

Gray Matters: Depression and the Brain 1996

The following program, "Gray Matters: Depression and the Brain," was produced in association with the Dana Alliance for Brain Initiatives.

[TICKING]

MAN: Winston Churchill called it "the black dog." It is mental depression. Abe Lincoln was so anguished by it, he cried, "I am now the most miserable man living. If what I feel were equally distributed to the whole human family..."

MIKE WALLACE: "If what I feel were equally distributed to the whole human family, there would not be one cheerful face on earth." Hello, I'm Mike Wallace. In 1973, I did that report for "60 Minutes," but I didn't fully understand those words of Lincoln and Churchill until 11 years later when depression hit home.

I'd reported for a documentary about the Vietnam War, and General William Westmoreland sued CBS and the producer and me for liable. And so for five months I sat in a drafty New York courtroom listening to witnesses and lawyers question my integrity. As a journalist I felt that in a sense I was on trial for my life, and I sank into a desperate and prolonged depression.

[MUSIC]

Depression has been called the common cold of mental illness, not because the symptoms are mild, but because the disease is so widespread. Roughly one person in five will experience a major depression in the course of a lifetime. During the next hour we'll show how brain science has helped to understand depression, to improve treatments, and to save lives, including my own. We'll talk to brain scientists who are heading the fight against depression. And throughout the program you'll hear music from composers who struggled with depression in their own lives. Rachmaninoff, Tchaikovsky, Berlioz, Ives, and others.

[MUSIC]

And I'll talk with columnist Art Buchwald, and novelist William Styron, friends of mine who helped me overcome three bouts of depression, and who have experienced the illness themselves. As Bill Styron once wrote, "Depression is a wimp of a word for an illness that creates a howling tempest in the brain."

[MUSIC]

Art Buchwald, Bill Styron and I have summer homes about a quarter-mile apart on Martha's Vineyard. We've known each other for more than 25 years. We go to the

Vineyard each summer to escape the demands of city life at the beach or on the tennis court. And it is also the place where an unexpected bond took hold.

I remember very well a rainy afternoon in our slippers, each of us suffering rather quietly about the way we felt. Each of us in a depression. Walked side by side happy in the fact that there were three of us, and comparing notes as to who felt worse.

A few months ago we got together there to discuss our experiences with depression. First, Art Buchwald.

ART BUCHWALD: The interesting thing about the Vineyard, where we all had our depressions in a sense, is that while it's a thing of joy now. When you have a depression the darkness closes in on you and all the things that you love work against you. And it exposes you to dark trees, dark people. It's a terrible thing.

MAN: And I think the contrast between your inner torment and often the rather beautiful landscape you happen to be walking through or observing is one of the most amazing things about the whole experience. Because it emphasizes the fact that depression is so profoundly destructive to the psyche that nothing having to do with the outer world, nothing external can really alter it.

[MUSIC]

MIKE WALLACE: Depression is the modern name for what used to be called melancholy. Robert Burton, an English scholar, wrote an influential book about depression more than 300 years ago. "If there is hell upon earth," he said, "it is to be found in the heart of a melancholy man."

Depression can affect people at every stage of life, but it does not strike at random, it often runs in families. Women get depression twice as often as men, and the illness tends to be recurrent. If you've had one episode of depression, you're clearly at risk for more.

Dr. Harold Sackheim is chief of the Department of Biological Psychiatry at the New York State Psychiatric Institute.

DR. SACKHEIM: At least half of the people who experience a major depression and likely more will have that episode of illness repeated during their life. Once the illness becomes recurrent, once it repeats, the likelihood of additional episodes increases. Across the life span depression is an illness which doesn't burn out.

MIKE WALLACE: At puberty, following childbirth, after a heart attack, or during old age—these are some stages of life when we are particularly prone to the illness. And depression can be a hidden traveler with brain disorders like multiple sclerosis or epilepsy, stroke, Alzheimer's Disease. We sometimes see people suffering from those illnesses and assume their sadness or their lethargy is a natural part of the disease. But

often they are actually experiencing depression, which can be treated independently of the other illness.

Depression has physical symptoms, but it can't be diagnosed like pneumonia or a broken leg. Instead doctors listen as patients recount their experience. Bill Styron and Art Buchwald describe a few telltale signs.

STYRON: It was not immediate, but over the period of several weeks it got worse and worse. I began to feel agitated; I began to feel fragile.

BUCHWALD: All you want to do is sleep, you don't want to talk to anyone. The normal things that you do in a day seem impossible. Getting your breakfast, going downstairs and reading the newspaper. And that scares the hell out of you because you've been doing it all your life, and suddenly you can't even read a newspaper.

STYRON: I felt like an absolute loathsome, complete worthless object, who hadn't done anything, and whose entire trajectory of life had gone up and then was plunged down into absolute zero, pit.

MIKE WALLACE: Dr. Raymond DePaulo of the Johns Hopkins University School of Medicine has worked extensively with depressed patients. He recalls one patient who at first seemed very irrational, and who was described by his son as having a stranglehold on reality.

DR. DePAULO: Each day that he would see me he would tell me, Dr. DePaulo, I believe that today is the worst day in my life. And he would tell me this 20, 40, 50 times. Obviously he didn't respond to my first treatment, but as long as you're in the depression there is something in a sense freshly horrible about it. Each minute is a new event, and it's like getting hit in the face once a minute, once a second, any kind of time frame that you want to put on it.

DR. FRANK: I think it's very important to distinguish between the sadness and despair that we all feel when things don't go our way, and the clinical syndrome of depression. We all have times when our mood drops, sometimes for no apparent reason, but often because bad things have happened to us. But we're able to lift ourselves out of that bad mood.

MIKE WALLACE: Dr. Ellen Frank is a professor at the Western Psychiatric Institute in Pittsburgh. And she says that clinical depression sets off a whole series of changes, beginning with the patient's mood.

DR. FRANK: Typically the change in mood is to one of depression, but sometimes it's to one of anger or irritability. But coupled with that change in mood we also see marked changes in sleep, in appetite, in energy, in the ability to concentrate, and think, and remember.

Perhaps the most profound and disturbing change associated with major depression is the loss of interest and loss of pleasure in usual activities. So that things which were ordinarily very enjoyable are no longer of any interest. And the loss of motivation: One of my patients once told me that filling the sugar bowl felt like climbing Mount Everest.

MIKE WALLACE: But for all the pain that depressed people experience, they're mostly expected to keep functioning—on the job, at home, with their families. William Styron, the author of *Darkness Visible* and *Sophie's Choice*, calls people with depression the walking wounded. Everyone understands if you stay home from work with the flu, but people with depression are expected to soldier on. Again, Bill Styron.

STYRON: The pain and indeed the agony are with you almost every minute. But you cannot lie in bed and let this alleviate itself, because there's no alleviation in bed. In bed you're just as badly off as you are when you're walking around. So what you do? You make a choice between two impossible horrors. Instead of lying in bed you get up and you begin to walk around. And you make conversation with people, knowing each moment that this conversation is likely to be a sort of piece of catatonic play-acting—that you're really not saying anything that makes sense. And you're just staggering through your daily life because you are indeed like someone who has been wounded, but forced to walk around.

[MUSIC]

MIKE WALLACE: Depression has been with us forever. But until we began to study the brain scientifically we had no way of knowing that depression is, in fact, a brain disorder.

DR. HYMAN: It's important to recognize that understanding the human brain, how it works and how things go wrong in diseases like depression may be the most difficult project that humankind has every undertaken.

MIKE WALLACE: Dr. Steven Hyman is Director of the National Institute of Mental Health.

DR. HYMAN: The brain is made up of perhaps 100 billion different cells, and they're not all uniform. There are literally thousands of different kinds of cells in the brain. And each one of these cells may make a thousand or 10 thousand connections with neighboring and in some cases distant cells in the brain.

In order to really understand what causes depression we're going to have to understand, in the context of the overall workings of the brain, what controls emotion and emotional states, and how those relate to all kinds of both cognitive or thinking functions, because depression affects thinking as well as emotion and also bodily functions, because we know that depression affects things like energy levels, and appetite, and sleep. So we really have our work cut out for us.

[MUSIC]

MIKE WALLACE: Before World War II, there was no reliable drug treatment for depression. Then we got lucky. Two different drugs—one designed to treat tuberculosis, the other designed for psychosis—were serendipitously found to help patients with depression as well. As a result of those discoveries, we now know that depression can be treated with drugs that stabilize the levels of brain chemicals. Especially serotonin, norepinephrine, and dopamine. Drugs such as imipramine and nortriptyline were introduced in the 1950s and are still widely prescribed. But since then researchers have developed an array of antidepressant drugs, including Prozac, Paxil, Zoloft, and others. Dr. Harold Sackheim.

DR. SACKHEIM: We are making great strides in going beyond some of the early notions we had about how these drugs work, to a much richer understanding of the underlying biology. What we're beginning to see for the very first time in the treatment of depression in particular are drugs that were designed to treat depression from the start—not accidental discoveries, which were all of the original antidepressants.

And so that's really a testament to the fact that we're getting a much richer understanding as to how it is we can intervene in the brain to address these illnesses.

MIKE WALLACE: The best news about depression is that treatment usually works. In most cases even patients with severe depression can be helped. Usually the best treatment is a combination of drugs and talk therapy. And statistically at least, the treatments are very effective. Roughly 80 percent of the patients who seek treatment get much better within a few months.

That sounds simple, but usually it's not simple at all. We still don't know which drug will work for which patient. We don't really understand why these drugs are effective, or why it usually takes several weeks to see any results. Brain science has tried to understand how the antidepressant drugs actually affect the chemistry of the brain. There have been remarkable advances based on studying the brain at the molecular level. Again, Dr. Steven Hyman.

DR. HYMAN: We've discovered in the last few years that there are at least 14 different kinds of receptors for serotonin in the brain. Now if that were not enough, it turns out that the world inside of cells is as complicated as the world outside of cells. And one of the things that anyone who's taken antidepressants knows—and it's very frustrating—is they take a long time to work. And we have to ask as scientists, what could be taking so long? And recognize that there are clues in this.

And what appears to be happening is that when you take the drug—and let's say you increase the amount of serotonin in your brain—you're bombarding now at least some of these 14 different serotonin receptors with more serotonin than the brain has ever seen before. And in response to this bombardment the cells adapt. They are basically trying to defend their normal equilibrium. And there are slow adaptive processes that actually

change the chemical composition of the nerve cells. And what we believe is that it's in this process of adaptation that the actual therapeutic response to antidepressants occurs.

MIKE WALLACE: Dr. Samuel Barondes is a professor of neurobiology and psychiatry at the University of California in San Francisco.

DR. BARONDES: Some people respond very well and very quickly. I mean some people really get better quickly. Some people don't get better whatever you do. I mean they really are very, very tough cases. It may well be that they have different diseases. I mean we lump them altogether and call them all depression, but they may be—it's like heart disease. It used to be in the 19th century that all heart disease was heart disease, but, you know, now there are dozens and dozens of different kinds of heart disease. And some of them have a better prognosis and are treatable in one way, and some have a terrible prognosis and require a heart transplant. So it may well be that depression is not depression is not depression.

[MUSIC]

MIKE WALLACE: Because we don't yet understand the underlying causes of depression, our treatments are still not entirely reliable. For many patients there's an element of trial and error as doctors test first one drug and then another. If you were suffering from a fever or a broken bone, this kind of experimentation would be troubling enough, but in the case of depression it can be devastating.

During an episode of major depression, some patients feel they can hardly get through the next hour, let alone waiting weeks for the effects of the medicine to take hold. Bill Styron recalls that by the time he decided to see a psychiatrist he was already in the depths of his depression.

STYRON: By this time in the deep autumn, I was very close to doing something very harmful to myself. I had suicidal thoughts all the time. I went to this guy, and I blurted out—I think it was our second session—I said, Doctor, how long? I said, I've never felt so terrible in my life. How long do you think this will last?

He had a rather ingratiating sort of Uriah Heep, butter-won't-melt-in-my-mouth attitude—he couldn't have been more accommodating. But he looked at me with these gelid eyes and he said, "Six months to a year." Now, he committed an atrocity upon me at that moment, because in the horrible state of depression I was in, 24 more hours was hard enough to think of. Instead of saying, "I can't tell you. I will say this, that there's no doubt about it, you're going to get better eventually. It may take a certain amount of time." He made it impossible for me really to live with myself. It's one of the worse things that a doctor's ever done.

MIKE WALLACE: So doctors have a very delicate task. They need to make careful judgments about which drug might work and in which doses. If the first drug they prescribe doesn't work, they may need to choose another one. And all the while they need

to encourage their despondent patients to hang on and to believe they really will get better.

[MUSIC]

I'm Mike Wallace, and you're listening to "Gray Matters: Depression and the Brain."

DR. JAMISON: There's a particular kind of pain, elation, loneliness, and terror involved in this kind of madness. When you're high it's tremendous. The ideas and feelings are fast and frequent, like shooting stars, and you follow them until you find better and brighter ones.

MIKE WALLACE: Dr. Kay Jamison of the Johns Hopkins University School of Medicine is sitting in the study of her home in Washington, D.C., reading from her memoir, *An Unquiet Mind*. She's an expert on manic depression, a mood disorder that includes the soaring highs of mania, as well as the despair of depression. Dr. Jamison has manic depression herself.

DR. JAMISON: Shyness goes. The right words and gestures are suddenly there. The power to captivate others a felt certainty. There are interests found in uninteresting people. Sensuality is pervasive, and the desire to seduce and be seduced irresistible. Feelings of ease, intensity, power, well-being, financial omnipotence, and euphoria pervade one's marrow, but somewhere this changes. The fast ideas are far too fast, and there are far too many. Overwhelming confusion replaces clarity. Memory goes. Humor and absorption on friends' faces are replaced by fear and concern.

Everything previously moving with the grain is now against. You are irritable, angry, frightened, uncontrollable, and enmeshed totally in the blackest caves of the mind.

MIKE WALLACE: Manic depression, also known as bipolar depression, is marked by pronounced changes in mood, behavior, and energy. It is less common than conventional depression, but still it affects 2 to 3 million Americans. Manic depression has a very strong tendency to run in families. Art Buchwald knows what it's like.

BUCHWALD: There're certain stages that I can describe. Number one is the manic stage. That's about three or four months. I got from 88th Street to 42nd Street on Fifth Avenue in six minutes. But everything I did was so—there's nothing I couldn't do.

MIKE WALLACE: And he couldn't have been a nicer guy. He would ... (that's right, [CHUCKLES] Arty just took out a couple of \$10 bills). He would give you money, he would buy you gifts, he would let you call a ball out that was in, in tennis. He was just having a good time. He was having such a good time, such an uncharacteristically good time, and I didn't realize that he was in that kind of shape. I asked his wife, Ann, and she said, "Well, I'm worried about it." And, sure enough, all of a sudden the manic phase turned down.

BUCHWALD: So the second stage was I wanted to kill myself. And I knew it, and I even worked it out—you work it out. You don't just want to kill yourself, you know how you're going to do it: go to the 16th floor, you go out the window... It's all planned.

And then as I wrote in a book, my biggest fear was that de Gaulle would die the same day and I'd never make The New York Times obituaries.

[SOME LAUGHTER IN BACKGROUND]

MIKE WALLACE: But manic depression is no laughing matter. As Dr. Jamison points out, it is very dangerous. When people think about depression, she says...

DR. JAMISON: Death does not come to mind. Misery for other people comes to mind, misery for the individual comes to mind, will power comes to mind, Prozac comes to mind, lots of things come to mind—death does not. I think if you have people in your life who've committed suicide, or you yourself have attempted suicide, death is much more on your mind with these diseases. And I think that that is the single most underemphasized aspect of the mood disorders in general—both depression and manic depression—is they kill people, they kill people all the time. Twenty percent of the people with manic-depressive illness will die by suicide unless they get treated. That's a horrifying rate of death.

MIKE WALLACE: Suicide kills more Americans than homicide. Every year in this country 30 thousand people take their own lives. And a significant number of those suicide victims suffered from depression or manic depression. Because manic depression especially is so dangerous, it is vital for patients with the illness to stay on medication, lithium in most cases.

With medicine manic depression can usually be kept under control. Without it, patients are at high risk for a relapse.

DR. JAMISON: We have very good treatments that work almost all the time. The problem is that most people—or not most people, probably 30, to 40, to 50 percent of patients who have manic-depressive illness—will stop their medication at one time or another. And some people stop it repeatedly.

MIKE WALLACE: Dr. Jamison says we shouldn't be surprised.

DR. JAMISON: It's very hard. It's very hard if you're 17 years old and you've gone psychotic for the first time, and somebody tells you you're supposed to be on medication the rest of your life. Most adults have a problem taking antibiotics for 10 days.

In classic studies in medicine, physicians being prescribed antibiotics for upper respiratory infections, for example—and even though they know that if they stop their antibiotic as soon as the symptoms go away, if they don't take it for 10 days their illness

is going to come back. And these are doctors. Fifty percent of doctors will not take the full 10 days.

So you're asking patients who have illnesses that don't always seem like illnesses, where if the drug is working properly there are no symptoms so there's no motivation and there's no reminder. And you're seriously expecting that people are going to take these medications with often very troubling side effects. I don't know, it defies logic to me.

MIKE WALLACE: And, says Dr. Ellen Frank, it's not only patients who resist the idea of medication.

DR. FRANK: I think we have a view in this country that grows out of our puritan, our pioneer spirit, that you're only truly well if you're well off medicine. And so the patient, the family members, and the doctor conspire to find out if the patient is truly well. And so they take them off medication, or they agree to taking the patient off medication. And the results are almost always, in patients with multiple episodes of depression, a disaster. But we have defined wellness in this country as something has to be done independently.

Now, we've gotten over it with certain diseases. We don't define a well diabetic as someone who's off insulin. We define a well diabetic as someone whose blood sugar's under control. We don't define a well hypertensive as someone who's off anti-hypertensive medication. We define a well hypertensive as someone who has a blood pressure within a certain range. We're going to need to do some more work to define a well person with a history of depression as someone who is continuing to take their medication.

[MUSIC]

MIKE WALLACE: Antidepressant drugs may be most effective when they are combined with psychotherapy. Two kinds of talk therapy have proven to be especially valuable. The first, cognitive therapy, addresses the way patients look at themselves and the world. Dr. Ellen Frank explains.

DR. FRANK: And the treatment really consists of teaching the individual to identify this tendency to have automatic negative thoughts, and to see how irrational those thoughts are, and learn to correct those thoughts for himself or for herself. And through this process of almost debate, the patient begins to set up a debate with himself or herself, and begins to be able to argue against her own irrational thoughts.

MIKE WALLACE: Major depression is often precipitated by painful life experience. The second type of talk therapy, interpersonal therapy, confronts these problems directly. Dr. Myrna Weissman of the Columbia University College of Physicians and Surgeons says there are four common triggers for depression.

DR. WEISSMAN: One is grief. Depression associated with an unresolved grief. Someone has died in the family, and the patient never resolved that, they never mourned,

or they were angry. The second are role disputes, and that's very often marital disputes. He doesn't understand me; she wants to have a different lifestyle. And these disputes are either at an impasse where there's smoldering resentment, or there's a renegotiation going on but it's hot and heavy, or they're in a period of desolation. He wants to leave, but he doesn't know how to maneuver it.

The third problem area is transitions, role transitions. People who are in the midst of some major life change, like promotion, demotion, retirement, children leaving home, after the divorce becoming a single person again. And the last are what we call interpersonal deficits, and that's people who have trouble either initiating or sustaining relationships. And they report they feel lonely and bored. Or they can get into a relationship, but then it just doesn't go anywhere.

[MUSIC]

MIKE WALLACE: Interpersonal therapy addresses these problems in an effort to help patients cope better with their daily lives. Both forms of talk therapy are designed to be effective within 16 to 20 weeks. And in most cases through intelligent trials of one or more drugs plus psychotherapy, patients do improve. Their symptoms recede, they feel more energetic, and they eat better, and sleep better, feel better.

But there is no cure for depression. Depression can be alleviated, it can be suppressed, but we can never be sure it has been vanquished. Often a patient will feel fine for several months or even several years, and then slip into another depression.

Patients who do not respond well to medicine or psychotherapy have yet another, more dramatic option. Electric shock treatment. It has a bad image in this country, personified perhaps by Nurse Ratched who tormented her patients in "One Flew Over the Cuckoo's Nest." But electroconvulsive therapy, or ECT as it's called, is now generally accepted by the medical community. Dr. Ellen Frank explains how ECT works.

DR. FRANK: Electroconvulsive therapy consists of providing a relatively strong electrical impulse—these days to a single half of the brain—while the patient is under anesthesia, and essentially it creates a seizure or a convulsion. We don't know why creating that seizure treats depression, but it clearly rearranges the brain chemistry. We know that in the context of the seizure the soup in which the brain is sitting changes briefly, but markedly. And it's probably that rearrangement of the neurochemicals that relieve the depression. Exactly how that happens I don't think anyone knows.

MIKE WALLACE: The seizure usually lasts for about a minute. Most patients get better with six to 12 ECT treatments over a period of several weeks. But most people are still afraid of ECT, as Dr. Harold Sackheim admits.

DR. SACKHEIM: There's little doubt that ECT generates fear and considerable uncertainty in the public. I think in part that's understandable, because ECT is bizarre. It would be hard to think, if one were looking objectively from the outside, that giving a

patient general anesthesia, essentially putting them to sleep, applying electrodes to their head, passing electricity through the brain, producing a seizure would be therapeutic—that one would do that for someone's good.

But from the point of view of caring for people, the questions become what good does the treatment do and what harm does the treatment do? Not what does a treatment look like. Because we have to realize that when we are treating with biological treatments in any form of medicine, not just psychiatry, but in all forms of medicine, we are changing the body. And particularly in psychiatry and neurology, we are changing the brain.

It's hidden from us when patients take pills. With ECT it's very obvious that we're changing the brain. But we're changing the brain with both no less.

MIKE WALLACE: Since ECT was introduced in the 1930s, we've learned to apply it more precisely.

DR. SACKHEIM: We know remarkably that people vary by 40-fold in how much electricity they need to produce a seizure. And that standard practice decades ago was essentially to use the high end. So that meant that at each and every treatment many individuals were getting 10, 20, 30 times the dose of electricity that they needed to produce a seizure.

Related to this work, what we found is that depending where in the brain we stimulate and how much we stimulate with, how much electricity we give, we can have forms of ECT where only about 15 percent of patients will get well, or forms of ECT where 70 percent of patients will get well. A remarkable difference in the efficacy of the treatment, which is contingent on the setting of a dial and where in the brain we stimulate.

MIKE WALLACE: Dr. Sackheim and others believe that ECT is not only an effective treatment for depression, it may be the most effective. And it is certainly the fastest. But ECT also causes some memory loss. And the question is, how serious is that risk?

DR. SACKHEIM: The major effect of ECT on memory will be a loss of memories for events that happened surrounding the ECT course, particularly events in one's own life. So who took you to the hospital? Who visited you while you were in the hospital? What gifts you gave somebody a month before receiving the treatment? There will be gaps in memory for events like this, and these gaps may be—in fact, I think commonly are—permanent.

It is not that years of one's life will be wiped out. There will be distinct gaps. That effect will last typically for about one to two weeks, and then it will dissipate.

MIKE WALLACE: Because of the memory loss and the uneasiness of most patients and other factors, ECT remains a secondary treatment for depression. It is generally used when other treatments don't work.

Whatever the method—medicine, talk therapy, or ECT—depression is now highly treatable. The tragedy of depression is that most people suffer in silence. Of the people who experience depression only about one in three comes forward. Again, Bill Styron.

STYRON: By September— after I left the Vineyard, I was back in Connecticut—I was feeling more and more monstrous and horrible. And I was fighting the idea of going to a therapist. I have to confess that all my life I had prided myself on an independence, which prevented me from going to psychiatrists for anything. So I fought that.

MIKE WALLACE: There is a tendency to downplay mental illness. We still tell friends and family members to pull themselves out of it. And many people with depression just blame themselves. Again, Dr. Steven Hyman, who's director of the National Institute of Mental Health.

DR. HYMAN: Patients suffer with stigma because mental disorders are not widely understood, unfortunately, to be real disorders, real brain disorders. And patients are embarrassed. And, of course, depression itself creates a trap because patients don't feel that they're very worthwhile, so they feel they're not deserving of treatment. And so the stigma, in essence, creates this reverberation with the disease, which can be incredibly painful.

And one also sees the families. The families are often made to feel shame; they're embarrassed. But having the disease is nobody's fault, just as it's nobody's fault that they get diabetes or cancer.

[MUSIC]

MIKE WALLACE: For all we've come to understand about depression, there is much more that we don't know. Why is one person more prone to depression than another? Why does a particular drug help one patient, but not another? Why does one person recover quickly while another suffers for years? New brain-imaging techniques may offer some clues. With PET scans, that is, Positron Emission Tomography, we can actually see the brain at work. But as Dr. Hyman points out, that is only a first step.

DR. HYMAN: If you just take someone who's depressed and someone who's not depressed, and you take a picture of both of their brains without any sort of hypothesis ahead of time, it's really very hard to make sense of what you're seeing. What you really want to do is come up with something that makes the brain of the depressed and the nondepressed person go to work maybe processing some emotional information, so you can actually see a circuit that should work in a certain way, now in essence malfunctioning. So we would like to develop the basic science of emotion so that we can better use these noninvasive neuroimaging tools to see what circuits might not be working in depression. And then it would be very nice to see improvement with different kinds of therapies, whether psychotherapy or pharmacotherapy.

MIKE WALLACE: Genetics may also provide some answers. Dr. Samuel Barondes is an expert on psychiatric genetics.

DR. BARONDES: The reason that there's so much interest in the genetics of mental illness now is not because we've suddenly discovered that genes are important, or that there's a familial tendency to have problems like depression, but because the power of the field of genetics has grown so immensely in the past five or 10 years because the tools for studying, finding, and then modifying genes are so powerful, and because there is this broad, systematic attempt that goes on worldwide to fully determine the structure of all human genes and try to find out what each of them does. So that those of us who are interested in psychiatric genetics are deeply dependent on the grand project that's ongoing, without which we really would be hopelessly lost.

But because the human genome is being worked out in its minute structural detail, it's become feasible to really undertake a complicated problem like depression.

MIKE WALLACE: Genetics holds out the promise that we might finally isolate the biological roots of depression, and then develop drugs that are better tailored to the individual patient.

DR. BARONDES: If one really knows that there is some specific gene variant in some person who is very inclined to become depressed, it should be possible in time to devise drug treatments that would be useful in ameliorating or preventing the depression.

Now that might not be easy. The genes that are involved might not be genes that lend themselves readily to the creation of drugs to modify their function. So it remains to be seen exactly how this will all play out. But the next critical step, obviously, is to try to find the players, try to understand what they do, and then try to use whatever tricks one can to modify their effects.

MIKE WALLACE: Dr. Barondes is confident that genetic research will eventually lead to major breakthroughs in our understanding of the human brain.

DR. BARONDES: I have personally been extremely interested in the genetic underpinnings of mental illness ever since I began my work in psychiatry decades ago. And have been just biding my time recognizing what a formidable problem it is. And the extraordinary thing about where we are today is that there is really light at the end of the tunnel. There really is. It's going to work. It may take 10 or 20 years to work—it's not going to take 100 years. It may also happen next month.

So it's real. The technology is so powerful that we really do have hope of sorting these things out. And even though it may take a lot of time, and a lot of work, and a lot of confirmation, it's a real enterprise now.

[MUSIC]

MIKE WALLACE: Back in Martha's Vineyard, I spoke with Bill Styron and Art Buchwald about a simple form of healing that we all sought out: reassurance and empathy from someone who understood what we were going through. As I sank into depression during the Westmoreland trial, I turned first to my family doctor.

And I used to call him about 11, 11:30 at night and say, "Frank, I don't think I can take it anymore. I really think that I'm going to do something serious..." "No, you're not." I was telling him I was going to commit suicide. "No, you're not, you're OK. Not that you're OK, but you're going to be OK, and use a little strength and so forth." And that's when I began to call this fellow—he was my...

BUCHWALD: They can't see you when you say this fellow—it's radio.

MIKE WALLACE: That's right. This fellow: Buchwald. And he would stay with me on the telephone, night after night, after night, listening and listening, and giving me the benefit of his understanding of what happens when you are clinically depressed. And I'm certain that I would never have survived if it weren't for Buchwald. And I believe he did the same thing more or less with Styron.

STYRON: I have to give him credit. He's basically a funny man and we all know that, but he is capable of depth. In effect, he was the Virgil to our Dante, because he'd been there before, like Virgil, unlike Dante, we had not been there. And he really charted the depths, and it was very, very useful to have Art on the phone. Because we needed it. Because this is a new experience for everyone, it's totally terrifying. And you need someone who has been there to give you parameters and an understanding of where you're going.

BUCHWALD: I've been getting very good credit from these two gentlemen for helping them, and I'm delighted to get it. But I wish to say that by helping them I really was helping myself. And it's like an AA thing. When I spoke to Styron and was able to tell him real brilliant things that, funny enough, they came out of the blue. I didn't even know why I was using those words. And talked to Wallace. I felt, my God, I must be better if I can tell other people what the problem is. So I don't want to take full credit for this as a noble gesture, I really was helping myself.

MIKE WALLACE: I didn't look at it this way at the time, but Bill Styron and Art Buchwald, my neighbors and longtime friends, became my informal support group. And for many patients with depression, this kind of support is a lifeline.

RESNICK: Do support groups really make you better? Can they help you get better?

MIKE WALLACE: Wendy Resnick is a psychiatric nurse at Johns Hopkins University Hospital in Baltimore. Here she's leading a training session for people who would like to start support groups in their communities.

RESNICK: ... See, OK, does it really make a difference? But it's very hard to measure the things that come out of support groups, because they're so—they're spiritual...

MIKE WALLACE: Participants travel to Baltimore on a Saturday from nearby cities like Washington and Philadelphia...

MIKE WALLACE: Most of them have long histories of struggling with depression. They're interested in exploring how support groups can pick up where diagnosis and treatment leave off.

RESNICK: What we can do is we can talk about living with this illness on a daily basis. We can share experiences related to living with this illness.

Now if out of that comes health-producing behaviors for people, healthy behaviors, good feelings, friendships, connections, then that's a wonderful thing. And those, in fact, are things that we know happen in these groups.

MIKE WALLACE: In 1984, Wendy Resnick and Dr. Raymond DePaulo started an organization for professionals, patients, and families, called DRADA, the Depression and Related Affective Disorders Association. As Dr. DePaulo recalls, they began with only 10 families.

DR. DEPAULO: It was just clear that there was just a huge need, and that people were going to extraordinary lengths to get information about depression and manic-depressive illness, and that it wasn't readily available to them. And when you see families scouring, literally scouring the medical literature and trying to interpret those awfully written papers that we write, you know that people are desperate.

MIKE WALLACE: DRADA now has more than a thousand members and some 60 support groups. DRADA also holds an annual conference where speakers like Kay Jamison, Bill Styron, actor Drew Carey, and I have spoken about our experiences. And our stories are all too familiar to those who attend.

WOMAN: Three years ago I was a graduate student at UC-Berkeley. I became very ill. I'd had real definitive episodes of depression before, but I didn't understand that I had the disease. Because of the stigma about mental illness, people in my family hadn't been very open about other members of my family that also had manic depression and schizophrenia. And only after I became sick did it sort of come out that there was a lot of that on my dad's side of the family.

WALGROVE: My name's Norma Walgrove, and I'm a nurse therapist, and this is about the third time I've come to DRADA. And I also find it very helpful in terms of making clients of mine aware that the organization exists so that they can become a part of support groups, as well as to experience the fact that there is hope for those who are experiencing either mania or depression.

Plus, I like the collegiality of seeing other people who are working in mental health, and to hear about what's going on that's new in terms of medications and research.

WOMAN: My father had bipolar. He killed himself in 1969. My brother is bipolar and was diagnosed when he was 20 in 1982. I was diagnosed just three and a half years ago, and I had a lot of information before I started having episodes. But when it started affecting me, of course, it's a different story.

MIKE WALLACE: Dr. DePaulo remains hopeful.

DR. DEPAULO: Probably one great misperception about what I do is that my work must be depressing because I work with patients with depression. And actually that's not the case at all. In fact, one of the things that's very rewarding about this work is that most of your patients get well, and they get well in a relatively short period of time—that is, months.

Once you and they understand what the mission is—what the problem is—and once the mission is [set], the hardest thing is to keep the patient and doctor on task and patient enough to wait and see if a particular therapeutic intervention's going to work. So the fact that it's such a rewarding piece of work, I think, is probably not well known.

[MUSIC]

MIKE WALLACE: Although we still don't know what causes depression, new scientific tools are helping us to get to the bottom of it. Meantime, as we learn more about how depression affects the brain, we may find better ways to treat the illness. Dr. Ellen Frank.

DR. FRANK: I'm much more optimistic that we will find really specific treatments, that we are homing in on ways of identifying the right treatment for the right individual before we start. I think we're probably less than 10 years away from that.

And what we're finally starting to see are brain scientists collaborating with clinicians like me, and doing their imaging in the patients who are being treated with a variety of treatments, so we can actually see what the brain effects of four, or five, or six different treatments are. And I think from that we'll be able to figure out—before we start treatment—what's our best shot treatment with a given individual.

MIKE WALLACE: Until the promise of brain research is fully realized, depression still comes down to the pain that patients feel, and the courage it takes to endure. Dr. Raymond DePaulo.

DR. DEPAULO: How do patients tolerate this experience is something that in some ways is hard to explain. I think I understand something about it, or at least I feel something about it, and that is simply that these are very tough and brave people. One of the things that—once they're well—that the patients and I and their families are able to celebrate is the patient's courage for waiting, for hanging in there, and for doing that. These are extraordinarily difficult things to sit through. And, you know, not all patients do that. And

patients do it to varying degrees. But it's not something you and I would take on for almost any price.

MIKE WALLACE: Doctors will tell you that depression is often a recurrent disease, that people who've had one episode of major depression are vulnerable to having another. But along with the vulnerability comes perhaps a certain hope. My friends Art Buchwald and Bill Styron seem confident.

BUCHWALD: To have a reversal episode—you think about it, but not a lot. And there's always a possibility that you can have a recurrence of it. I think we're so much stronger now that ordinarily when something comes along we can handle it before it becomes depressing.

STYRON: Yeah, I think after having survived the horror of such an episode, I think the analogy is almost like being immune. It's as if you've received some sort of shot, which if it doesn't make you immune it makes you quite resistant to future episodes. Because you're psychologically, I think, better equipped to see the darkness coming and to more or less take steps to prevent it from really happening to you.

[MUSIC]

MIKE WALLACE: Bill Styron evokes Milton's description of hell as a place where there is no light, but rather "darkness visible." And those of us who've emerged from the darkness of depression hope that with a little help we can manage to remain in the light. I'm Mike Wallace.

[MUSIC]

GARRICK UTLEY: And I'm Garrick Utley. Depression has been described as the cancer of the 21st century. It hits one out of every five people around the world at least once during a lifetime. Over any six-month period it is estimated that between 5 and 7 percent of the world's population will be suffering from a serious depression.

A new study by the World Health Organization estimates that by the year 2020, depression will be the second most burdensome illness in the world. The economic and social costs of that are staggering.

The good news is that there's a wider range of medications available now to help treat depression, and these medications have fewer side effects, giving patients more options in their treatment. New research has given scientists a clear understanding of how these drugs work. It's thought that the medications may actually burrow their way inside individual brain cells to change the activity of genes. This is a time-consuming process, which may explain why it takes a while for prescription antidepressants to work.

As for the question, is there one specific gene that causes depression? Recent studies suggest that the answer is no. However, it does look increasingly certain that there are

genes and many of them that make people vulnerable to the disease. I'm Garrick Utley, and you've been listening to a special edition of "Gray Matters: Depression and the Brain."

[MUSIC]

WOMAN: "Gray Matters: Depression and the Brain" is one of a 13-part series. For a cassette, CD, or transcript of this show, or for any of the "Gray Matters" programs, call 1-800-65-BRAIN. At that number you may leave your comments or also request a free pamphlet answering your questions about brain research. That's 1-800-65-BRAIN.

This program was produced in association with The Dana Alliance for Brain Initiatives. The Dana Alliance is a nonprofit organization made up of 200 leading neuroscientists, including seven Nobel Laureates. The Dana Alliance's commitment is to advance public education about the progress and promise of brain research.

[MUSIC]

MAN: PRI, Public Radio International.

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