Mod.28

MODULE 28: SCHIZOPHRENIA: PHARMACOLOGICAL TREATMENT

AUGUSTINE
ST. ELIZABETH'S HOSPITAL

George Page (V/O):
Before the advent of modern anti-psychotic medications, most sufferers of schizophrenia were unable to live or function independently.

AUGUSTINE (off meds)

Dr. Bigelow (V/O):
Could you share with us something that's going on in your mind? How are you feeling?

AUGUSTINE

Augustine (O/C):
I'm feeling okay. There's kind of a mantle on my mask. All I have is thoughts going across my head of all sorts.

DR. BIGELOW

Dr. Bigelow (O/C):
Do they make sense?

Augustine (V/O):
No.

DR. BIGELOW

Dr. Bigelow (O/C):
Augustine, is there anything that you'd like to tell us or ask us?

Augustine (V/O):
No.

AUGUSTINE

Dr. Bigelow (V/O):
You're about getting ready to change your medications aren't you?

AUGUSTINE

Augustine (O/C):
Yes.

Dr. Bigelow (V/O):
When's that...

AUGUSTINE

Augustine (O/C):
I'm looking forward to that.

Dr. Bigelow (V/O):
You're looking forward to that?

AUGUSTINE

Augustine (O/C):
Yes.

DR. SCHEIBEL
UCLA MEDICAL CENTER

Dr. Scheibel (O/C):
I can remember when I was a resident in psychiatry, we had nothing specific with which to treat our patients, except perhaps shock treatment which seldom helped, or cool baths. We had to tie them into a bathtub under a canvas restraint and it was a pretty awful situation. I remember that I went away for a year of fellowship abroad, 1953 and 54, and when I returned, the new drug chlorpromazine, which we knew as Thorazine, had just been made available, and it was the difference between night and day. Suddenly, we had an agent, which while not curing the disease, made it possible for at least some of these patients to be reclaimed, to even live a half way normal life with their families and in some cases going out to work, so that the field changed enormously at that point.

BRAIN VISUAL

George Page (V/O):
Anti-psychotic drugs alleviate the symptoms of schizophrenia by normalizing the chemistry of the brain. In the brain,

NEURAL NET

George Page (V/O):
the nerves never actually touch. They're separated by small gaps known as synapses. Chemicals released from one nerve ending attach to the surface of the next nerve ending causing the nerve to respond electrically. In the case of schizophrenia, there seems to be excessive activity at the synapses that use the neurotransmitter, dopamine. Anti-psychotic drugs reduce this activity.

DR. BARCHUS
STANFORD MEDICAL SCHOOL

Dr. Barchus (O/C):
Well, it was found relatively quickly that these neuroleptics all seemed to act on one particular type of neurotransmitter, the so-called dopamine system, nerve cells which use dopamine as a transmitter. And that they block the receptors for dopamine over here. So that led rise to a theory of schizophrenia that schizophrenia is a relative excess of dopamine. We don't know if it's a true excess, or just in some way or another, there's a balance and we're restoring it to normal by blocking the effects of dopamine.

AUGUSTINE

George Page (V/O):
The effectiveness of anti-psychotic drugs in alleviating symptoms is shown in Augustine's behavior after four weeks on medication.

Augustine (O/C):
I wanted to become a patriarch, a doctor of the church, a world leader. Things of that sort.

FOUR WEEKS LATER

Dr. Kirch (V/O):
Fairly grand ideas.

AUGUSTINE (ON MEDS)

Augustine (O/C):
Yeah. I don't have them anymore.

Dr. Kirch (V/O):
Back then did you really believe those things? Were you really caught up in them?

Augustine (O/C):
I was caught up in them, but I didn't believe I could make it.

Dr. Kirch (V/O):
You didn't think you'd make it?

Augustine (O/C):
Right.

Dr. Kirch (V/O):
What do you think now? What do you think the future holds for you now?

Augustine (O/C):
Work.

Dr. Kirch (V/O):
Work?

Augustine (O/C):
Work.

DR. SCHEIBEL

Dr. Scheibel (O/C):
Very recently, there have been other exciting, exciting things happening. Second and third generations of drugs, rather

Dr. Scheibel (O/C):
different molecules, have become available. The exciting thing is they seem to have the capacity to help that 25 to 30 percent of patients who we never could touch before with the usual neuroleptic or psychotic type of drugs. These drugs seem to work in a slightly different way. They work on different molecules in the brain, we call them receptor systems, and it may well be that by changing the structure of the drug molecule that we're dealing with, we may gradually close in on most of these sick molecular components in the brains of schizophrenics and eventually we may be able to help all of our patients. But again, I must stress that this is amelioration and stabilization. It's not cure yet, and cure is what we want. In other words, we have to learn how to prevent.

STEVE AND DR. BIGELOW

Dr. Bigelow (O/C):
You're taking a research medication now, aren't you?

STEVE

Steve (O/C):
Yes, it's very helpful to me.

Dr. Bigelow (V/O):
Well, that's good news. What's it doing for you?

Steve (O/C):
Well, it clears up my mind for thinking and I feel a little healthier.

Dr. Bigelow (V/O):
Good.

SHOT OF DOCTORS

Dr. Barchus (V/O):
One can imagine a day in the future, when we will have sub-typed the illness, both biochemically and behaviorally and will be able to treat the individual ideally with more specific medication and with a better long-term prognosis. That's sort of a dream that propels people like myself to continue our research.

DR. BIGELOW

STEVE

Dr. Bigelow (V/O):
Steve, I see you moving your lips as if you are saying something. But I don't hear anything.

Steve (O/C):
I'm not saying anything.

Dr. Bigelow (V/O):
Are you aware that you are moving your mouth as if you were speaking?

Steve (O/C):
No I wasn't.

SHOTS OF DOCTORS

Dr. Bigelow (V/O):
You weren't. Is it possible you were hearing things when your mouth was moving?

Steve (V/O):
No.

Dr. Bigelow (V/O):
Thanks for coming in Steve.

Mod.29

MODULE 29: AUTISM

CHILDREN DISPLAYING AUTISM
AUTISM NE CENTER BOSTON

George Page (V/O):
The developmental disorder known as autism was first described in 1943. It appears in about 5 out of every 10,000 births and occurs more often in boys than in girls. It is found throughout the world in families of all racial, ethnic, and social backgrounds.

AUTISM NE CENTER BOSTON

George Page (V/O):
As recently as the 1970's, researchers believed that autism was environmentally and psychologically based. And that it was caused by parenting style, especially mother-child interactions. This long-held belief brought blame and humiliation to parents of autistic children. It affected the diagnosis of autism, as well as the intervention strategies used in educating and caring for autistic individuals.

DR. BAUMAN AND DR. KEMPLER

George Page (V/O):
Among the leading investigators of autism are Dr. Margaret Bauman, Director of the Autism Research Foundation in Boston, and her colleague, Dr. Thomas Kempler. Their team has been studying brain tissue at autopsy

BRAIN SLIDES

George Page (V/O):
hoping to find clues to the neurological basis of the disorder. They compare tissue from people who suffered from autism with tissue from normal individuals. They have found some remarkable differences.

BRAIN SLIDES

DR. BAUMAN

Dr. Bauman (O/C):
Our research uses a technique called "whole brain serial section." and this is a very old technique . It's also a fairly expensive technique and not very glitzy. Basically what we do is we take an entire brain and we embed it in something called celloidin which firms it up and it has to sit there about 8-10 months, until it's hard enough for us to do something with. After which we section it in a very standardized protocol. And we can do this with an age and sex matched control as well so that all the material that we get is processed identically. We then take that material and we use a comparison microscope which is basically two microscopes next to each other connected by a bridge. And we can then take the same sections out of each brain a normal and an age matched autistic brain and we can look at these identical sections side by side

COMPARISON MICROSCOPE

DR. BAUMAN

ul

Dr. Bauman (V/O):
at the same field of view, with the same magnification and we can compare. And I think that's been extremely usef

because I think without that technique we would never have found what we found. The brain findings here are very subtle and they are not able to picked up by more standard methods of looking at neuropathology. So while this is a old technique and an expensive technique, I think in this circumstance it is the only way that you can survey a brain when you don't know what you are looking for. We didn't have any idea of what we were looking for when we got started. And I think this is the only way that you
can really survey a brain with
any kind of comfort.

DR. BAUMAN

Dr. Bauman (O/C):
By using the standardized technique, we have been able to identify two circuits within the brain, and by circuits we mean that the abnormalities are not site specific. That is to say that there are a number of sites which may be at different areas throughout the brain that are connected to each other and which talk back and forth to each other if you will.

VISUAL OF BRAIN

DR. BAUMAN

Dr. Bauman (V/O):
Those two circuits include the limbic system which is responsible for memory, learning, behavior, emotion, and the cerebellar circuit which was in some ways more of a surprise to us at that time. The abnormalities have been found using this whole brain serial section technique and the abnormalities consist of two different abnormalities actually. The limbic system looks like a developmentally more immature system. It's not brain damage. There isn't cell loss there. In fact, the cells are too many, too small. There are more neurons than we would expect to see and the ones that are there are too small. And it looks like the system of a much younger person...not only in terms of the patient's chronological age, but in terms of the rest of the brain itself. The cerebellar circuits look a little bit different in that there are a number of cell populations that are missing. We're not clear whether or not those cell populations arrived at their designated site and then later disappeared or whether they never arrived in the first place. But it's

Dr. Bauman (V/O):
the population that helps us speculate about when this might have occurred in the prenatal period. So in some ways they are somewhat different but they give us two pieces of information that I think are helpful.

AUTISTIC CHILDREN

George Page (V/O):
Dr. Bauman's research contradicts the theory that autism is a psychological disorder. Rather, it is associated with with brain malfunction. This may be traced to a lack of normal neural growth and development during the prenatal period.

DR. BAUMAN

Dr. Bauman (O/C):
This is not something that happens at birth. This is not something that happens because you were a bad mother. This is something that was preprogrammed sometime early in development sometime prior to the end of the second trimester. I don't think we are in a position at this point to say just when that happens or in fact what the cause is, but we can at least make some estimate about the timing.

COUNTRY CANADA: TEMPLE GRANDIN

George Page (V/O):
Growing up with autism doesn't necessarily mean that a person cannot achieve a high level of professional competence. In fact, for one person, it turned into an advantage. Meet Dr. Temple Grandin, a professor of animal sciences at Colorado State University.

COUNTRY CANADA: DR. GRANDIN

Narrator on movie (O/C):
Dr. Grandin.

Dr. Grandin (O/C):
It's a real pleasure to be here today, and we'll start out...I mean I was very autistic and very messed up as a young child.

TEMPLE AS A CHILD

George Page (V/O):
Temple Grandin's professional achievement would never have been predicted on the basis of her early childhood. She was three years old before she spoke her first words. She was emotionally withdrawn. Doctors recommended that she be institutionalized in a facility for the mentally disabled. But special attention from her parents and teachers enabled her to succeed in school.

TEMPLE GRANDIN

Temple (O/C):
Well the first thing was being put into a really good educational program by age two and a half. I can't emphasize the importance enough of early intervention in autism. I had about 20,25 hours a week in a small classroom. I also had a nanny that spent many hours a day playing games with me. It's very important to keep autistic children engaged with the world because if you let them tune out they are just going to go deeper into autism and deeper into all the sensory problems.

COUNTRY CANADA: TEMPLE TALKING BEFORE STUDENTS

Temple (O/C):
Here in Canada, the two biggest plants in Alberta that process about a half of all the feedlot cattle in Canada, they use systems I've designed. So when you go get a steak here in Canada, you've got a 50% probability it's been through one of my systems. And I don't think that's doing to badly for somebody they thought was mentally retarded and they wanted to send me away to an institution.

COUNTRY CANADA: TEMPLE TALKING BEFORE STUDENTS

George Page (V/O):
Unlike many autistics, Dr. Grandin has been able to overcome the barriers to social interaction. Her progression from social isolation to prominence in her field has been remarkable. It is due, in part, to her autism and the special way it enables her to view the world.

DR. GRANDIN

Temple (O/C):
I think totally in pictures. I don't have any language based thought. Well animals also would think in pictures. I think like videotapes in my head. And it's so easy for me to imagine what it would feel like to be a cow in certain situations.

COUNTRY CANADA: TEMPLE WITH CATTLE

George Page (V/O):
This special ability to think in pictures allows her to perceive the world as an animal would. Her special affinity for cattle gives her a humane approach for designing cattle facilities. The holding pens she designs have gentle curves, to take advantage of the cattle's natural tendency to circle, and also to obscure what lies ahead.

COUNTRY CANADA: TEMPLE WITH MANAGER

Temple (O/C):
...that the animals think they are going back to where they came from. They are coming on around and they think they are going back to the corrals.

SQUEEZE MACHINE

George Page (V/O):
When feeling stressed, Dr. Grandin takes advantage of another lesson she learned from observing cattle: she calls it her "squeeze machine."

DR. GRANDIN

Temple (O/C):
Well when I got into puberty, I started having very intense anxiety attacks. It felt like a total state of stage fright all the time. I once told a TV reporter it would be like first time you ever interviewed somebody really big and you were just so scared you just didn't know what to do. That's the way I felt all the time for absolutely no reason, and I was desperate for relief from this. Well, one day I watched cattle going through the squeeze chute at my aunt's ranch. And I noticed that some of the animals when they are put in the squeeze chute tended to relax. And so I thought, well I ought to try this. So I went and I tried it, and it would temporarily relieve the nervous attacks. Many autistic children

seek pressure. I've had parent after parent say to me: my child gets under the sofa cushion; my child gets under the mattress. Therapists will often use pressure, getting under mattresses, to help calm down and relax children with autism. So then after trying the cattle chute at the ranch I then built a cattle chute-like device that I could get into, that would apply pressure, where I could

Temple (O/C):
control the amount of pressure. At first, I tended to just sort of pull away from it, but then gradually I learned to tolerate more pressure. When I was a little child, I couldn't stand to be held because I just got this engulfing, tidal wave stimulation just coming over me.

SQUEEZE MACHINE: TEMPLE IN HER APARTMENT WITH SQUEEZE MACHINE

George Page (V/O):
When Temple feels the need to relax, she crawls into her own version of a cattle chute, which she keeps in her study.

SQUEEZE MACHINE

Temple (O/C):
I'll demonstrate to you how it works. You get in here like this. You put your head through here like this. And by working this control

SQUEEZE MACHINE
TEMPLE IN SQUEEZE MACHINE

I can let a little pressure off; I can put a little bit of pressure on. Now the things that bother cattle are the same things that upset a person with autism, high pitched noise, sudden jerky motion, With a hyperaroused nervous system, I'm just always constantly vigilant. Any little stimuli just sets the whole nervous system off. You know

Temple (O/C):
being an autistic person is sort of like being a wild animal out in the woods full of predators. I'll stay in here anywhere from fifteen minutes to forty five minutes. Sometimes I fall asleep in here.

COUNTRY CANADA: DR. GRANDIN

Dr. Grandin (O/C):
A lot of things that people consider important, I don't consider important. People get concerned about having you know a gold plated bathroom, having a corner office. That doesn't mean anything. You know I'd like to say when I get to the top of the stairway to heaven, that I did something of value for society.

COUNTRY CANADA

George Page (V/O):
Temple Grandin is certainly an extraordinary example of

a person able to overcome the effects of autism. But what does the future hold for the countless others stricken by this disorder?

DR. BAUMAN

Dr. Bauman (O/C):
There are many issues that remain to be investigated. I think the anatomy has allowed us to say, yes, there is something definitely wrong with these brains. We now know where that is

Dr. Bauman (O/C):
and we're comfortable that those findings are reasonably consistent from case to case. But that's not going to help the kids a whole lot. We need to be able to take it to the next step to find out what it is about these brains that is abnormal other than the structure. And in all probability, there is a neurochemical profile that goes along with this abnormal structure. And I think that, in mind at least, is the next step: that we need to look at the brain tissue from a neurochemical perspective to try to find out what's abnormal about the chemical profile here. If we can pinpoint that, and it may be more than one thing. I don't know that it's necessarily going to be

AUTISTIC CHILD

one neurochemical substance, and it may be several, or it may be different proportions in different people. But I think in all likelihood, there's going to be some abnormality that goes along with this abnormal structure. If we can do that, then we can think about some more specific treatments for these children.

Mod. 30

MODULE 30: UNDERSTANDING THE BRAIN THROUGH EPILEPSY

JASON HAVING SEIZURE

Dr. Dreifuss (V/O):
Jason is suffering, or we believe him to be suffering from a condition which is almost pure epilepsy, or what we call primary epilepsy.

DR. DREIFUSS
University of Virginia
VA Medical Center
Charlottesville, VA

Dr. Dreifuss (O/C):
Epilepsy is in some ways a caricature of normal brain function. It is nature's experiment of how the brain works and when we look at a person in an epileptic seizure, it's really a distortion of what one...expects normal brain function to be. But it does teach us a lot about the circuitry of the brain and how it works.

ALLISON ANIMATION
Brain model

George Page (V/O):
If we could penetrate a normal brain with a high-powered microscope and observe neurons in action, we might see them switching on and off in an orderly fashion.

Crystal brain

Neural net

During an epileptic seizure, Jason's brain undergoes an electrical storm. The discharge begins in the center of the brain. Then the rest of this brain is switched on, uncontrollably. For a few seconds,

George Page (V/O):
the storm encounters no resistance. It short-circuits every one of the brain's more complex functions: movement, mood, thought: everything.

DR. DREIFUSS' OFFICE
Charlottesville, VA

Dr. Dreifuss (O/C):
Most transactions in the nervous system are conducted...as electrical messages...and the actual...

ALLISON ANIMATION
Synapse

Dr. Dreifuss (V/O):
conduct of them...electrical impulse across the...junction between nerve cells is a chemical process.

George Page (V/O):
In the brain, nerves never actually touch. They're separated by small gaps known as synapses. Chemicals released from one nerve ending attach to the surface of the next nerve ending and cause the nerve to respond electrically. There are two types of chemicals, or neurotransmitters: one type excites the next nerve, causing it to fire. The other inhibits the next nerve from firing.

edit "synapses"

DR. DREIFUSS' OFFICE

Dr. Dreifuss (O/C):
And we feel that in Jason's case...he has primary epilepsy, which we think is due to a relative lack of an inhibitory neuro-transmitter system, allowing normal discharges to become abnormally dispersed through the nervous system.

ALLISON ANIMATION
Neural Net

Dr. Dreifuss (V/O):
and during this time his brain ceases its normal function.

JASON'S BEDROOM
JASON HAVING SEIZURE

Dr. Dreifuss (V/O):
He loses contact. His eyes feel glazed. He tends to drop forward, and..and then almost immediately, his...seizure is again over and he's back to normal.

JASON IN BED
BLUE RIDGE HOSPITAL

George Page (V/O):
Jason stayed at Blue Ridge Hospital in Charlottesville, Virginia, for six weeks, under Dr. Dreifuss' care. One goal was to help him overcome his horror of medication. The other was to induce seizures through deep-breathing, so that the electrical discharges of his brain could be monitored. Dr. Dreifuss would then be able to prescribe the drug most appropriate for his epilepsy.

Nurse (V/O):
You're doing great. Come on. One, two buckle my shoe. What did I say Jason?

Jason (O/C):
One, two buckle my shoe.

JESSE SALB'S EEG TOPOGRAPHIC MAPS

George Page (V/O):
An epileptic seizure shows up clearly in Jesse Salb's images of the brain. The electrical storm of epilepsy strikes like this...slowed down we can see how it blocks the normal functioning of the brain, with light colors representing positive electrical charges, darker ones, negative charges.

INT. UNIVERSITY OF VA. MEDICAL CENTER

George Page (V/O):
Doctors have tried to control epilepsy chemically for almost 300 years. Today, one effective new drug is valproic acid, under development since the 1960's, the medicine Dr. Dreifuss ultimately selected for Jason.

BLUE RIDGE HOSPITAL

JASON

While we cannot be certain how valproic acid works in Jason's brain, Dr. Dreifuss suspects the medication encourages the presence

ALLISON ANIMATION Neurotransmitters	George Page (V/O): of a neurotransmitter called GABA. GABA is a chemical that inhibits firing. It seems to control the wild electrical discharge of epilepsy. It seems to keep the excitatory chemicals in check.
DR. DREIFUSS	Dr. Dreifuss (O/C): Now, in Jason's condition, the seizure...that he has is being to some extent, controlled by our being able to influence the amount of GABA in his nervous system by the administration of this drug.
JASON PLAYING BASKETBALL	George Page (V/O): For Jason, seizure control has been made possible by anti-convulsant or anti-epileptic drugs. For others however, seizure control is not possible through medications and alternative treatments are being tried. One of those is to surgically remove the part of the brain causing the seizures.
ASHLEY HORRIGAN CLIMBING TREE	George Page (V/O): Ashley is 14 years old and she has had epilepsy since she was 4. Until surgery 7 months ago, she was

George Page (V/O):
unable to climb a tree, play at the park or spend the night away from home. The risk of a seizure was too great. Her mother, Terri, describes what Ashley's seizures looked like.

TERRI HORRIGAN/CSU

Terri Horrigan (O/C):
There's times when Ashley would have a seizure and she would stand up and she could walk about, and she would have automatic lip smacking, and automatic movements, and she would be pulling at her shirt or something and she would...and you could call her name, and she'd say "huh?" You'd say, "Ashley, are you okay?" "Yeah." "What color is your shirt?" "Ashley, what's your teacher's name?" "Uh." And you'd say, "Ashley, are you okay?" "Yeah." Pretty soon she'd rub her nose, and she'd be, "Oh, I'm just so tired." "I'm really tired; I just want to lay down." And then you knew that if she did sit down and lay down that she probably had a seizure. And if you

Terri (O/C):
could ask her, "Ashley, you know, do you remember me asking you any questions or do you remember anything I said?" She wouldn't remember anything.

ASHLEY AT SCHOOL

George Page (V/O):
Before her surgery, Ashley explained to her classmates the operations and testing procedures she would undergo at Swedish Medical Center in Denver, Colorado.

Ashley (O/C):
It can be very scary.

SWEDISH MEDICAL CENTER
TERRI AND ASHLEY

George Page (V/O):
The techniques involved in Ashley's case will have risks.

Terri (V/O):
One would be to be left mute, one would be paralysis, one would be hemorrhage, uh, stroke. The first step is to discover what is causing Ashley's epilepsy.

ASHLEY

DR. MICHAEL HANDLER, M.D.
Swedish Medical Center
VIEWING SCANS

Dr. Handler (O/C):
We don't see a reason on the films, for her to be having seizures. That's why we have to go after it electrically, we have to go find it electrically.

PREP FOR SURGERY

George Page (V/O):
A grid of electrodes will be placed on the surface of her brain. These electrodes will help doctors make a map of her brain functions. The surgeon must first cut through three layers: Ashley's scalp, her skull, and the brain covering.
Underneath, is Ashley's brain.

SURGERY

C/U BRAIN

FAMILY IN WAITING AREA

George Page (V/O):
Down the hall, her family waits.
With the brain exposed, the surgeon puts the first electronic grid in place. In all, six grids will be used to make a window into Ashley's brain.
The site is closed.
With the grids in place, she will live with them inside her head for a week.
When a seizure occurs, the grid will show doctors its location. Ashley will then return for surgery to remove the part of the brain that's causing her epilepsy.

SURGERY

C/U GRID

POST-SURGERY

C/U ASHLEY POST-SURGERY

George Page (V/O):
But if the doctors find that the brain tissue causing her seizures is the same tissue that controls

	George Page (V/O): a major function, such as speech or sight, then Ashley must make a choice: either lose that function or live with her seizures for life.
DR. PAUL LEVISOHN, M.D. SWEDISH MEDICAL CENTER	George Page (V/O): Ashley's doctor, has mapped out those portions of her brain that affect speech, memory, and motor ability. But he still doesn't know what part is producing her seizures.
ASHLEY IN HOSPITAL BED	Finally, Ashley has a seizure. It's exactly what the doctors had hoped.
DOCTORS VIEWING MAPS	Dr. Levisohn (O/C): The speech area is here, but the seizures are beginning down here.
ASHLEY	George Page (V/O): Ashley can now have the surgery without fear of losing other critical functions, but there are still risks.
DR. LEVISOHN AND ASHLEY	Dr. Levisohn (O/C): 80% likelihood that it's going to happen, but there's a small chance that despite everything we've done, we didn't find the right place and that your seizures will continue.

ASHLEY

Ashley (O/C):
I think it's all worth it.

PREP FOR SURGERY

George Page (V/O):
This is a dangerous procedure. The surgeon is going deep inside Ashley's brain using a microscope to identify the critical tissue. When he locates the area that's producing seizures, he will remove it. He must be thorough enough to remove the entire section and yet be very careful not to damage anything else. The surgery takes over six hours.

C/U BRAIN

SURGERY

WAITING ROOM

ASHLEY POST-SURGERY

George Page (V/O):
The operation is over but the question remains, is the epilepsy gone?

ASHLEY AT SCHOOL

George Page (V/O):
Two weeks later, Ashley returns to school without having had a single seizure. Now if the stress of going back to school does not trigger a seizure, it will indicate that the operation has been a success.

TERRI HORRIGAN AND ASHLEY

Terri (O/C):
There are not very many

Terri (O/C):
people that would go through it with the bravery that she had. But you can see that she does have hair. Now wouldn't you be proud of her if she was your daughter and went through all that.

Students (V/O):
Yeah. (Clapping)

ASHLEY

George Page (V/O):
Before surgery, Ashley had some mild verbal memory and word finding problems. Since surgery, her word finding is better, but memory difficulties persist.

ASHLEY CSU

Ashley (O/C):
For school, for like homework, I'll have to write down what I have and then the teachers like check the homework. If I'm missing something, then they like write it down for me to do because sometimes I just forget what I have.

ASHLEY PLAYING

George Page (V/O):
But for Ashley, mild memory difficulties are a great tradeoff for being free from seizures. She is now able to do all the things any child her age would want to do.

Mod-31

MODULE 31: BRAIN TRANSPLANTS IN PARKINSON'S PATIENTS

TREMBLING HAND

George Page (V/O):
Parkinson's Disease is a relatively common neurological disorder, in which patients slowly develop rigidity, tremor, slowness of movement, and difficulty maintaining balance.

INT. DR. DAVID MARSDEN;S OFFICE
Institute of Psychiatry
DR. MARSDEN
VIDIFONT 12
Dr. Marsden
King's College Hospital
Medical Center, London

Dr. Marsden (O/C):
The muscles themselves are normal; the nerves supplying the muscles are normal; the spinal cord and the local mechanisms for controlling muscles are entirely normal, and, indeed, even the more sophisticated motor mechanisms coming from the brain itself are capable of functioning normally.

EXT. LONDON NEWS
England

Dr. Marsden (V/O):
Somebody with Parkinson's Disease, given a big enough stimulus, may leap into action in an amazing way. The classical example is the...patient who finds difficulty crossing the road because of his gait problems; he may be very slowly cruising across the road when, suddenly, the car horn goes, and he races to the

MAN WALKING

EXT. LONDON NEWS

Dr. Marsden (V/O):
opposite side, running, but when he hits the pavement, he can't walk again. So that the basic mechanisms are there; it's the starter motor

PATIENT ENTERS HOUSE
ALLISON ANIMATION
NEURAL NET

Dr. Marsden (V/O):
that won't work. And it looks as though the starter motor is this particular system of this particular chemical called dopamine.

George Page (V/O):
The neurotransmitter dopamine is the chemical substance, that bridges synaptic gaps between nerve cells within the basal ganglia. This chemical is being supplied to those synapses by a nearby region called the substantia nigra.

ALLISON ANIMATION
Brain model

George Page (V/O):
In sufferers of Parkinson's disease, this area wastes away. Without the dopamine it supplies, they cannot make full use of the motor programs that the basal ganglia provide.

FRENCH FOOTAGE
EXT. CLINIQUE
M/S MME. MOFFLET AND SON

George Page (V/O):
For Madame Mofflet in France, the disease has advanced considerably. For her, even to walk, her husband and son must give her minute goals to attain.

Mme. Mofflet (V/O):
I loved life. I loved everything. And really, the disease took everything away from me. It grabs you by the throat, and it's a horrible feeling; you feel as if you're about to choke.

INT. DR'S. OFFICE
MME MOFFLET

George Page (V/O):
At the age of forty-five, she would be housebound were it not for a kind of cure she's about to take: a so-called miracle drug that was introduced in 1970. Called L-DOPA, it's a drug the brain transforms into dopamine, restoring the victim of Parkinson's to near-normal movement.

NATURE MAGAZINE
PET SCAN PHOTO-COLOR

George Page (V/O):
In these remarkable PET scans, we can see regions of the brain that are active when a patient absorbs L-DOPA. In the center of the scan, the basal ganglia shows heightened activity as a result of the drug flooding in. It's effects in this central region are what cause those dramatic results.

FRENCH FOOTAGE
EXT. CLINIQUE DES MALADIES DU SYSTEME NERVEUX
MME. MOFFLET WALKING

Mme. Mofflet (V/O):
The minute I take the drug, I feel a gradual relief and everything becomes normal again. I'm much happier. I find myself singing often.

MME. MOFFLET

George Page (V/O):
But L-DOPA is neither a permanent cure, nor free from side effects, and scientists have begun to look for other cures. One of the most promising new approaches involves the implantation of fetal tissue into the basal ganglia of Parkinson's patients.

Dr. Curt Freed
University of Colorado
Health Sciences Center

Dr. Freed (O/C):
The idea of using fetal tissue to help patients with Parkinson's disease actually came from animal experiments that started about 15 years ago. Two groups in Sweden, one Lars Olson in Stockholm, and another group, Anders Bjorkland in Lund, in southern Sweden, did some critical experiments in the rat in which they showed that you could take dopamine cells from very early in fetal development when the rat embryo was about a half an inch long. You could transplant that into a rat model of Parkinson's disease and make that disease improve.

DR. OLSON'S LAB

George Page (V/O):
And Dr. Olson and his colleagues had shown in this laboratory that in animals several sorts of cell implants could take root in the brain. This kind of research proved that the animal brain can accept and exploit transplanted cellular material. It took ten years of painstaking work before this technique could be applied to even one human being. In experiments performed on mice, minute quantities of embryonic brain tissue were implanted into the basal ganglia of adult animals.

MICE

DR. LARS OLSON

Dr. Olson (O/C):
They will not be rejected because the brain is a...is what is known as an immunologically privileged site. That is to say, things grafted to the brain are not rejected the way they are in other parts of the body.

DR. OLSON'S LAB

George Page (V/O):
In the mice the implanted cells flourished, sending out new fibers and producing the missing neurotransmitter, dopamine. Exactly that same strategy has been applied to humans.

DR. FREED

Dr. Freed (O/C):
We at the University of Colorado were in at the beginning of this application to humans. That was in 1988. That's when the first experiments were being done around the world, and we performed the first experiment in the United States in a patient with Parkinson's disease.

SURGERY

George Page (V/O):
In their most recent clinical investigations, Dr. Freed and his colleagues use a double-blind procedure. This means that neither the patient, nor the doctors evaluating the outcome, know whether the patient is actually receiving the fetal transplant. This

George Page (V/O):
is the first such study authorized by the National Institute for Health in this new and controversial area of medical research.

SURGERY

Dr. Freed (V/O):
Half of the patients are getting such transplants, the other half of the patients are going to the operating room, are receiving exactly the same kind of treatment in the operating room, except that the patients do not actually have needles and tissue implanted in their brains, but they do have the skin incised over the skull. They have holes drilled in the skull but they do not have a needle implanted.

SURGERY

Dr. Freed (V/O):
The patients are awake during surgery, and so it is quite challenging to have the activity and timing in the operating room be very close, so that even the anesthesiologist who is in the room doesn't know what surgical procedure is being performed.

DR. FREED

Dr. Freed (O/C):
The patients that we operate on have all been referred from Columbia-Presbyterian Hospital in New York. Our colleagues there, Dr. Stanley Fawn,

Dr. Freed (O/C):
and Dr. David Eidelberg, are actually evaluating these patients, but they don't know whether the individual patient has received a tissue implant or a placebo operation.

PATIENT PRE-SURGERY
PRE-DRUG DOSE
MARGARET

George Page (V/O):
Margaret, although not a part of the double-blind study, was one of Dr. Freed's transplant patients.
In this video, made four months before her surgery, and prior to her morning dose of L-DOPA, she shows great difficulty with voluntary movements, even simple things like walking and sitting in a chair. When she was asked to do repetitive, stereotyped movements, she was very slow, especially with the right hand.

PATIENT POST-SURGERY
PRE-DRUG DOSE

George Page (V/O):
Here she is seen a year after transplant surgery, again, before her initial dose of L-DOPA.
She is now able to walk normally, and can perform repetitive movements rapidly. This indicates her brain is now producing dopamine on its own.

PATIENT POST-SURGERY
ON L-DOPA

MARGARET PLAYING TENNIS

George Page (V/O):
Seventeen months after surgery, Margaret is now able to play tennis, running for the ball, and hitting it well. Her transplanted brain tissue is producing more and more dopamine as her recovery continues.

DR. FREED

Dr. Freed (O/C):
There are actually some very exciting research possibilities though that are almost unique to the transplant business for Parkinson's disease, and that is that we are able to custom design cells that may actually be able to be grown in the laboratory and replace the cells that are missing in the Parkinson patient. It turns out that the brain, like the skin, can reproduce in tissue culture, namely multiply cells that are normal cells, that are not cancerous cells. And then those cells may be transplantable. If that's the case, then we could have an infinite number of cells available for transplant without having to resort to aborted fetal tissue. I would say that the timeline for such available cells would be ten years away, not more than twenty years away, probably not less than five years away.

MARGARET PLAYING TENNIS

Dr. Freed (O/C):
...and that's really the excitement of this field scientifically, is being able to custom design a neuron to meet the needs of a group of people like the Parkinson's population.

Mod.32

MODULE 32: NEUROREHABILITATION

BRAIN-INJURED INDIVIDUAL
USING WALKER IN HIS HOME
(Scott H.)

George Page (V/O):
Brain functions can be understood by examples of how brain injury affects behavior. But what happens after a person's brain is injured because of trauma, stroke, brain tumor, or neurological disease? What can be done to help brain-injured people return to their greatest level of independence and function?

COGNITIVE THERAPY SESSION
BRAIN INJURY RECOVERY PROGRAM
FORT COLLINS, CO

George Page (V/O):
Brain injury rehabilitation is relatively new as a specialty. In 1980, there were less than a dozen brain injury rehabilitation centers in the United States. Now, however, excellent facilities, like this one in Fort Collins, Colorado, are available in many areas.

DR. THOMAS BENNETT

CLINICAL DIRECTOR
BRAIN INJURY RECOVERY PROGRAM
BIN 631/10:18-11:32

Dr. Bennett (O/C):
As a neuropsychologist assessing the impact of brain injury on behavior, I was frustrated by the lack of community based programs that brought together a lot of disciplines and really tried to provide an integrated approach to brain injury

Dr. Bennett (O/C):
rehabilitation. So my colleagues and I at the Brain Injury Recovery Program brought together cognitive rehabilitation, speech and language therapy, occupational therapy, neurology, and neuropsychology. And we use physical therapists from the community, and then we do re-entry activities such as return to work, return to school or just trying to help the person return to their normal activities. We use a model of community reintegration where we will teach somebody something to do in our clinic to get around a brain injury problem or actually try to remediate a difficulty they are having such as a problem with attention and a problem with memory. And then we have them go out and practice it at work or at school or in their home and then they come back and then we go through it again and then try to get them back to the highest level of functioning that is possible.

BRAIN INJURY RECOVERY PROGRAM
JANET INSTRUCTING CONNIE ON COOKING;

Janet (O/C):
Okay, Connie, today we're going to do a cooking activity using the microwave oven. And I've put the recipe in this plastic cover so that you can check off the ingredients as you add them, and then check off the steps as you've completed them, so you can hopefully stay on task.

JANET AND CONNIE

George Page (V/O):
People with brain injuries are being discharged from hospital settings earlier than in the past. Programs like this allow brain-injured individuals to continue receiving supervision and rehabilitation in their own communities.

CHRISTY DITTMAR, OTR
Program Coordinator
Brain Injury Recovery Program

Christy Dittmar (O/C):
At the Brain Injury Recovery Program, treatment plans are developed individually for each client and that is based on that assessment information that's gained from the rehab team. Treatment includes individual and group therapy, and oftentimes the family participates directly. We encourage that as much as possible. For the more involved person, they may be in the program as much as six hours a day, five days a week. And for the person that needs less intensive rehab, they may be in the program two to four hours an average per week.

COGNITIVE REHABILITATION SESSION
BRAIN INJURY RECOVERY PROGRAM

THAIS B.

George Page (V/O):
Depending on a person's needs, a variety of interventions are used. Cognitive rehabilitation therapy uses computerized and table activities to remediate problems in such areas as speed of processing, attention, and problem solving. For students, cognitive rehabilitation provides compensatory academic strategies.

LYNN INTRODUCING A SPEECH THERAPY ACTIVITY TO ROB

Lynn (O/C):
Rob, today we're going to work on word-finding skills and in particular we are going to work on an exercise called synonym naming. So I am going to show you a list of words...

George Page (V/O):
Speech and language therapy addresses problems in communication, verbal comprehension, reading, writing, spelling, and arithmetic. Home-based education can be combined with therapy for students not yet ready to return to school.

JANET AND CONNIE DISCUSS MEMORY BOOK
BRAIN INJURY RECOVERY PROGRAM

Janet (O/C):
So Connie, how are things going with using your memory book?

Connie (O/C):
I think it's going very well.

Janet (O/C):
You've been good in scheduling appointments. Are you still doing that as well?

(CLOSE-UP MEMORY BOOK)

(JANET AND CLIENT WORK ON DEXTERITY EXERCISE)

(JANET AND CLIENT ON THERAPY BALLS)

George Page (V/O):
Occupational therapy is involved in many aspects of rehabilitation-from assessing and providing treatment for activities of daily living, such as cooking, home organization, and driving;
to providing compensatory strategies for reducing problems with memory, organizational skills, problem solving, and decision making;
to treating problems with balance, visual-perception, and motor skills.

THAIS B.

George Page (V/O):
Thais is a 16 year old junior in high-school. She suffered a serious brain injury in an automobile accident. Before her injury, she was a straight A student and an athlete, and active in band, orchestra, and many extracurricular activities.

THAIS B.

Thais (O/C):
I have had a lot of speech and language problems, like my vocabulary has gotten a lot smaller, like I can't remember like words. Like for the first couple weeks, people would ask me, you know, well what happened? You know like, "What's gotten messed up like from your accident? And I always want to say, you know, my vocabulary's not as big, but I couldn't remember the word vocabulary. And I'd try to describe it, but it would take me like fifty words to describe the word vocabulary.

THAIS

Thais (O/C):
The way I think, I don't think flexibly. I only think like in one tunnel. You know like there's this whole area. There's this whole world that I can think of. You know all these ways of fixing things or answers to problems, but I only think of like one tunnel.

Thais (O/C):
Like, going back to school. It was kind of weird because everybody you know from the looks of me, they knew that I had like gotten hit in the head. But

Thais (O/C):
they you know didn't realize that like with a brain injury you know like all this stuff that goes on like your vocabulary and just the way you think is different. They just figured oh yeah, you know, you have like, your nose was the only thing that got you know wrong, you know got messed up in your brain injury. And they didn't expect me to like be different like emotionally, you know just like the way I act and stuff. They figured oh yeah, "Same old Thais."

THAIS' MOTHER PATRICE

Patrice (O/C):
For the first you know three or four days, when she woke up she still had no idea of where she was or what she was doing; she had no memory at all of what had happened. But all of the previous memories were intact as best as we could tell.

PATRICE

Patrice (O/C):
We had some problems getting along for a while. And a lot of that was the fact that she really didn't recognize that the brain injury was causing some of the problems she was having.

PATRICE

Patrice (O/C):
But, I think that she does realize now that there are some things that she's had problems with and will continue to have problems with that are the effects of the brain injury, and that no matter how much effort she puts forth, it's not going to make that any easier.

THAUT'S GAIT LAB WITH PATIENT

George Page (V/O):
Individuals with brain injuries often have trouble walking normally. One new treatment combines the body's natural rhythms with the rehabilitation process. Dr. Michael Thaut, of the Center for Biomedical Research in Music, uses music and rhythmic patterns in rehabilitating patients with gait disturbances.

CBRM TAPE WITH MUSIC BACKGROUND

MICHAEL THAUT
CENTER FOR BIOMEDICAL RESEARCH IN MUSIC

Dr. Thaut (O/C):
I think what we are studying from a mechanism point of view is a very interesting aspect of the interaction between the auditory and the motor system, and it relates to rhythmic entrainment mechanisms. In other words, the auditory rhythm, the frequency of the auditory rhythm interacts and locks into movement rhythmicity.

The entrainment effect is very promising for rehabilitation because apparently we can drive from the outside, from the periphery, we can drive damaged timing networks that usually drive internally, walking ability. We apparently can drive those from the periphery through sensory stimulation, and so replace or restabilize some of the damaged internal networks.

George Page (V/O):
JEAN
Compensatory strategies and environmental modifications, allow many persons with even severe brain injuries to return to independent living and productive employment.

This is Jean. Injured in an accident, she was able to return to her prior job after rehabilitation.

Jean (O/C):
JEAN
I survived a brain injury when I was thrown off the back of a motorcycle on October 15, 1988. I was unconscious for about one week and hospitalized for five weeks before I was transferred to a rehabilitation facility where I spent almost five months in recovery.

Jean (O/C):
At the rehabilitation hospital, they said I probably wasn't able to live alone or would never work at the profession I was working in again. But that's not what happened. I was able to resume independent living and return to my old job following treatment at the Brain Injury Recovery Program.

Jean (V/O):
Rehabilitation helped me get my life back. It helped me gain a confidence that was lost after I was injured and it helped me with both personal and professional skills so I could get back on the job.

Jean (V/O):
My advice to someone who has suffered a severe brain injury would be to seek professional support and rehabilitation and don't give up. Continue the process no matter how hard it feels.

NEURONS FIRING

George Page (V/O):
Just how the brain recovers from injury and why rehabilitation helps is unclear. There is usually some immediate recovery due to a general healing of the physiology of the brain. Longer term recovery is

George Page (V/O):
more mysterious. There may be some regeneration of damaged pathways. Another possibility is neural reorganization, where areas that once played a minor role in a cognitive process take on a more dominant role. Finally, rerouting signals around damaged areas in the brain may contribute to recovery. All of these possibilities await verification.

CONNIE COOKING

George Page (V/O):
The damaged brain seems to learn and apply compensatory strategies acquired in rehabilitation. This ability of the brain to be aware of its injury and circumvent the resulting problems is yet another example of the brain's extraordinary capabilities, and adds to its aura of mystery.