around the circumference of the cornea. The evolution of smaller surgical incisions was matched by the development of new lens implants created out of different materials (such as acrylic and silicone) that could be folded to allow the lens to be inserted through a tiny wound. Ultrasonography is used to break the lens into minute fragments that can be aspirated. A combined ultrasonographic, irrigation, and aspiration allows the removal of any lens through a small incision (< 3 mm). The development of new lens implants using different materials, which could be folded to allow the lens to be inserted through a tiny wound.

There are many other medical-surgical specialties where the knowledge of “who needs this procedure?” and “how to perform this procedure” are important. But why do these physicians, after they graduate high school, must go to school for 12 more years just to learn how to perform this one procedure? Could a trained technician perform this?

Most of the debt that physicians have accumulated from the cost of college and medical school. The median medical school debt, not including loans from pre-medical education, was about \$200,000 among 2019 graduates with medical school loans. The median debt for premedical loans was \$25,000.

Newly minted doctors who attended private medical schools tend to have more student debt than those who attended public ones, according to AAMC's data. The median student loan balance was \$215,005 among graduates with debt from a private medical school, compared to \$193,186 among medical graduates with debt from a public one. Thus, in addition to making enough money for essential items like food, housing, young physicians who are completing their residency, have huge loans to pay back and this might have a great influence on the specialty that they select.

I believe that currently, the most difficult job is being a primary care physician, pediatrician, or a general internist. The reason being, is that the first thing they must



do is after taking a history of the present illness, as well as a patient's past medical history, is to then perform a full examination. After the history and examination are completed, these physicians must develop a differential diagnosis. This diagnosis should first be anatomic, such which organs is malfunctioning. Then the decisions about what are the possible causes of this malfunction may be (e.g., infection, tumor, trauma, degenerative disease, vascular disease, etc.) The physician then might perform the tests that can help to identify the possible disease with which this patient is suffering.

Those doctors who perform procedures make much money. For example, the average orthopedists' pay in 2019, ranked highest at \$482,000, followed by plastic surgeons, at \$471,000 and otolaryngologists at \$461,000. Unlike those physicians who are performing procedures, correctly performing a full evaluation requires a physician who has a detailed and broad knowledge of diseases to perform a complete and detailed history and examination. However, many of the physicians who often perform these complete and complex examinations, such as pediatricians, make at average of \$225,000 a year and those who practice family medicine make on average \$231,000 a year. Fortunately, most, but not all medical students do not select a specialty based just on income.

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## **Education of the General Population.**

According to Robert Hahn's and Benedict Truman's paper, *Education Improves Public Health and Promotes Health Equity* (2015), researchers and practitioners have investigated three principal relationships between education and health. The first relationship is that health is a prerequisite for education. For example, hungry children or children who cannot hear or see well, are hindered in their learning. Second, education about health that does occur in schools "is a central tool of public health." Third, physical education in schools teaches about the importance of physical activity for developing and maintaining health. In this paper the authors discuss the relationships between education and health. They propose that education as a personal attribute is a central conceptual component and essential element of health, and they summarize the extensive literature demonstrating that formal education is an important factor in maintaining and improving health. Those programs that close gaps in education between low-income or racial and ethnic minorities and higher-income and majority populations are needed to for health equity. Health practitioners, teachers and health departments can and should collaborate to implement educational programs and policies that promote health.

These authors also summarize the extensive literature demonstrating that formal education is an important contributing element of health. For example, there is evidence of a dose-response correlation between years of education and several health-related risks. A survey of adults over 25 years of age, revealed that the prevalence of several risk behaviors is higher among those with fewer than nine years of formal education and those who have nine to 12 years of formal education have a decline in risk and this decline continues with additional years of education. Wages and

income are not health outcomes but are closely linked with health outcomes because higher wages provide access to health care, healthy food, and a safe environment. Whereas educational attainment is strongly associated with health, this association increases with aging. With increasing age, the gap in symptom-free days increases between those with a college degree, those with a high school education and those who do not have a high school degree. The rates of circulatory diseases, diabetes, liver disease, and several psychological disorders have higher rates among those with lower level of education. There is also evidence that there is a strong association between educational attainment and mortality from a variety of diseases (CDC National Center for Health Statistics. Health, United States, 2008. Hyattsville, MD). For example, in 2005 a man at age 25 living in the United States, who has less than a high school education could expect to live to the age of 69.2 years. In contrast, a man with a graduate degree could expect to live more than 15 years longer than a man who did not complete high school. At age 25 years, a woman in the United States with less than a high school education could expect to live to age 74.9 years; however, a woman with a graduate degree could expect to live about to the age of 85 Rostron, Boies, and Arias [3].

In our society, the child's education is highly correlated with the level of their parent's education. Therefore, unfortunately the children of parents with little education, who could greatly benefit from higher levels of education, are least likely to receive this education [4].

We must learn the methods by which we can correct this problem.

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